THE STATE OF SOUTH CAROLINA
In The Court of Appeals

APPEAL FROM SPARTANBURG COUNTY
Court of Common Pleas

R. Keith Kelly, Circuit Court Judge

RECEIVED
OCT 18 2018
SC Court of Appeals

Appellate Case No. 2017-002522
Case No. 2010-CP-5743

Gregory J. Feldman, MD, Joseph A. Boscia, III, MD, and Upstate Lung & Critical Care Specialists, PC, Appellants,

v.

Ray E. "Chuck" Thompson, and Charles M. Fogarty, MD, Respondents.

RECORD ON APPEAL
VOLUME VII

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STATE OF SOUTH CAROLINA COURT OF COMMON PLEAS

COUNTY OF SPARTANBURG C. A. NO. 2006-CP-42-1728

William Mark Casey,

Plaintiff,

vs.

Gregory J. Feldman, MD, Joseph A. Boscia III, MD, Upstate Lung and Critical Care Specialists, PC, and Devendra Shantha, MD,

Defendants.

COPY

Deposition of ***CHARLES M. FOGARTY, M.D.***

Pursuant to notice of deposition and/or agreement in the above-entitled case, a deposition was taken on the 22nd day of December 2008, commencing at approximately 10:15 a.m. attended by counsel as follows:

Appearances:

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Spartanburg, South Carolina 29306
Attorney for Defendant, Dr. Devendra Shantha.

Also Attending: Dr. Gregory Feldman
Mitzi Higgins (paralegal)

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Videographer: Michael A. Arrison
Cert. Legal Video Specialist

Deposition Reported By: Joanne S. Quebe, CR
Depositions And ..., Inc.
(864) 585-0642

Pursuant to notice and/or agreement to take depositions, the within deposition was taken by the above reporter, a notary public, as required under the code of laws of South Carolina, 1976, section 19-17-10, and circuit court rule 30, et al., by consent of all parties at the Law Offices of The Ward Law Firm, 233 South Pine Street, Spartanburg, South Carolina.

WAIVER:

Counsel and the deponent agreed that both the reading over of and signing of the deposition are hereby dispensed with and **WAIVED.**

** ** **

BY VIDEOGRAPHER:

This is the videotape deposition of Dr. Charles Fogarty taken by the defendants in the matter of William Mark Casey, plaintiff versus Gregory J. Feldman, M.D., et al, defendants, filed in the Court of Common Pleas, State of South Carolina, Spartanburg County. Case Number 2006-CP-42-1728. This deposition is being held at the Ward Law Firm, 233 South Pine Street, Spartanburg, South Carolina on Monday, December 22nd, 2008. My name is Mike Arrison. I'm from the firm of Carolina Legal Video Services. The court reporter is Joanne Quebe from Depositions And, Incorporated. We're going on the

record at 10:15 a.m. Counsel will now state their appearance for the record.

BY MR. KING:

I'm Spencer King with the Ward Law Firm. I represent Dr. Gregory Feldman, his partner, Dr. Joseph Boscia, III. Their practice is Upstate Lung and Critical Care Specialists.

BY MR. MANN:

My name is Milton Mann. I'm assistant counsel with Mr. King. I represent Doctors Feldman, Boscia, and their group, Upstate Lung and Critical Care.

BY MR. GUNN:

I'm Billy Gunn of Spartanburg and I am the attorney for Dr. Deve Shantha.

BY MR. TURNER:

Noel Turner, with Burts, Turner, Rhodes and Thompson and my partner, Chuck Thompson and I represent the plaintiff, William Mark Casey.

BY MR. THOMPSON:

And I'm Chuck Thompson and I represent the plaintiff, Mark Casey.

BY VIDEOGRAPHER:

The court reporter will now swear in the witness.

BY COURT REPORTER:

Dr. Fogarty, do you swear that the testimony you're

about to give is the truth, the whole truth and nothing but the truth to the best of your knowledge so help you God?

BY THE WITNESS:

I do.

CHARLES M. FOGARTY, M.D., being duly sworn, testified as follows:

DIRECT EXAMINATION BY MR. KING:

Q. Good morning, Dr. Fogarty. Spencer King. I introduced myself a minute ago on the record. We are about to begin the taking of your deposition. You have been identified by the plaintiff attorneys, sitting across from me, Mr. Thompson and Mr. Turner. You have been identified in the litigation involving Mr. William Mark Casey against my clients and Dr. Shantha. You have been identified both as a fact witness and an expert witness. Thus the reason for the taking of your deposition. You have previously had depositions taken in other matters, have you not?

A. Yes, sir.

Q. You have the right to read and sign this deposition to ensure that the court reporter does not make mistakes, or you may waive that. It is your privilege. Just instruct the court reporter what

you want.

BY THE WITNESS:

I'll probably waive that privilege. Yeah, I'll waive the privilege.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Okay. Dr. Fogarty, you are a pulmonologist?

A. Yes, sir.

Q. What is the name of your practice?

A. Lung and Chest Medical Associates.

Q. And it's located on Boiling Springs Highway?

A. 2030 North Church Place, which is just off of Boiling Springs Highway.

Q. Is that your only location?

A. No, sir. Do you want me to ---

Q. Please. Yes, sir.

A. I spend my mornings at our research office which is Spartanburg Medical Research. And that's at 485 Simuel Road.

Q. I'm sorry?

A. 485 Simuel, S-I-M-U-E-L, Road.

Q. I gotcha.

A. It's right next to the old Metromont, currently the Cemex cement plant. And then on weekends I round at the Restorative Care Hospital.

Q. How many physicians are with your group?

A. Four. We have Dr. Smith. We have Dr. Clark, Dr. Mendoza and Dr. Cruez.
Q. Are all the physicians with your group primarily pulmonologists?
A. Yes, sir.
Q. And what is pulmonology?
A. Pulmonology is a subspecialty of internal medicine with a focus on diseases involving the chest, focusing mainly on the lungs and associated blood vessels, chest wall, but not including the heart.
Q. Doctor, do you have any employees with your group that you know to be related by either blood or marriage to any of the litigants in this party or any of the attorneys in this case?
A. I do not currently have any employees in either group, to my knowledge.
Q. Has Mr. Thompson's wife, Maria, previously been employed by your group?
A. Yes, sir. She was previously employed at Lung and Chest.
Q. What was the period of her employment?
A. She worked there as a transcriptionist for -- on and off, I don't know, for -- I really don't know. I'd say -- it seems like forever, but certainly for a long period of time.

Q. When did she last work, approximately?
A. I'm not sure of the exact date. But as we merged into electronic records, the need for transcription went way down. I would say probably sometime last year, the start of this year.
Q. Doctor, give us kind of a capsule of your education and training.
A. I went to Providence College, Providence, Rhode Island and completed a bachelor of science in 1966. It seems like ancient history. I did my medical school training at the University of Rochester. Completed that in 1970. I then stayed on at the University of Rochester, Strong Memorial Hospital from 1971 through '75 with two years out in the military. That was the Vietnam era. After completing my internal medicine residency in 1975 I then went to the University of Pennsylvania -- Hospital University of Pennsylvania and completed a pulmonary fellowship there from 1975 through 1978.
Q. Is that it?
A. That's pretty much the end of my residency and fellowship training, sir. Uh-huh (affirmative response).
Q. You may have said this, where did you do your internal medicine training?

A. At the University of Rochester, Strong Memorial Hospital.
Q. You may have said that. I'm sorry. I didn't get that.
A. I actually have a outline copy of the CV.
Q. Do you have it with you?
A. Yes, I do. Here. I just made two copies.
BY MR. KING:
That's fine. We'll mark that as Exhibit 1.
(COURT REPORTER MARKS EIGHT-PAGE DOCUMENT AS DEFENDANTS' EXHIBIT NO. 1; ATTACHED TO DEPOSITION).
DIRECT EXAMINATION RESUMED BY MR. KING:
Q. Doctor, are you board certified?
A. Yes, sir.
Q. In what fields?
A. Internal medicine and pulmonary disease.
Q. And when were you first boarded in internal medicine?
A. That would have been around 1975. I think the dates would be on the CV on page three. It's 1975.
Q. Is internal medicine a specialty that requires you to be re-boarded periodically?
A. It currently does. At the time that I took the internal medicine boards, there was no requirement for periodic re-boarding.

Q. And how about pulmonology; when did you become first boarded as a pulmonologist?
A. 1978.
Q. Same question, do you have to retake those boards?
A. You do now. At the time that I took them, you did not.
Q. And I take it that because you took them in 1978 and you did -- because of the passage of time, you're grandfathered in, you don't have to retake them?
A. Yes, sir.
Q. Are you board certified in critical care?
A. I was board certified and that required a ten-year re-certification. And along with several other peers hitting their late fifties, early sixties, I realized that to sit for the exam you really needed to spend 25 percent of your time in critical care, and that I was no longer spending that much time in critical care. Therefore I did not take the board certification.
Q. When were you last boarded in critical care?
A. That would be on the CV. That would be 1999.
Q. What is critical care?
A. Critical care is a -- again a subspecialty that focuses on the care of acutely ill patients. And

in an intensive care setting, that would start with respiratory support, but also involve other organ support. So a critical care specialist would have some expertise in areas of renal insufficiency, in cardiac insufficiency, in gastrointestinal. Involve the ability to manage acute critical problems involving organ systems such as those.

Q. You told me that you also have a facility, if I understood, known as Spartanburg Medical Research?

A. Yes, sir.

Q. And what type research is done at that location?

A. That facility functions as kind of a support group for physicians such as myself. It includes other physicians. And depending on the physician, the research would include, in my case, primarily pulmonary problems, chronic obstructive lung disease, asthma, emphysema, pulmonary hypertension, infections, bronchitis, pneumonias. We do have other physicians who -- I forget, we have a pediatrician, pediatric allergist. So at that facility studies involving asthma and allergies in children are conducted. We also have an adult allergist. And there are also a couple of family practitioners whose studies involving diabetes, hypertension might be ongoing. And we have a

rheumatologist, so studies involving arthritis, gout, would be among the studies conducted.

Q. Is that the extent of the physicians who practice there in doing research?

A. Well, when we say "practice there," it's a -- the other physicians in our group, for example, are involved with studies that insofar as everybody can't be everywhere, insofar I'm not in the intensive care unit, they're not at the research office. So they're involved. But as far as the day-to-day conduct of the clinical trials with their patients, I would be doing the conduct of them.

Q. Help me, Doctor, I'm confused as to -- am I wrong that you see patients at the Research Center?

A. No, that's correct, sir.

Q. You do?

A. Yes, sir.

Q. What determines whether you're going to see a patient at the research center versus seeing a patient at your office?

A. Patients seen at the Research -- with your indulgence, let me go back just a bit. There are significant potential ethical conflicts with patients and clinical trials. And at the time that

I initially started doing clinical trials, the location was the same as the practice office. But I became aware that the patient might be confused, as far as whether he was coming in for regular care, for a regular visit, or coming in for care relating to the specifics of the study. So in the mid 1990s we started a separate location, although less convenient. And so if I was seeing a patient, it could be the same patient, for an acute problem, I might see him at the main Lung and Chest office. If I was seeing him for a visit specified by a study protocol and the patient was on that study and gave informed consent and so forth, I would be seeing him at the research office. Does that help you out, sir?

Q. It does. And let me see if I understand. One distinction as a layman I would make, if I'm being seen as a patient in your office, you would be charging me for your charges?

A. Yes, sir.

Q. If I ---

A. In general.

Q. Okay. If I see you at the research, as a part of a clinical trial, then I likely would not be charged?

A. Yes, sir. One of the reasons for the separate

location was the potential for inadvertent double billing, which has become a serious concern for hospitals as well as practitioners. You're seeing the patient strictly for a study. The sponsor is paying for that visit. But on the way out, the patient goes by the exit clerk and the exit clerk doesn't know and gives that patient a bill. So that's part of the reason for the separate location.

Q. Who dictates or who establishes what clinical trials will be conducted?

A. That would be the doctor that's the principle investigator. So to help you out, we might get a call from a drug company that has a drug, for the sake of argument that's already on the market, Rituxan is an example. It's on the market for oncology, but it looks like it's a benefit for arthritis. We then ask the rheumatologist if he would be interested in participating in that study. If he says no, then that's the end. If he says he's interested, then we would proceed to get the proper documents and so forth in place to do that study.

BY MR. THOMPSON:

Spencer, let me inject, if I might. You had filed

a motion earlier that as to research operations, particularly Dr. Feldman and Dr. Boscia, that that was going to be off limits. At least that's what you indicated in your motion and verbally. And my question now is, you know, you've got a little background from Dr. Fogarty on the research. And I would object to any further questioning in that regard.

BY MR. KING:

I probably have two more questions. You know, if you ---

BY MR. THOMPSON:

It's not proper ---

BY MR. KING:

If you feel like ---

BY MR. THOMPSON:

--- to go any further then ---

BY MR. KING:

I'm going to ask a couple more questions. If you feel like that I am into privileged and confidential territory, instruct him not to answer and we'll deal with it later.

BY THE WITNESS:

I'll try not to be longwinded.

BY MR. THOMPSON:

A couple more questions. Go ahead.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. My question, Doctor, is the clinical trials related to relationships with drug companies?

A. In general the clinical trial starts with a pharmaceutical company, in our case. It could start with the doctor. We have a doctor in town that has a product -- a device that he approached us on doing a study. But in general it starts with a drug company that has a product. And then they go through several steps to -- including preliminary testing with animals and so forth, and then the FDA. So we do not get involved until there have been several steps and the drug or the product has been pretty extensively vetted.

BY MR. KING:

Chuck, that's -- I was just trying to get a general idea of what Dr. Fogarty's work is. I'm not ---

BY MR. THOMPSON:

I have no problem with that.

BY MR. KING:

--- going to pursue that any further.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Doctor, do you consider yourself that you are an expert in neurology?

A. In what?
Q. Neurology?
A. I would have the expertise of a general internist, but not of a neurologist.
Q. What training would you have in neurology?
A. The training that an internist has. I did a rotation with Dr. Griggs who went on to author several textbooks and so forth. But that would be the extent of my formal training in neurology.
Q. And when was this?
A. That would be back in 1974, '75.
Q. And the name was Grigg?
A. Griggs, G-R-I-G-G-S.
Q. Griggs. Do you know his first name?
A. At this point, no.
Q. And he is the author of ---
A. Several textbooks.
Q. --- textbooks?
A. What I want to convey is that that's -- wetted my interest in neurology. My college roommate was Jack Nolte, who is professor of neuro-anatomy and the author of several textbooks on how the brain functions. So while I have only the formal training of a general internist, I have had a -- more than a passing interest.

Q. Do you have any advanced training in radiology?
A. No, sir.
Q. Do you consider that you are an expert in radiology?
A. I have the expertise in radiology that a pulmonologist would have, but not that of a radiologist.
Q. Do you have training in neurosurgery?
A. In what?
Q. Neurosurgery?
A. No, sir.
Q. And don't consider yourself as an expert in neurosurgery?
A. No, sir.
Q. Doctor, your practice does not deal with brain disease?
A. We do not see brain disease. We do deal with brain disease. A good many of our patients have -- are elderly and have problems with memory, dementia. Pretty much any internist taking care of geriatric patients is dealing with a subset of patients that have brain disease.
Q. Do you deal with patients with brain injury?
A. Not primarily. We see patients that have had brain injury, but not primarily, sir.

Q. How about brain disorders?
A. I'm not sure what you mean by brain disorders. You mean like seizures and epilepsy?
Q. Correct.
A. Again, we see patients that have epilepsy and refill their medications, but we do not -- that's -- we would follow up on a plan of action that's been established by a neurologist or someone with more expertise.
Q. So if I understand what your answer was, if you have a patient that you are seeing primarily because of a pulmonary issue, they also may have dementia?
A. Yes, sir.
Q. Would you be the physician treating the dementia, or would that be someone else?
A. It depends on the situation. If the patient is what we call "end stage severe," then we might actually assume primary care of that patient, just as the nephrologist assumes primary care of the patient on dialysis. But otherwise we would be deferring to that patient's family practitioner. And we would still be following them in consultation with neurology.
Q. Doctor, do you currently have privileges in any

hospitals?
A. Yes, sir.
Q. Where?
A. Spartanburg Regional, Spartanburg Restorative Care, and Mary Black.
Q. Have your privileges at Spartanburg Regional ever been under any type of review?
A. No, sir.
Q. Have you privileges at Restorative Care been under any type of review?
A. No, sir.
Q. And same question for Mary Black?
A. No, sir.
Q. What are the type privileges that you have at Spartanburg Regional?
A. The privileges I have at Spartanburg Regional would be those of pulmonologist. To maintain privileges, one needs to do a certain number of procedures. So, for example, in the past in critical care, I would have been putting in a fair number of Swan-Ganz catheters and chest tubes. Since I'm no longer performing those services with any regular frequency, I informed the medical staff I wished to relinquish those procedures. Now, in a emergency situation, I can still -- I'm still permitted to

proceed. But unless it's a pressing situation, I'm saying that let's get someone else that's doing more of this in the way of -- for example, Swan-Ganz catheters and chest tubes.

Q. Do you do bronchoscopes?

A. Yes, sir.

Q. How often would you do a bronchoscope?

A. Recently not that frequently. I would say probably a half dozen to a dozen a year.

Q. Okay. What type bronchoscopes are these?

A. Flexible. There are -- there's a large channel adults scope. It's a six millimeter, roughly, outer diameter with a two point seven millimeter inner channel. There's the regular adult scope; it's approximately a five point seven millimeter outer diameter with a two point two millimeter suction channel. And then there is what we call the pediatric scope which is a smaller outer diameter approximately -- under five millimeters and it has a suction channel that's generally less than two millimeters. And then there's also a fiber optic laryngoscope which one can actually use in the office to pass down the nose and look at the vocal cords and the upper part of the trachea.

Q. Do you do rigid bronchoscopes?

A. No, sir.
Q. Have you ever?
A. Only under supervision.
Q. Have you removed foreign bodies from the bronchus?
A. Yes, sir.
Q. When is the last time you removed a foreign body from a bronchus?
A. When Dr. Feldman came to Spartanburg and joined our practice, I basically stopped doing YAG laser procedures and removal of foreign body procedures.
Q. And about when was this? About what time was this? Roughly year wise.
A. I'd say around 1992.
Q. Dr. Fogarty, we -- the notice of deposition asked you to bring records with you. Have you seen that notice?
A. Yes, sir. Mr. Thompson showed me the notice this weekend.
Q. Did you bring those records?
A. Yes, sir.
Q. Can I see what you brought?
A. Do you want to put the box on the ---
Q. Yeah, that's probably the best thing.
A. Okay.
BY MR. GUNN:

Spencer, are you going to take a minute to go through those?

BY MR. KING:

Yeah, that's fine.

BY MR. GUNN:

I'm not suggesting you to do that.

BY MR. KING:

That's probably a good idea. Yeah, we'll go off the record now.

BY VIDEOGRAPHER:

Off the record at 10:45 a.m.

(OFF THE RECORD).

BY VIDEOGRAPHER:

On the record at 11:02 a.m.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Dr. Fogarty, we went off the record a minute ago for you to produce records that you were asked to bring today. And we've had an off the record discussion. First off, you have your chart of treatment of Mr. Casey. And whereas my records did not show that you saw him after 2006. From the records you've brought today, you have continued to see him, have you not?

A. Yes, sir. As I mentioned my kind of graph (phonetic) discussions, after seeing Mr. Casey in

June or whatever of '05, I continued to see him basically at six-month intervals. I've continued to see him at six-month intervals up to the present.

Q. And the most recent note that I have in your records is December 8th, 2008; ---

A. Yes, sir.

Q. --- is that correct?

A. A couple weeks ago.

Q. And you've told us that in the last year or two you have gone to computer generated records?

A. Yes, sir.

Q. And in preparation for today's deposition you went into the computer and printed out the records of visits?

A. I didn't do it, but I asked our office manager. Otherwise you would have nothing for this year.

BY MR. KING:

We'll mark as the next exhibit the records from Dr. Fogarty's office, beginning with the visit of January 3rd, 2007 through the record visit of December 8, 2008. That will be -- what is that? What's that number?

BY COURT REPORTER:

Exhibit 2.

(COURT REPORTER MARKS 18-PAGE DOCUMENT AS DEFENDANTS' EXHIBIT NO. 2; ATTACHED TO DEPOSITION).

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Doctor, you said that as this litigation has proceeded, you have received a number of depositions of witnesses and parties; correct?

A. Yes, sir.

Q. And you have not read all of those depositions?

A. That's correct, sir.

Q. You've told us that you had -- and I'm going from memory, that you reviewed the deposition of Dr. Feldman?

A. Yes, sir.

Q. Dr. Boscia?

A. Yes, sir.

Q. Dr. Paladuga?

A. Yes, sir.

Q. Dr. Nguyenduy?

A. Yes, sir.

Q. Dr. Shantha you don't recall reviewing?

A. That's correct, sir.

Q. How about Dr. Gonda, do you recall reading Dr. Gonda's deposition?

A. No, sir.

Q. Do you know who Dr. Gonda is so far as Mr. Casey?

A. Yes, he's -- I've been sending him copies of some of the office notes. He is Mr. Casey's primary care physician.
Q. And you have brought a number of texts of previous review here today, have you not?
A. Yes, sir.
Q. The first one, and this is not necessarily the order in which we took them out of the box. It's almost kind of a reverse order, but the first one I have is the -- is that The CIBA Collection of Medical Illustrations, Volume seven?
A. Yes. CIBA's a now bought out Swedish -- a Swiss pharmaceutical company.
Q. And what is the significance of this volume, please, sir?
A. It's a recognized authoritative reference. Dr. Netter, although deceased, is recognized for his ability as a physician, as well as an artist, to portray meaningful medical illustrations.
Q. And what illustrations in here do you believe are appropriate to this case?
A. Well, I believe that this here -- there are other ones, but the key one for this case is this illustration (indicating). There are other illustrations relating to the blood pressure in the

pulmonary vasculature that we can -- I can make the points I want to make without referring to those illustrations.

Q. And you're referring to an illustration on page 241?

A. Yes, sir. It's basically a chapter. It continues for a couple pages.

Q. Can you tell me where it ends?

A. It ends on page 244.

Q. And Doctor, why do you believe that these illustrations are relevant?

A. They portray a tear in the left bronchus and the collapse of the lung with air in the plural cavity. And they portray the patient in significant distress.

BY MR. KING:

Let's mark this as the next exhibit.

BY COURT REPORTER:

3.

BY MR. KING:

And I'm going to ask the court reporter in all cases if she will make arrangements to copy the parts that we've identified. And then if she could just return the text either to Dr. Fogarty or to y'all, whichever you want her to do. Just tell

her.

(COURT REPORTER MARKS DOCUMENT AS DEFENDANTS' EXHIBIT NO. 3; ATTACHED TO DEPOSITION).

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. The next one, Doctor, I have is Atlas of the Human Body?

A. Yes, sir.

Q. Tell me about that volume.

A. Well, the anatomy of the chest is complicated, particularly the anatomy of the blood vessels around the trachea and the right and left main bronchi. And it's difficult to give a three-dimensional picture of that in a two-dimensional format, but this atlas has a nice depiction of the trachea and then the left main bronchus, the left upper lobe bronchus, the left lower lobe bronchus. And it has a depiction of the pulmonary artery, the aorta and the pulmonary vein and they're nicely labeled. And I've made copies of those.

Q. Doctor, would you hold that up for the cameraman. You've made multiple copies ---

A. Yes, sir.

Q. --- of plate 47C?

A. Yes, sir.

Q. Which is the thoracic organs, deeper view model?
A. Yes, sir. And it's going to be tough. This is left; right?
Q. The right.
A. No, this is left. This is left. So on the left here, up here is the aorta and then the pulmonary artery. And then down here -- I need a sharper. And then down here is the pulmonary vein in between the left upper and left lower lobe bronchi.
Q. Again, point to -- show me where the left -- the left bronchus is.
A. This is the left bronchus (indicating).
Q. Is that in blue?
A. Yes, sir.
Q. That's in blue. Okay.
A. Yes, sir.
Q. And where is the pulmonary vein?
A. Well, there are lots of pulmonary veins. But it depicts a pulmonary vein right there (indicating). And I want to mention that everybody -- this is a model and that there may be variations in any given case.
Q. And where is the pulmonary artery?
A. The pulmonary artery is -- we have this arrow here. And let's see, yeah, it says, "left pulmonary

artery" right there. And that's going to -- and that is on top of the left vein bronchus. And then on top of the pulmonary artery is the aortic arch.

Q. Is the pulmonary artery closer to the bronchus than the pulmonary vein?

A. No, they're both touching the bronchus. They're just touching in different places.

Q. Is there any other drawings, illustrations out of that volume that you deem to be appropriate here?

A. Not at this time, sir.

BY MR. KING:

We'll just mark this one as ---

BY COURT REPORTER:

4.

BY MR. KING:

Yeah.

BY THE WITNESS:

You probably want this to say where it came from.

BY MR. KING:

Yeah, that's what I'm -- thank you on that.

BY THE WITNESS:

Yeah, you're probably going to need to have that cover plate.

(COURT REPORTER MARKS DRAWING AS DEFENDANTS' EXHIBIT NO. 4; ATTACHED TO DEPOSITION).

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. The next volume we have is The Human Body, Doctor, and that's by -- editor in chief is Charles Clayman, M.D.?

A. Yes, sir. This is aimed more at lay people. So this is an atlas that is aimed at a lay audience, that I selected it because it has again a nice depiction of the anatomy -- let me sit sideways here. Let me take a step back. What I did here was to enlarge with the magic of the Xerox machine this picture here, and that's on page 104. And what this picture shows is the aorta. It shows the pulmonary artery. This is a frontal projection, so this is just like me looking like this (indicating). It shows in the frontal projection the space between the aorta and the pulmonary artery which is called the "aorta pulmonary window." Now, some of these labels I put on. So we need to -- I want to make clear that some of these labels are not in the picture. And so this arrow here going up to aorta pulmonary window was placed there by myself. This is an original line (indicating). This is the pulmonary artery (indicating). This is the pulmonary vein (indicating). Now, it's a little tricky here, but

this is the main windpipe, the trachea. And that is coming down and with some imagination is coming down like this (indicating). And then it's branching into the left upper lobe bronchus and the left lower lobe bronchus. And the reason I selected this picture is because I believe it gives an accurate depiction of the location of the aorta pulmonary window, which is fairly close to the trachea. And the pulmonary artery which here is on top of the left main bronchus, and as we go further out to the left upper lobe bronchus. And the pulmonary veins, which are coming -- simplistically the arteries tend to run a little more vertically and the veins tend to run a little more horizontally. And these veins are coming in horizontally from the lungs. They've already been through the lungs. And they're right next to the left upper lobe bronchus, kind of in between the left upper and left lower lobe. And when we talk about locations on bronchoscopy, since we're usually looking at a picture flat, we would say that this dimension here is at about 9:00 o'clock and this dimension here (indicating), if we're looking at a clock through a bronchoscope is at about 3:00 o'clock.

Q. And you're referring to the view that the physician has ---

A. How we usually describe it, right.

Q. With the patient lying down?

A. Right. In other words, if we're looking -- and I have another picture which will make the same point, but I thought this -- as a physician I find some of these pictures complicated. And I thought this was a nice demonstration.

Q. I was trying to get us a pointer that you could point those out.

A. Well, see, with that being in the way here. Do you have a lighter pointer?

Q. I had asked if we could get a laser pointer, and that's -- we're currently looking for it.

A. So again to review, this is the aorta (indicating), receives the blood vessels going to the brain, the right and left carotid vessels. The right brachiocephalic. The space here is where the aorta goes over the pulmonary artery and that's called the aorta pulmonary window. And it's just -- you can see why they call it a window. It's just a very -- potentially a very narrow space. This is the pulmonary artery. This is the left pulmonary artery. You need to be careful because the right

pulmonary artery you can't see. It's coming in there (indicating). So this is the left pulmonary artery (indicating). Coming down here is the trachea, and then this is the left main bronchus that we can't really see in here (indicating). And then what we can see is several inches out from where it takes off from the trachea the left main bronchus divides into the left upper lobe, which is here (indicating), and the left lower lobe which is here (indicating). And we can see that the space in between the left upper lobe and the left lower lobe -- all these spaces have a lot of blood vessels. But the space here typically has the pulmonary veins coming in horizontally. And they're going into the left upper part of the heart, the left atrium. And then they would go into the left ventricle. And then they would go straight out the aorta through the systemic circulation.

Q. Thank you, Doctor. Any other illustrations in that text that you believe to be appropriate?

A. That's the main one at this time, sir. And again, you will want the book, I guess, to ---

Q. It's The Human Body?

A. Yes, Illustrated Guide.

(COURT REPORTER MARKS DIAGRAM AS DEFENDANTS' EXHIBIT NO. 5; ATTACHED TO DEPOSITION).

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Now, the next one, Doctor, is Flexible Bronchoscopy, second edition. The first editor is Ko-Pen Wang?

A. Wang, yes.

Q. Wang, M.D. Doctor, what in that text do you believe to be appropriate?

A. Well, there's several chapters. But again, what I believe -- in terms of the anatomy, there are some color pictures -- I think they're colored pictures. Maybe not. Yes. So there's a chapter -- the chapter on "Applied Anatomy of the Airways," it is relevant, and it shows what you would see both externally and what you would see looking through the bronchoscope. So this is looking externally and this is what you would see through the bronchoscope. And, let's see, plate five six -- plate five six is particularly relevant. So this shows the bronchoscope sitting at the left takeoff of the left bronchus and the right bronchus. It shoes the aorta which is just highlighted here. And the pulmonary artery. And what that would mean is that this little space here is the aorta

pulmonary window, which is fairly high up on the left main bronchus. Fairly proximal. The left main bronchus. And then it shows that if you go several inches further down, the -- you can't really see it in this dimension, but it shows that the -- we need to go to this picture here, but it would show that the left upper lobe bronchus is coming out this way, and the left lower lobe bronchus is going down. And this pulmonary vein here would be going in between the left upper, which is on top and the left lower ---

Q. The left upper bronchus?

A. Bronchus is on top. The left lower lobe, which we can't really see, because in this plain it's coming out and going down. And in this picture here, plate five seven, shows the bronchoscope further out. And it shows the picture that one would see if we were further out. And it shows the subdivisions of the left upper lobe and again depending on how you're oriented, the upper upper part of the lobe is -- if you're looking at the patient supine, it's like they peel off laterally, so the left upper lobe would be to the left. And the lingulate would be more to the -- if you will, this is to the left, and the lingula is more to the

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right. And again, it shows that the pulmonary veins are coming in on this direction, which would be more in the 3:00 o'clock dimension if we're describing something with the usual terminology we do with the patient supine. And the pulmonary artery would be more in the 9:00 o'clock position. That's the -- that chapter is on the anatomy. But there is a chapter -- a couple of chapters that are just worthwhile as general references as a whole chapter.

Q. The chapter that you've been -- the drawings that you've been ---

A. Would be plates five six and five seven.

Q. Are contained in "Applied Anatomy of the Airways," which is chapter five?

A. Yes, sir.

Q. And then other ---

BY MR. KING:

Let's mark that as ---

BY COURT REPORTER:

Number 6.

(COURT REPORTER MARKS DRAWINGS AS DEFENDANTS' EXHIBIT NO. 6; ATTACHED TO DEPOSITION).

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. You said there are other chapters that are ---

A. Right. There are two chapters. This Dr. Wang is the inventor of the Wang needle and a noted expert. There's a chapter on "Bronchoscopy in Foreign Body Removal. That's chapter 19, page 197 through page 209, is a very worthwhile chapter.

Q. May I see that, please, sir?

A. Yes, sir.

Q. Do you consider this to be authoritative?

A. Yes, sir.

Q. And that is ---

A. That chapter is by Dr. Mehta.

Q. "Bronchoscopy in Foreign Body Removal," chapter 19?

A. Yes, sir.

BY COURT REPORTER:

Do you want that as a separate ---

BY MR. KING:

I do.

BY COURT REPORTER:

Number 7.

(COURT REPORTER MARKS DOCUMENT AS DEFENDANTS' EXHIBIT NO. 7; ATTACHED TO DEPOSITION).

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Other sections or chapters in that book that you believe to be appropriate?

A. I think that may be. Let me get my glasses out

here. I believe that's the main chapter, yeah.

Q. And then the last hardbound we have is a text entitled Interventional Pulmonology?

A. Yes, sir. And this text is notable for its introductory chapter on "Laser Bronchoscopy," page -- starting at page 43 and going through to page 67. And I think that's -- for this discussion that's the main chapter.

Q. And this is Interventional Pulmonology, is it Beamis and Mathur? Mathur?

A. Yes, sir.

Q. And you ---

A. We should look at the authors that -- you need to be careful, the authors of that chapter though -- the authors of this chapter, "Laser Bronchoscopy" are James Fenton and Mr. -- and Dr. Beamis.

Q. And that's chapter five?

A. Yes, sir.

BY MR. KING:

Next exhibit.

BY COURT REPORTER:

That would be Number 8.

(COURT REPORTER MARKS DOCUMENT AS DEFENDANTS' EXHIBIT NO. 8; ATTACHED TO DEPOSITION).

DIRECT EXAMINATION RESUMED BY MR. KING:

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Q. Now, I believe this is a Pocket Atlas, ---
A. Yeah, that's probably ---
Q. --- of Radiographic Anatomy, and you, I think, mentioned ---
A. Well, the main ---
Q. --- one drawing on page 185?
A. Well, the main reason for this is -- any of the dozen atlases would do, but it depicts a standard chest film. And then it depicts the anatomy that goes with that chest film.
Q. So that's actually -- actually that's 184 and 185?
A. Yes, sir.

BY MR. KING:

We'll combine those into one exhibit. And that's 9?

BY COURT REPORTER:

9.

(COURT REPORTER MARKS DOCUMENT AS DEFENDANTS' EXHIBIT NO. 9; ATTACHED TO DEPOSITION).

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Doctor, you have a number of articles that you have brought.
A. With the court's permission, it might be -- it might save the court some time if I put those in some kind of order at the next break. They're

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supposed to be order. I don't know if they're in order.

Q. Are you saying -- I just picked up one ---

A. Yeah.

Q. --- and there are a number -- there appears to be a number of articles in there?

A. The idea is that each folder is supposed to represent a concept of interest. So one folder would represent articles relating to complications of the YAG laser and another might represent air emboli. Another might represent neurologic impairment. But I'm not sure that those are in as logical an order as they could be.

BY MR. KING:

Then at this point then, why don't we take ---

BY THE WITNESS:

I don't want to change or add anything. I just want to ---

BY MR. KING:

--- a recess and let Dr. Fogarty go through these and put them in the order he deems appropriate. So we're off the record.

BY VIDEOGRAPHER:

Off the record at 11:29 a.m.

(OFF THE RECORD).

BY VIDEOGRAPHER:

On the record at 11:44 a.m.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Doctor, you were kind of organizing some literature that you had accumulated; correct?

A. Yes, sir.

Q. And whichever package you want to talk to us about first.

A. It's still not as organized as I'd like, but this first packet are some articles that make the point that flexible fiber optic bronchoscopy is used to remove approximately two-thirds of most foreign bodies. And there's also a chapter in the previous text by Dr. Mehta that makes the same point. Those are a couple articles referring to the successful use of flexible bronchoscopy in the removal of foreign bodies. The main reference -- those are just really submitted -- that's another chapter in another text by Dr. Mehta. So the initial articles are in support that the chapter is not an isolated opinion.

Q. The first article is an article by -- is it A.H. Limper and U.B. Prakash?

A. Prakash, yeah.

Q. Prakash. And did that come out of the Annuls of

Internal Medicine? Am I right there, 1990?

A. Yeah. I'd have to look at it here. Yes. And the point of the article is that sentence that was underlined.

Q. Which is "Fiber optic bronchoscope was successful in 14 of 23 patients"?

A. Yes, sir.

Q. "And rigid bronchoscope was successful in 43 of 44 patients."

A. Yes, sir.

Q. "Including six of seven patients in which previous fiber optic bronchoscope had failed."

A. Yes, sir.

Q. And that's for removal of foreign bodies?

A. Yes, sir.

Q. Which were the two procedures used in this case?

A. Yes, sir.

Q. Now, there are other articles that you -- would you just list those for us, what's in this package?

A. Oh, okay, sir. This initial article was in 1990. And over the last 20 years the success rate with using the fiber optic bronchoscopy to remove foreign bodies has greatly improved. So the subsequent articles refer to higher success rates. So particularly in foreign countries where women

tend to have hat pins, this next article is from the Saudi Medical Journal, year 2007, volume 28, page 913. And it mentions that the flexible fiber optic bronchoscopy was used to remove a foreign body -- was used to identify or remove a foreign body and it was successfully performed. In essentially all patients, it had 93 percent.

Q. Success rate?

A. Yeah. The next article is from Turkey, extraction of pins from the airway with flexible bronchoscopy by Dr. Gencer, G-E-N-C-E-R. And the conclusion here is: "Standard flexible bronchoscopy is used increasingly in the treatment of tracheobronchial foreign aspiration in adults and older children." And the conclusion was, "Our study suggests that fiber optic bronchoscopy is a safe, easy and successful method used in the removal of foreign bodies, such as pins." And his results was that it was successfully applied in all cases, the removal of the pins. So not to belabor this, the success rate in part's a function of the skill of the person behind it. So the point of the article is that there's a range of success rates. And that we have improved with time and it is a function of the person doing the procedure. The equipment, the

instrumentation at hand is a variety of devices. There are even probes that are metallic. So you put the probe down and if you're going for a piece of metal, just like the auto mechanic goes for that screw in the middle of the engine with his long metal probe, that there are devices like that that are now available.

BY MR. KING:

Let's mark this as the next exhibit. And I've kind of lost count of how many ---

BY COURT REPORTER:

Number 10.

BY MR. KING:

--- articles are in here. But if we just label these -- these entire package will be labeled 10, and then A through however far you go in the alphabet. And again, like these you're going to copy these and give back the originals back to Dr. Fogarty.

BY COURT REPORTER:

Right.

(COURT REPORTER MARKS DOCUMENTS AS DEFENDANTS' EXHIBIT NO. 10; ATTACHED TO DEPOSITION).

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Now, your next package, Doctor?

A. The next package is an article mentioning the -- some of the risks of a bronchial laser resection. And it's by Dr. Mathew. And it makes the point that "Laser resection in the right and left upper lobe bronchi is difficult due to the lung anatomy. Another danger in the upper lobe bronchi is close contact with the pulmonary artery, particularly on the left. For these reasons, resection in the upper lobes is -- indications for resection in the upper lobes are limited." It also refers to the risk of higher powers of laser settings and longer durations. And that text that we gave there's also a similar chapter. To the point that we did not want to leave the court with one isolated text, that's the supporting article drawing the same conclusions as the text in the Interventional Bronchoscopy book.

Q. And the quote that you made a minute ago comes from page 62 of that article, "That laser resection in the right and left upper lobe bronchial is difficult due to the lung anatomy. This is true even with a flexible fiber optic bronchial scope because of the rigidity of the laser fiber prevents anticoagulation of the tip of the fiber optic bronchial scope. Another danger is the upper lobe

bronchi is in close contact with the pulmonary artery, particularly on the left. For these reasons, indications for resection in the upper lobe are limited." Is that what you just read?

A. Yes, sir. And that chapter makes this same conclusion as the textbook reference that you have.

Q. Doctor, are there different types of lasers?

A. Yes, sir.

Q. Do you know what type laser was used in this case, the case involving Mr. Casey?

A. Yes, sir.

Q. What type?

A. It was the YAG. And the chapter -- the introductory chapter on the laser bronchoscopy type goes over the differences between the carbon dioxide laser and the YAG laser.

Q. Is the laser used in this case gas cooled?

A. No, sir.

Q. It's water cooled?

A. Current lasers are water cooled.

Q. And the one used here is water cooled?

A. Where?

Q. In this case?

A. Oh. In terms of that article, I'd have to check. As far as the perforation, that would have nothing

to do with whether it's water or gas cooled. That'd have to do with the power of the beam.

Q. This article is written, I think, in 1990?

A. That ---

Q. Oh, I'm sorry, there's two -- well, it says there -- or 2000, I'm sorry. I'm sorry. It says, "Received January 28, 2000."

A. Yeah.

Q. Do we know when this article was written?

A. I'd have to look at the article.

Q. See if you can tell us what ---

A. You really can't tell when it was written.

Q. Okay. My question ---

A. Your point is -- the point as far as the contraindication of the left upper lobe being technically difficult, that would be independent of whether it's an older water cooled -- older gas cooled. And since -- at the time I was doing bronchoscopy in 1992, we were using water cooled lasers. So unless they had a -- without knowing the specifics, I would submit unless they had a very old model ---

Q. The older models are gas?

A. Yes, sir. In fact, I don't know that there are any in use in the area.

Q. So the newer models are water and you would assume that the laser used ---
A. Yeah.
Q. --- in this case ---
A. Though it would not be critical to the conclusion.
Q. Would not change?
A. No, sir.
Q. Would it matter as to whether or not it was a contact probe?
A. Not as far as the laser. A point is in the textbook on the laser -- chapter by Dr. Beamis, Dr. Mehta makes the point that the YAG laser can penetrate a distance easily of six millimeters and that you cannot tell what's happening on the other side. You can see the first millimeter, but you can't see what's happening on the other side. So there is the risk that if this -- if there's a lymph node on the other side, then that's not as critical. But if on the other side of the bronchus there's a blood vessel, that could be a problem.
Q. And is that heat being generated by the laser?
A. By the laser coming into contact. The amount of heat that's generated is a function of the laser that's emitted in the absorption of that light by the tissue.

Q. Now, this article mentions close exposure of the pulmonary artery. It doesn't mention the pulmonary vein.

A. That's correct, sir.

BY MR. KING:

And this will be?

BY COURT REPORTER:

Number 11.

BY MR. KING:

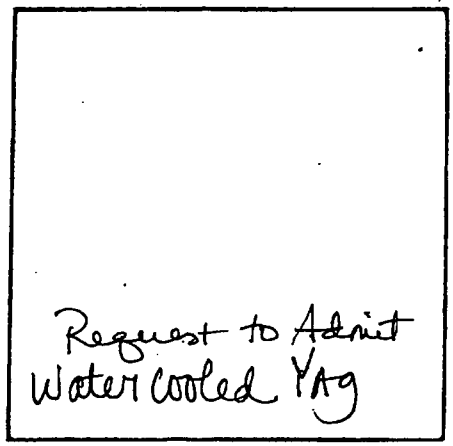
Number 11. Okay.

(COURT REPORTER MARKS DOCUMENTS AS DEFENDANTS' EXHIBIT NO. 11; ATTACHED TO DEPOSITION).

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Your next accumulation of articles, please, sir.

A. These are a couple of articles relating to cases where -- both in an animal model -- I think these are both -- these are both animal models where the laser was used to vaporize metal. And the reason is that there are stents that are inserted that have expandable metal. And they may or may not be coated by silicone. And it was just to review the various types of stents and the amount of energy that could be given without vaporizing the metal stent. Now, keep in mind that the metal stent is just a sliver of metal. But they conclude that


Request to Admit
Water Cooled YAG

there is a potential for significant tissue damage and that one needs to be aware of the amount of metal and the coating.

Q. Is that ---

A. Those are two animal model studies.

Q. Two animal studies. Both of these are on stents?

A. Yes, sir. Which are used in people and -- of course, you may need to laser in an area where there's a stent and you may intentionally laser through that sliver of metal. But just a study letting the laser endoscopist appreciate the appropriate settings and what the risks are.

BY COURT REPORTER:

Number 12.

(COURT REPORTER MARKS DOCUMENTS AS DEFENDANTS' EXHIBIT NO. 12; ATTACHED TO DEPOSITION).

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. And the next package?

A. These articles relate to pulmonary venous emboli as a complication of laser treatment. Some of these occurred with the gas cooled laser, some occurred with a water cooled laser. Some occurred with the laser used in the nose. So just a variety of articles saying that the potential, if you poke a hole in the bronchus or in the case of the nose, if

you poke a hole in the tissue there is the potential for air to go through to the other side.

Q. On the other side of the bronchus?

A. Yes, sir.

Q. And did you use the term node, N-O-D-E? Did I understand you ---

A. I said, nose -- I said, ---

Q. Are you saying nose or node?

A. In this article, one of the emboli occurred when they were using the laser in the nose.

Q. In the nose?

A. In the nose, yes. It was an ENT procedure. So they were doing ---

Q. And what is on the other side of the bronchus?

A. Well, it depends on the anatomy. And, of course, ordinarily you would obtain a CT scan of the lungs so that you would know what is on the other side in the area that you're proposing to laser.

Q. Have you seen the CT that was done on Mr. Casey?

A. I don't believe I've seen the actual CT. I saw the CT report.

Q. But have not seen the actual CT?

A. No, sir.

BY MR. KING:

Off the record a minute.

BY VIDEOGRAPHER:

Off the record at 12:01 p.m.

(OFF THE RECORD).

(COURT REPORTER MARKS DOCUMENTS AS DEFENDANTS' EXHIBIT NO. 13; ATTACHED TO DEPOSITION).

BY VIDEOGRAPHER:

On the record at 12:11 p.m.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Doctor, we have handed you a CT scan of the chest that was done on Mr. Casey on May 28th, 2004. And first off, let me ask you, what does that CT show you?

A. I'm not sure I understand your question. It shows me -- it's labeled as belonging to William Casey. And the date is May 20, 2004, 21:39 is the time that this was printed out, I guess. And it shows the lung. It shows the ascending descending aorta. It shows the trachea. This is on the left. And then as we keep going lower, it shows the left and the right, I believe, bronchi. And I'd have to have slices to be sure, because I don't read CTs by myself. I always read them with the radiologist. But it would be likely that at this point the left upper and left lower were getting -- had gone down a ways. I don't know how close these slices are.

And then this is the heart. And it shows that the lung fields are -- there's nothing unremarkable in the lung fields. And I'd -- yeah, that's as far as I'd comment at this point. And of course, it shows the spine.

Q. So you would be dependent upon the radiologist to read that CT?

A. Yes, sir.

Q. Can you tell us whether that shows what is on the other side of the bronchus?

A. It -- well, in so far as it's a three-dimensional slice. It gives you an idea, particularly if you're using contrast and you compare the contrast with the non-contrast, then in so far as blood vessels are more prominent with the contrast, if you compare the two, you would get some help in deciding whether it was a lymph node on the other side of the bronchus or a blood vessel.

Q. And this one was done without contrast?

A. That's correct, sir.

Q. So can you see the -- what is on the other side?

A. Well, some things you know from your basic anatomy. But the answer is that if I was trying to sort out a lymph node from a vessel, I mean, you know from basic anatomy that that has to be the descending

aorta and this has to be the ascending aorta (indicating). But as you get further out, and I would submit that, you know, you could get fooled without contrast in knowing whether you had a lymph node. So particularly if I was doing a laser -- in our text it mentions that kind of the standard procedure for a laser bronchoscopy in the left upper lobe area would be to have a CT at your disposal. And if I was doing left upper or left lower lobe, I would want contrast so that I could be sure that the tissue that was adjacent to the bronchus I was planning on lasering didn't light up.

Q. Now what further articles do you have?

A. These are a collection of articles on micro bubbles and how little tiny bubbles can get into the circulation with a variety of procedures, be they open heart surgery, laser endoscopy, conventional endoscopy. And how they can elude detection because of little tiny bubbles. And go on to cause -- settle problems in whatever area they end up lodging in. I'll be happy to, for the convenience of the court, to provide a formal bibliography listing a couple of sentences as to the take home points from these articles if it

would help out.

Q. Are any of these articles discussing bronchoscope, other than the one from Anesthesia, 1988, "Systemic Embolism During Laser Bronchoscopy"?

A. A couple of them do deal with just conventional bronchial biopsy without the laser.

Q. Is this the only one that does with laser?

A. I'd have to check. I believe there's -- in the previous articles there were lasers. So the -- and we've already covered the issue of the laser poking holes. Now the next question is, if you poke a hole -- but these are dealing with is, if some gas, by whatever mechanism, gets into a blood vessel, what's the outcome. So these articles are not dealing with the issue of the laser. They're dealing with the issue by whatever mechanism -- what happens when small blood vessels -- once small air bubbles -- or for that matter, small particles of debris.

Q. Do any of these case histories discuss tiny bubbles getting to the brain?

A. Not in an individual case history. Well, what they discuss -- there is somewhere in here there's a case where they actually looked in the patient's retina and were able to see air bubbles in the

retina, presumably going to the brain.

Q. That's the only one, that's in the retina?

A. Probably; yes, sir.

BY MR. KING:

Let's mark these.

WITNESS CONTINUES:

A. But the air bubbles -- the tiny air bubbles are going to go wherever the circulation goes.

BY COURT REPORTER:

14.

(COURT REPORTER MARKS DOCUMENTS AS DEFENDANTS' EXHIBIT NO. 14; ATTACHED TO DEPOSITION).

WITNESS CONTINUES:

A. So they could go to the left toe. It's just that if it goes to the left -- let's pretend that this air bubble goes to a little tiny blood vessel in my fingertip, then when it's all over, I've got a little black spot there. Because it blocked off the blood vessel and the tissue on the back side of that blood vessel dies. If I get a little black spot on this fingertip, it's not a major problem. If I get a little black spot in the hippocampus part of my brain, my memory's not what it should be.

Q. What's the next articles you have?

A. These are articles dealing with the neuro-cognitive impairment. And this is a Scientific American article dealing with someone that had open heart surgery and sailed through it, but just realized that they weren't the same person. They tested out fine. The surgery's a success. No change in vital signs. And then the subsequent articles are additional articles on the -- just the increased risk with the anesthesia per se, older patients per se, length of surgery. For postoperative cognitive dysfunction which could be simply some initial confusion or delirium. They go on to make the point that this -- that these problems have been reported after folks have a knee replacement or a shoulder surgery. And it doesn't have to be an air bubble. The mechanism, you know, may vary from case to case. But what you end up with is someone that had a procedure and by whatever mechanism neurologically they've lost something after the procedure. So these are just abstracts from the neurologist. And it's a major challenge any time you're putting someone to sleep, because it's very hard to monitor for this. You can have an oxygen saturation in your finger that is fine. The oxygen saturation in this fingertip could be normal, but

there could still be a little tiny particle that goes to a blood vessel in his finger that knocks off part of the fingertip.

Q. And these articles discuss cognitive dysfunction following general anesthesia?

A. Yes, sir. And procedures. And they don't offer any solutions. They say they were missing a lot of this. And we need to advise -- we need to be aware of the risks to advise patients and be on the lookout. And we need better tools for monitoring.

BY MR. KING:

This is what?

BY COURT REPORTER:

15.

(COURT REPORTER MARKS DOCUMENTS AS DEFENDANTS' EXHIBIT NO. 15; ATTACHED TO DEPOSITION).

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. And your next article?

A. These -- I apologize, these are really just miscellaneous articles on systemic air embolism following bronchoscopy, some with the water cooled lasers, some with gas cooled. It's again making the point that this is not an unheard of complication. That's several abstracts.

(COURT REPORTER MARKS DOCUMENTS AS DEFENDANTS' EXHIBIT

NO. 16; ATTACHED TO DEPOSITION).

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Doctor, did those articles come off the internet?

A. Well, it depends. Several of the articles were from journals that I subscribe to. But I no longer rip pages. Like the New England Journal, I've spent years ripping pages and filing them. And it's all a waste of time. So I would say that the answer is that the majority of them came off of the Internet, even if I had access to them in our library. So several of the articles -- I go to the medial library once a month and kind of sit and pour through their journals. But I would say that -- some of them I may have printed out at the library. And the library's wonderful. Because if you ask them to print stuff out at the Regional, they will print it out for you. And some of it I may have printed off the Internet.

Q. But did the -- did you do your own research?

A. Oh, yeah. Yes, sir. What I did -- the way I usually start on these things is to use a reference called "Up-to-Date" which then they give you a general overview. I did not include Up-to-Date as a reference. Instead I picked references from the Up-to-Date, which is kind of a textbook online and

went from there. Other techniques would be just to do a Google search or a Pub Med search on air emboli on the YAG laser bronchoscopy. Let me take a step back to clarify this for the court. If I have a patient with an interesting problem, then I will often -- it's so easy, just see what's available on the Internet.

Q. When did you do this research in procuring these articles?

A. This has been ongoing. I initially did some preliminary research when I saw Mr. Casey. And I had just seen the wife of a physician who had had open heart surgery. And she was thinking about -- she had a separate career. And she was thinking about giving up her career, even though the surgery was successful, because she could not organize her day. And she just -- you know, she was fine. She was reading books in the book club and all, but she just felt she was not comfortable. And, of course, that was easy for me to say to this patient that surgery success, you don't have any energy but it's not because your lungs are puny. Your lungs are fine. But you most likely, you know, had something happen to settle -- happen to your -- the thinking higher executive parts of your brain. Whether that

was from the anesthesia, from particles, from bubbles, you know, we're never going to know. And since you had your open heart surgery like a year ago, you know, it's unlikely that this is going to change a whole bunch. So having been through that experience with that patient, when I saw Mr. Casey and was aware from our chart review that he had had a lot of air, not to mention tissue trauma, that something similar might have gone on with his complaints of no energy, shortness of breath but normal breathing tests, and his lack of response to medicines. And at that point I did a quick search. And while he was still there, based on -- I actually had one of these texts in the office -- I think I actually had access to both of them in the office at the time. But based on a quick search, I said, you know, you may -- I kind of said, this is in your head but it's not in your head. This is not -- because this whole issue of are you just being lazy? If you push yourself and work out more and take more notes and think harder, this will get better. Or is this something real? And based on the other patient -- I'd actually seen more than one patient, of this physician's wife -- it's fresh in your memory. I said, you know, this is probably

what's going on.

Q. You said both texts, what are both texts?

A. The two texts that I left you with.

Q. I'm sorry.

A. These textbooks here (indicating). Let's see, this here.

Q. Okay. Interventional ---

A. Let's see here. Some of these textbooks I kept at Lung and Chest. But I have shifted more and more texts -- textbooks over to the medical office. But this book would have been at my office at Lung and Chest.

Q. And that's pulmonary?

A. Interventional Pulmonology.

Q. And the other one?

A. And I think this one was too, upstairs.

Q. Flexible Bronchoscopy?

A. Yeah. These textbooks here would -- these are aimed at lay people. This one I would not have looked at initially. That would have been sitting elsewhere.

Q. Doctor, what are the basic facts that occurred involving Mr. Casey that are going to bring him to your care and treatment?

A. That brought him to my care initially?

Q. Yes. Yes, sir.
A. As I mentioned in my summary, Mr. Casey ---
Q. Let me interrupt.
A. Yes, sir.
Q. I'm sorry. Poor question. I'm sorry. This morning when you arrived, you gave me copies of some notes that you had prepared?
A. Yes, sir. Realizing that I might have neurocognitive impairment, I went through -- I briefly reviewed Mr. Casey's chart. That's this thing. Over the weekend. And last night -- yesterday afternoon, thanks to the football game last night, I ended up completing this report. So I may have started the report on Saturday and finished last night.
Q. And this is dated December 20th?
A. Yes, sir.
Q. 2008?
A. Yes, sir.

BY MR. KING:

Let's mark that as the next exhibit.

BY COURT REPORTER:

17.

(COURT REPORTER MARKS TEN-PAGE DOCUMENT AS DEFENDANTS' EXHIBIT NO. 17; ATTACHED TO DEPOSITION).

BY MR. GUNN:

Spencer, is that the one with 345 lines? The pages aren't numbered.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Is that correct? To answer Mr. Gunn's question, it actually ends ---

A. Yes, sir.

Q. --- on line 345?

A. Yes, sir. I knew -- this is a new software program. I found the button to line the page, but I didn't find the button to number the page, so ---

Q. Doctor, have you ---

BY MR. GUNN:

That would be preferable.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Have you rendered any other written reports in this case?

A. I did not render a written report, but I did render a list of findings, conclusions, questions. As I mentioned, that's a two-page list that I failed to produce. I can produce it. I think -- I don't know if it's two pages or three pages. But ---

BY MR. TURNER:

That is -- I want to say it's five pages.

BY THE WITNESS:

Fives pages, okay.

BY MR. TURNER:

Dr. Boscia, Dr. Feldman, and Dr. Shantha.

BY MR. MANN:

That's it.

BY THE WITNESS:

I think there's something else.

BY MR. THOMPSON:

It's what we provided to you, Spencer, earlier.

BY THE WITNESS:

Well, that's the gist. I think when I initially prepared it, it was more condensed, so ---

BY MR. TURNER:

That was to get some guidance as to the parameters that he ---

BY MR. GUNN:

Did y'all put it in the form of a letter?

BY MR. TURNER:

--- would testify about.

BY MR. KING:

I'm showing a -- we've got a cover letter from Noel dated October 30th to the three -- including John Rogers. To you, Milton, John Rogers and myself. And then attached five pages, criticisms.

BY THE WITNESS:

I think there are two other pages, unless you reformatted this. And I'll go -- it might be buried or misfiled. But I should be able to retrieve that.

BY MR. GUNN:

Let me make sure, but this doesn't need to be on the -- I mean, this can be on the record. I'm not sure I have a copy of that. I've got a letter from plaintiff's counsel to us dated August 20th.

BY MR. KING:

This has a printed date of August 20th, Billy, a pen date of October 30th, and a fax date of October 30th. And a mailing affidavit of mailing of October 30th. I'm going to mark this as an exhibit.

BY THE WITNESS:

There are another couple of pages floating around. But they don't change -- there's nothing different in substance.

BY MR. THOMPSON:

Can I have mine back?

BY MR. KING:

Is that yours?

BY MR. THOMPSON:

Yeah.

BY COURT REPORTER:

Number 18.

(COURT REPORTER MARKS SIX-PAGE DOCUMENT AS DEFENDANTS' EXHIBIT NO. 18; ATTACHED TO DEPOSITION).

BY THE WITNESS:

And as I recall, the pages -- I'm sorry, sir, go ahead.

BY MR. GUNN:

Can I just ask him a question or two to make sure we're all singing from the same sheet of music here?

BY MR. THOMPSON:

I don't have a problem.

BY MR. TURNER:

I think what happened was, all the names were all on a fax sheet from August and that they just struck through the date and put October 30th, if that's right.

BY MR. GUNN:

Well, let me -- are the -- are the -- I see y'alls cover letter. The cover letter from plaintiff's counsel. And then attached to it, I do have that document. But I guess my question, and maybe this is -- maybe I'm jumping ahead to something that isn't my turn, but the attachment, was that

something that Dr. Fogarty offered or that y'all offered? That's what I need to know.

BY THE WITNESS:

I don't -- I -- I really don't -- I think what I authored was -- it wasn't on a letterhead and it was just a -- it's the same stuff, but ---

BY MR. THOMPSON:

This is something that ---

BY THE WITNESS:

It's the same stuff, but it was fewer pages.

BY MR. THOMPSON:

--- we offered, as to what we anticipated Dr. Fogarty ---

BY MR. GUNN:

Okay. That's fine. That's good.

BY MR. TURNER:

Which we prefaced on ---

BY THE WITNESS:

I prepared oh sometime about a year ago. This whole thing has been evolving over years and years.

BY MR. GUNN:

That answered my question.

BY THE WITNESS:

What I felt went on.

BY MR. GUNN:

And I'll get to it when it's my turn, if I need to.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. By way of clarification, Dr. Fogarty, there is an email or document that you generated that we don't have right now; is that correct?

A. I don't know if it's -- if it's -- it's a couple pages, is that what you're -- yeah.

Q. A couple pages, in some fashion?

A. I don't think it's an email. But what I recall is, it's on no letterhead. It would have been typed up in a word document. At this point the only record would be a paper record. But I'm pretty sure I can dig that up.

Q. If you can generate that off your computer, would you ---

A. Yeah.

Q. Do you think you can?

A. Yes, sir.

Q. Would you do that and make that available to Mr. Turner and Mr. Thompson?

A. Yes, sir.

Q. Who in turn will make it available to us. All right. Now, with that -- walking through that, Doctor, if you would, would you give us the facts as you understand it from going back when Mr. Casey

presented to the emergency room at Spartanburg Regional, came under the Boscia's care, then Dr. Feldman's care, up to the time that he comes under your care and treatment and take it us through kind of a summary of your group's care and treatment.

A. Well, paraphrasing what I have in the report, I initially saw Mark Casey as a follow-up from Dr. Smith and our nurse practitioner in mid 2005. And he was having some GI symptoms and had been on Strattera and Cymbalta really to help with his mental status. And I said to the first eval, which I'd have to look, I think it was our nurse practitioner, I said, "You might as well stop the Strattera and Cymbalta and I'll see Mr. Casey back in a couple of days and let's get an upper GI and I'll see him back and see if his stomach symptoms are any better." So I saw him back a couple days later, and that was my first encounter with Mark Casey as a patient. And during that time, between the two days, I'd looked at his chart and saw that he had seen Dr. Smith initially, I think in July of '04 really for a second opinion and a change in his care. He had been in the hospital in May and June of '04 initially for chest pain because he thought he was having a heart attack. And then he had this

chest film and it showed a piece of metal on the chest film. And he was told that he had something in his chest that needed to come out. And he had a flexible bronchoscopy. And then he was sent home and came back and had a rigid bronchoscopy. And as a result of the rigid bronchoscopy with the laser, he had some complications which led to -- I'm kind of telling this the way Mr. Casey told it to me. Had some complications which led to him having a lot of breathing troubles, needing to have a tube put down his windpipe, a tube put in his chest and put on a mechanical ventilator. And his face got all swollen with air -- subcutaneous air that had come out as a result of this complication of this procedure. He recovered physically from the procedure rapidly and was home within a couple days, I think around June 6. And -- but he continued to have the same complaints pretty much that -- when he went in the hospital, like his chest was sore. And when he saw Dr. -- either Boscia or Dr. Feldman in the office, at that time he learned that the CAT scan -- or somewhere in there he learned that the CAT scan which had been taken to see if there was a foreign body didn't show any foreign body. And this kind of shook his

confidence in the doctors. He was expecting an apology, I guess, or something. And at that point he went to Dr. Smith, which would have been in -- what did I say, July? July of '05.

Q. July 14th, 2005.

A. Yeah, July 14th. And Dr. Smith did a -- our usual history and pulmonary evaluation and told him, gee, your lung function tests are normal. So if you don't have any energy, if you're short of breath, if you're having trouble organizing yourself, it's not any permanent damage that was done to your lungs. You went through an awful lot. You had a scary experience. You almost died. And you could be having post traumatic stress. You know, maybe you need to see a psychiatrist. Maybe you need to get on some psychiatric medicine. So that was the thrust of Dr. Smith's initial evaluation. And over the next year, Dr. Smith was kind of the point person in our office and saw him periodically with the outcome that there really wasn't any change or improvement, despite the additional medication. When I saw him ---

Q. Let me stop you.

A. Go ahead.

Q. But from your review of the records, when the

approximate year before you became involved in his care and treatment,---

A. Yes, sir.

Q. --- when Dr. Smith was his ---

A. That's right, sir.

Q. --- principal point physician with your group, Dr. Smith clinically and diagnostic test-wise found normal pulmonary function?

A. Yes, sir.

Q. And he did at the initial visit opine that he may be -- that Mr. Casey may be suffering post traumatic stress?

A. Yes, sir.

Q. And post traumatic stress is not a malady or disease that your group treats?

A. Right. It was just an educated guess. I mean, he'd been through stress, and he'd been through trauma.

Q. And did Dr. Smith refer him to Dr. Jay Grace, who I believe is a psychologist?

A. I'd have to check the records, but I know from his note that he referred him for psychological and psychiatric help.

Q. Have you read -- you've told me you had not read Dr. Gonda's deposition. Do you have Dr. Gonda's

records?

A. I think you've given me all of the -- I probably do.

Q. You haven't read -- you haven't reviewed Dr. Gonda's records?

A. No.

Q. You don't think those would be helpful?

A. They might be.

BY MR. THOMPSON:

Can I show them to him?

BY MR. KING:

Sure.

BY THE WITNESS:

Okay. Okay. I would have skimmed those. I'm sorry. I thought you meant the deposition.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. No, I'm talking about his records.

A. The records, yes.

Q. You testified you hadn't read ---

A. Yeah. And I've -- I've pretty much skimmed the entire book. Yes, sir.

Q. So you have read his record?

A. Yes, sir.

Q. Is there a history in Dr. Gonda's records pre May/June of 2004 of drug abuse by Mr. Casey?

A. I'd have to look at the specifics. In terms of whether Dr. Gonda said he was abusing drugs or not, I'd have to look at that. If he says there was, I would accept that.
Q. You wouldn't challenge that?
A. No, sir.
Q. Did you conclude that Mr. Casey had been -- had abused prescriptive narcotics?
A. In my care of him; no, sir.
Q. Now, one of the problems that he had was nausea and vomiting ---
A. Yes.
Q. --- prior to your treatment?
A. Yes, sir.
Q. And what -- was that diagnosis -- what the cause of that was?
A. Well, it happened right after there'd been an adjustment in his Cymbalta and Strattera. So we didn't change anything except to tell him to stop those two drugs.
Q. And those were -- what's the Cymbalta and Strattera?
A. Well, Strattera is for an attention deficit -- again, I'm not -- I have to look these drugs up every time I go to use them. But these are

basically anti-anxiety, anti-depressant, attention deficit drugs used for conditions such as that.

Q. And do you know who was prescribing the Strattera and the Cymbalta?

A. No, sir. I assume that it was one of the -- those are prescription drugs, so it would be one of the psychiatrists or other physicians he was seeing.

Q. Your group wasn't prescribing those?

A. We might have refilled them, but we would not initiate a prescription for those drugs.

Q. They, you would anticipate, would be generated by a psychiatrist?

A. Or a family practitioner.

Q. Psychologists cannot prescribe medications can they, Doctor?

A. That's my understanding, sir.

Q. Tell us about the care and treatment after you became involved in Mr. Casey's care.

A. There are two aspects, from my standpoint, to Mr. Casey's care. One was my primary area of expertise, which is the chest. And we had the problem of his ongoing chest pain. On review of the records he had had chest pain intermittently, it's just that it had gotten worse, going back for years. He had even had a cardiac catheterization

which did not show any abnormality. Now, he did have risk factors. He had -- he's a smoker. He had hyperlipidemia. His CT actually showed some coronary calcification. And he is similar to a fair number of patients I have who have chronic pain and you're kind of telling them that, I'll prescribe pain medicine, but this is a chronic condition and you really need to learn to live with the condition on the one hand, but recognize that like the person who cries wolf one time too many, fits -- there's always the potential that chest pain could shift from being due to your chest wall to heart trouble. So we do need to keep an eye on things periodically. So the way we left from his cardiopulmonary end is that particularly since Dr. Smith was chief of staff at the time and was fairly busy, that I would be willing to see him. Each time I saw him, it took some time. Had to write notes. He seemed easily distracted. So it was -- each visit was a time consuming event. But I agreed to see him on a six-month basis. And I think I'm -- I'm -- probably was aware somewhere in there of the potential for drug abuse. Because I told him, "If this is a chronic pain condition and you need to realize that you cannot over take --

over use the medicine. Because if you do, then you're going to be labeled as a drug abuser." And we go from -- I mean, it can happen to a lot of people. And so on that end I've been seeing him essentially every six months. And he continues to have aches and pains that -- on the other side of the coin, he had aches and pains when he was working. And he was taking the Lortab. So I've been refilling his Lortab. He was taking Lortab prior to all of this happening.

Q. And you're still seeing him?

A. Yes. And -- so my mission is to refill his Lortab -- is to listen to his lungs, check his lung function tests, go over his history, make sure that -- he's still smoking. Make sure that his lungs haven't gotten any worse. That his heart's not any worse. And it's appropriate for me to continue refilling the Lortab as opposed to saying, "You need to go back and have another heart catheterization."

Q. From a pulmonary standpoint, is there any permanent injury to his lungs or pulmonary function not related to his cigarette abuse?

A. No, sir. That was one of the things that I told him, that the lungs are -- were blessed and

wonderful organs, and if you don't abuse it with the smoking, you can have an operation and the surgeon can remove a whole lobe of your lung and you can still function normally. So you can still have lung function tests that come out pretty close to normal. So each visit I'm encouraging him to quit smoking and, you know, your lungs are still okay, and don't -- don't make it worse.

Q. And other than filling the Lortab for aches and pains, anything else you were doing medically?

A. Just making sure that his lung function is stable and that there's nothing changed in the character of his pain to suggest that it's other than chest wall. And continuing to really bug him on the smoking. And I think Dr. Gonda -- faxing copies of our office visits to Dr. Gonda, and I believe he's keeping an eye on the cholesterol and his other general medical problems as well.

Q. Doctor, can you look at your chart, please, sir, and tell me what medications have been prescribed by your group for Mr. Casey?

A. Well, I'm -- right now, I'm probably the only -- the only medicines I'm personally aware of prescribed would be refills on the Lortab, because he's not on any pulmonary medicines. I doubt that

Lipitor, a cholesterol medicine, is Dr. Gonda should be prescribing.

Q. So the Lortab that you believe that y'all prescribe?

A. Right. And I've -- and I've discussed with him -- it would simpler -- because I think he's seeing a psychiatrist in Greenville. And he's on Adderall, which I don't know is doing a whole lot of good. But we want to avoid is two physicians prescribing the same drug. So at some point it would be simpler if the Greenville physician prescribed all of the controlled substances.

Q. Greenville, being the psychiatrist?

A. Yeah, I think -- and I'm embarrassed that I don't know the name of the psychiatrist.

Q. Doctor, I've been punched that we have one minute left on the video. So with that, we're ---

BY VIDEOGRAPHER:

This marks the end of tape number one, the deposition of Dr. Charles Fogarty. Off the record at 12:55 p.m.

(OFF THE RECORD).

BY VIDEOGRAPHER:

This is tape number two. We're on the record at 12:58 p.m.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Doctor, we have drug records from a pharmacy -- from various pharmacies. And what we're showing, and I'm going to ask you to look in your chart, that Dr. Gonda through January 18th, 2006 was prescribing Hydrocodone for Mr. Casey. And then beginning February 16th, 2006 it appears that you began prescribing the Hydrocodone.

A. That's probably right.

Q. What is Hydrocodone?

A. That's basically Lortab.

Q. That is ---

A. That is a generic name for -- it should be -- it probably says Hydrocodone slash APAP, something like that.

Q. And that's not a pulmonary medicine?

A. No, it's -- well, we -- I use a lot of cough suppressant medicine in pulmonary patients for people who have chronic pleuritic pain, chronic chest wall pain. So I would say that maybe one out of ten of our lung and chest patients are on medication like Lortab. And we're aware that these are controlled substances. And it's a double-edged treatment.

Q. What's the difference between Lortab and

Hydrocodone?

A. Lortab would be a brand name and Hydrocodone would be the generic. I'd have to look it up to be sure, but I believe Hydrocodone is the ingredient of Lortab.

Q. Doctor, you found and handed to me two pages.

A. Yes, sir.

Q. And are those the two pages that we had talked about that you thought we had not ---

A. Yes, sir.

BY MR. KING:

Mark those as an exhibit.

BY COURT REPORTER:

Number 19.

(COURT REPORTER MARKS TWO-PAGE DOCUMENT AS DEFENDANTS' EXHIBIT NO. 19; ATTACHED TO DEPOSITION).

(COURT REPORTER MARKS THREE-PAGE DOCUMENT AS DEFENDANTS' EXHIBIT NO. 20; ATTACHED TO DEPOSITION).

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Dr. Fogarty, I'm going to hand you your office note of July 21st, 2005.

A. Yes, sir.

Q. The Bates number is 440 through 438. Doctor, let me go to page three of your report, under the broad heading of "Comment."

A. I see it's page "tree."
Q. Page three, all right. The third paragraph under "Comment," would you read that to us, please, sir?
A. Sure. "With reference to the patient's difficulty concentrating, he undoubtedly had air emboli given his lengthy duration of anesthesia and laser perforation of the endrotracheal tree with resultant leakage of air into extra pleural and vascular extra pleural mediastinal and vascular spaces. Although he is fortunate not to have any gross motor deficit, he may well have a permanent neurologic deficit in which case the indication for taking medication may be moot and the patient may simply need to recognize that although he would like to go back to work, he may be chronically disabled by his neurologic impairment."
Q. Doctor, are there diagnostic studies or tests that would assist in diagnosing a neurological deficit?
A. Formal neurocognitive -- there are formal tests that can be done for neurocognitive impairment. Some of the references I gave you indicate this is a area that's on -- research that's ongoing and as far as what battery of tests to use, I'm not a psychologist or a psychiatrist and there may be some debate about the best ways to make the

diagnosis and monitor any progress.
Q. But aren't there diagnostic studies such as MRI, CAT scans, EEGs, that are ---
A. Those things are generally normal in neurocognitive impairment.
Q. Have you seen any diagnostic studies of the brain done on Mr. Casey?
A. Not to my knowledge.
Q. Would that helpful?
A. Based on my experience with the other patients that I've taken care of with this ailment, they've spent a lot of money and the tests didn't show anything.
Q. Other patients you've mentioned ---
A. I've got about a half dozen patients with -- this is a fairly common occurrence after open heart surgery. And obviously we have a lot of COPD patients that have had open heart surgery and we see them back.
Q. Do you have any patients who have had a bronchoscope that you thought had ---
A. Oh, no, sir. This ---
Q. This is the only one that ---
A. This is a kind of a only case in the world situation here.
Q. But do you know whether or not Mr. Casey has seen a

neurologist?
A. I believe in the -- he saw a psychologist.
Q. But to your knowledge has he seen a neurologist?
A. I believe he has, but I don't have those records.
Q. You don't have those records?
A. Yeah.
Q. All right. How about a neurosurgeon?
A. He could have seen a neurosurgeon. I wouldn't see the point. In terms of a neurocognitive impairment, the real experts there are the psychologists, because they do the detailed psychologic profiling.
Q. There's no anatomical change in the brain following the pneumothorax that Mr. Casey suffered?
A. To identify an anatomical change, one would need a microscope, because it would happen at the microscopic level. And the resolution of MRIs and CT scans is still not down to the level of individual capillaries.
Q. If he has permanent neurological deficit, the medical specialty that would diagnose and treat that would not be neurologists and neurosurgeons?
A. The diagnosis would probably be made by the clinical psychologist. If the test -- it gets back to whether the neurologist has an interest in

administering these batteries of tests. And, you know, I actually took a battery of similar tests. It's a fairly lengthy time commitment that's required by the doctor and the patient. I won't give you my results.

Q. You yourself took the test; is that what you're ---

A. I took a battery of tests. You're into a lot of things like reflex time. I just -- I was amazed at the variety of different tests out there.

Q. Have you seen tests like this conducted on Mr. Casey?

A. I've read the report where he's had tests conducted.

Q. And those were done by Dr. Randy Waid?

A. Yes, sir.

Q. And Dr. Grace? Are those the type tests you're ---

A. Yes, sir.

Q. --- referring to?

A. Yes, sir.

Q. Did you review those in detail?

A. No, sir.

Q. And whether or not they are consistent or inconsistent, you are not prepared to say?

A. I'm not prepared to say.

Q. What is the cause of the neurological deficit that

you mention here that Mr. Casey may be suffering?
A. I would -- in my opinion, the cause was the complications of the rigid bronchoscopy to laser the foreign body that wasn't there that resulted in a tear through the bronchial wall with perforation and destruction of the bronchial wall and adjacent tissue which resultant migration of air from high to atmospheric pressure to the area of lower pressure which would initially have been the pleural cavity and the vasculature. Primarily the pulmonary vasculature. But even without that mechanism, simplistically, one could say that he was having chest pain but able to organize his day and function. And then he had this catastrophic complication and hasn't been able to function since then. And I would not argue with someone that proposed an alternative mechanism such as an idiosyncratic reaction to the anesthesia. A little particle of tissue getting into the blood vessels. Localized change in oxygen. The bottom line is that with impairments like this, it's a little like you're looking at Charleston. The hurricane has been through town, but what you're looking at is the aftermath. And commenting or measuring on the hurricane is hard because all you're looking at is

the aftermath. And whether it was a hurricane or a tornado or something else, I would not be in a position to comment.

Q. I'm confused. My question to you, Doctor, was -- is what was the cause of -- if he has a permanent neurological deficit?

A. The cause was his surgical procedure.

Q. And you were telling me that the air went through -- the air escaped through the bronchial wall?

A. Right. Because we know it got up to his eyeballs.

Q. Got into the pleural space?

A. Yes, sir.

Q. And how did -- how does it cause neurological injury?

A. Well, there -- I -- several -- I've just went through the several -- the ways it could do it. It wouldn't have to be air. It could be a particle of tissue because we had a two-hour procedure where we were destroying a fair amount of tissue. And we had a laser that has penetration depth to six millimeters. And we've got blood vessels all over the place in a high risk area that the textbooks say, think twice about lasering in this area because of the risk of vascular penetration.

Q. I thought we -- I thought they said the risk of pulmonary arteries?

A. Well, vascular can be -- it depends on where you're lasering. If you're lasering it at 9:00 o'clock, it would be pulmonary artery. If you're lasering at 3:00 o'clock, it would be pulmonary vein.

Q. Does the pulmonary vein come in contact with the bronchus?

A. Yes, sir.

Q. It does?

A. Well, it's right next to the bronchus. It's right outside the bronchus.

Q. But it does come in contact?

A. Well, you have the -- as we showed in the picture, you've got the -- there are layers of tissue. You have the bronchus and then you have the tissue outside of the bronchus. You have a layer of mediastinal tissue. So these tissues are all wrapped in membranes. Kind of think of them like saran wrap. So in between that pulmonary vein, the net picture shows the pulmonary vein lying right on top of the bronchus. But there would actually be a very thin membrane of -- what we call mediastinal tissue, outside of that. But for all practical purposes, it's within a millimeter of the bronchus.

Q. There would not be nodes between the bronchus -- the wall of the bronchus and the pulmonary vein?

A. No, not -- well, there could be nodes. But ordinarily the nodes should be in a separate location.

Q. Now, if he has -- if Mr. Casey has neurological injury or deficit -- "neurological deficit," your word, where in the -- where in the body is that -- where did that deficit occur?

A. Well, the parts that -- the basal part of the forebrain is -- you're talking about animal models where you're taking out individual clusters of cells. You're down to the micron level. But as far as areas that control emotion, that control memory, the parts of the brain are organized into areas called the hippocampus, which is in the temporal lobe. And that has an influence on your immediate and -- your ability to process information for memory. You have the limbic system, which impacts on your emotional -- your ability to control yourself emotionally. And you have the forebrain, which would impact on your ability to organize and plan the day. And that's just -- again, I'm not a neurologist, so this is just stuff from general recall.

Q. So you would defer to a neurologist?
A. Yes, sir.
Q. Now -- but we are talking about the brain?
A. Yes, sir.
Q. And the mechanism of air escaping from the bronchus to reach the brain would be what?
A. That there's -- we're saying that if the air can travel two feet from the bronchus up to the eyeball, that the chances of some of that air traveling one millimeter from the bronchus to an adjacent blood vessel are pretty good.
Q. What evidence do we have that air reached the -- did you say the cornea?
A. He had subcutaneous air going up -- his eyeballs were swollen. I mean, air got -- air from the tear in the lungs got up -- enough air got out of the lungs, into the pleural space, that Dr. Shantha was worried that if he didn't put a tube down his windpipe that it would choke off his breathing. And then in spite of that, the air continued to go on up the neck and into the face.
Q. But does that mean that it got into the -- into either the arteries or the veins?
A. Oh, it increased the chances. You don't -- you don't even have to have a hole. The arteries and

the veins are not solid sheets. They have pores. These tissues all have pores which allow single blood cells, small particles, small bits of air -- of course, the air isn't supposed to be there. But if it is there -- when you give an injection of an anesthetic in the skin, that anesthetic -- those anesthesia molecules move from the skin into the blood vessel, even though you haven't put the needle in the blood vessel.

Q. Is there any evidence that in Mr. Casey's situation that air got into the arterial structures? Arteries or veins.

A. Just the evidence that he suffered -- it would be the same evidence that someone that's had open heart surgery has a neurocognitive impairment.

Q. But what is the neurological impairment that Mr. Casey has?

A. Mr. Casey has trouble -- just in terms of organizing his day. In terms of giving a coherent story without having to check with his notes. In terms of making decisions about what he's going to do. And in terms of being able to sit still in a chair while I go over a plan of exercise or smoking cessation. And then being able to tell me back what I've said. But from my standpoint, Mr. Casey

could function fine as someone flipping hamburgers under supervision in a restaurant. But as far as independent -- if I was to say, "go organize the kitchen and supervise the kitchen staff," that would be a problem.

Q. But anatomically there is no deficit?

A. Oh, no, anatomic there's a deficit. We just can't measure it with the tools that we have at hand. We could measure these deficits in an animal model.

Q. Wouldn't an air -- these tiny bubbles, wouldn't that be like a stroke?

A. A stroke is all relative. A stroke is generally referred to as a large bubble that takes off a large amount of tissues. Again, to use the example, if I have a big air bubble and it gets into the artery going to my hands, I could lose my entire hand. If it is a small air bubble and it goes into a capillary, then I just lose a pinhead size of tissue on my fingertip.

Q. Explain to me how these tiny bubbles -- if I understand, they're not treatable?

A. Well, if you recognize the problem immediately, you can put someone in a hyperbaric chamber. This is exactly what happens to divers with the bends. They have tiny bubbles that get into their system

if they come up too quickly. And depending on where those bubbles go, they may end up with brain damage. They may end up with knee damage. It just depends on where they end up.

Q. But would you not be able to diagnose through the use of diagnostic studies, would you not be able to diagnose the damage to the brain?

A. Not with the current tools that we have. Nothing -- the folks that have -- divers that have significant memory problems from repeated attacks of the bends have no discernable findings on CT scans. Dialysis patients that have a neuro kind of impairment, again from repeated opportunities for a particular material, air, to get into the brain with repeated dialysis don't have any demonstrable impairment on CT or MRI.

Q. But is the only evidence that Mr. Casey has permanent neurological deficits be his complaints that he has trouble with organization, decision making, restlessness?

A. Again, I'm not a neurologist or a clinical psychologist, but I don't think it's the complaints. I think it's his performance on objective psychometric testing.

Q. Such as conducted by Dr. Waid and Dr. Grace?

A. Yes, sir.
Q. Could there not be other causes for these disorders? These maladies?
A. Yes, sir.
Q. Such as?
A. I would be unaware of any. But it's a little like if you go into Charleston and the place is battered and you think it's a hurricane and someone says, could it be some other cause? Yeah, you could have had a tornado; extraterrestrial object could have hit the town. But the likelihood is that the town has a certain appearance. The likelihood is that it was a hurricane that did it. If a patient has a certain profile on psychometric testing for neurocognitive impairment and he's had abrupt onset of these symptoms after an event such as anesthesia or open heart surgery, the current medical consensus would say that that's the culprit.
Q. Could it be caused, Doctor, by use of medications, prescriptive medications?
A. If there had been a sudden change in the prescriptive medications. So what we're referring to is a sudden definable event and subsequent abrupt deterioration in functioning. If he had had a significant period of IV drug injection like IV

heroine where he's injecting something into his blood vessels, I would -- if I had additional information like that, I would want that to reformulate my opinion of the most likely cause.

Q. Doctor, if Mr. Casey suffered injury during the rigid bronchoscope with lasering, it would have been -- it would have been noticeable at the time; correct?

A. No, sir.

Q. Would it come on gradually.

A. Well, it's there, but you don't find what you're not looking for. The whole point of the article in the Scientific American Journal by the writer that sailed through open heart surgery and thought everything was going fine and then discovered that he couldn't write, it took twice as long and he couldn't organize his articles the way he used to. And unless you're doing fairly specific tests, way past what a neurologist or internist would do ordinarily, you're not going to pick up the deficit.

Q. But you wouldn't expect the deficit to -- if it's coming from tiny bubbles, you would not expect the deficit to worsen over a period of time; correct?

A. No, sir -- wait, if it's a fixed insult, I would

expect it to say the same, and then there might be worsening over time due to other factors.

Q. But actually, wouldn't you expect it to improve?

A. There might be some improvement if -- with strokes and small areas of damage. There's always the hope that doing mental exercises, trying harder. So I mentioned to Mr. Casey that he should take more notes. He should try doing things like crossword puzzles. So there's the potential for improvement.

Q. But the two types of neurological injury are either motor or sensory; correct?

A. No. You can have -- without -- one can be totally paralyzed, like Steven Hocking from ALS. So he really can't move anything and he can't feel much of anything, but his brain is going a mile a minute.

Q. But he does have diagnosable motor -- he has both motor and sensory deficits?

A. Right, but he doesn't have a cognitive deficit. His brain is going a mile a minute. So separate from motor and sensory is the deficit in the processing information, which doesn't require any -- to communicate that process he requires motor skill. But if I ask you to subtract backwards from seven and then add three to each

number and then divide by four, you don't need to feel anything or move anything to do that process. You should be able to do that all in your head.

Q. But in that case there's an anatomical injury; is there not?

A. Not that you can demonstrate on neurologic testing of the brain. You might be able to demonstrate it with the microscope in brain sections and find individual neurons that are damaged.

Q. But has Mr. Casey's condition from, again, pacing, fatigue, organization, has it not worsened since his March, April, May procedure in '04 to today?

A. I don't -- from my standpoint, I don't think his condition's gotten any worse since I initially saw him and today. I think the manifestations may be a little worse. So I think his inattentiveness is about the same. Now, manifestations like his teeth, he's not using dental floss the way he used to use dental floss. I've got to tell him to use his dental floss. But symat -- he may look a little worse, but I would say mentally -- and I haven't done the psychometric testing.

Q. Doctor, are you prepared to say based upon a probability of medical certainty that Mr. Casey is suffering permanent neurological deficit as we

speak?
A. Yes, sir.
Q. And are you saying based upon a probability of medical certainty that that neurological deficit came from air generated from the bronchus during the rigid bronchoscope?
A. I don't want to be that specific. I want to say came from the complications of the bronchoscopy.
Q. And what would be those complications?
A. The damage to the tissue.
Q. A particular tissue?
A. The bronchial tissue. Apparently a huge white chunk of something was vaporized. Damage to -- and knowing that the laser can go six millimeters, damage to the tissue on the other side of the cartilage, which in very high likelihood would include blood vessels. We have the anesthesia that went on for two hours. So the damage could include particulate material. We've got the anesthesia. We have the air bubbles themselves. And we have the whole issues of some transient hema-dynamic instability when his heart rate was going up. And that's usually the first sign of an air embolus is his heart rate went up and his blood pressure went up. They didn't go up by a whole bunch, but

again, -- so there were a lot of things going on, and I'm not in the position to unequivocally state that any one of them was the sole cause.

Q. Doctor, let me hand you -- show you the anesthesia record that accompanied the rigid bronchoscope. And you've seen that before?

A. Yes, sir.

Q. The surgery Dr. Feldman did was stopped at 13:56 or 1:56; is that correct?

A. Yes, sir.

Q. Is that correct?

A. I believe so, sir.

Q. In looking at that, what was the blood pressure when the surgery was stopped?

A. The blood pressure was -- I need my -- but it looks like the top number is 140.

Q. That's slightly above normal?

A. Well, not normal for someone that's under anesthesia, but it's slightly above normal for the awake person.

Q. And the blood pressure does not start to become more elevated until after the surgery is stopped; is that correct?

A. That's correct, sir. So we have two abrupt upticks. There's an abrupt uptick at about 13:15

or so, and then ---

Q. That's when it goes to the 140?

A. Yeah. And then there's abrupt uptick at about 14:30.

Q. And that's after the surgery is stopped?

A. Yes, sir. And to a lesser degree there's a slight uptick in the pulse rate.

Q. And is the pulse rate normal?

A. Yes, sir. Well, again, it's normal for an awake person. I'd say not normal for someone getting anesthesia.

BY MR. THOMPSON:

Object.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. And the comment was made at the conclusion when he was extubated initially that he was awake and responsive?

A. By -- you'd have to show me where that ---

Q. Bottom. Bottom.

A. Yes, sir.

BY MR. KING:

Let's mark this as an exhibit also.

BY COURT REPORTER:

21.

(COURT REPORTER MARKS ONE-PAGE DOCUMENT AS DEFENDANTS'

EXHIBIT NO. 21; ATTACHED TO DEPOSITION).

WITNESS CONTINUES:

A. They've got his pulses here as 126, which is a bit -- a bit fast.

Q. Now, after the surgery was concluded, Mr. Casey developed a pneumothorax; is that correct?

A. Probably not, sir. I mean, the pneumothorax was diagnosed after the surgery, but in my opinion the pneumothorax would have occurred as a result of trauma to the bronchial wall. And that would have occurred either at a time that the laser was being used to vaporize the tissue in the left upper lobe, or the forceps could have contributed to the perforation. And that would have ---

Q. Of the bronchial wall?

A. Right. And if you do enough biopsies, you can claw your way through just about anything. So I would say that the pneumothorax would have occurred at that time, and the uptick in the blood pressure would suggest that the patient was starting to respond to something. Something is going on that led his system to put out just a little bit more epinephrine, leading to the increase in blood pressure and pulse. And that -- typically the first response to air emboli is a mild increase in

the blood pressure and pulse. And then only when it's catastrophic do you see the reverse with low pulse rate and blood pressure.

Q. So the first tick in increase in blood pressure and pulse, are you referring to like -- it looked one -- maybe 13:15?

A. Something like that. I'm not saying that that's when it happened, but that's -- that would be a possibility. It could -- the air -- the actual perforation could have happened with the very first laser pulse.

Q. And why would that not be diagnosable?

A. Because only one droplet of air is getting through. If you poke a pinhole -- if you have -- to use the example of a carbon monoxide leak, since we've got a cold spell today, you can have a carbon monoxide leak going for a long period of time and then all of a sudden you've passed out. But the process has been going on for a long period of time. So that the very first laser pulse would be enough. Having done a fair number of laser procedures myself, I'm very much aware that you cannot tell what's happening on the back side of the laser pulse.

Q. With the amount of subcutaneous air that is going to be diagnosed in Mr. Casey, it's more than a pin

hole.

A. Well, that would represent a progression over a period of time and that would suggest that the hole was getting larger. So if you do a pinhole and then more and more air goes through that pinhole, at some point the pinhole gets larger.

Q. And a pneumothorax is a complication of a bronchoscope?

A. It can be. In this case, it was clearly a complication of the perforation.

Q. This was a relatively small pneumothorax?

A. I wasn't there, and the size of the pneumothorax is not really germane if there's a way for air to leak out. The pneumothorax means that air is in the chest. Now, if air is building up at a certain rate, but air is leaking out at a certain rate, then you can have a pneumothorax that doesn't look that big but still have a significant problem.

Q. This was not a tension pneumothorax?

A. Dr. Nguyenduy indicated that it was a tension pneumothorax. And again, this is relative. There is a clear difference between a pneumothorax. So a pneumothorax is a different entity than a tension pneumothorax. If I am treating tuberculosis in the old days, I can take a syringe and create a tiny

hole in the pleura and inject some air into the pleural space and I've created maybe a cupful of air into the lungs. That hole is fixed. The hole is now closed. So what we have is a cup full of air in the space in between the chest wall and the lungs. That's a pneumothorax. It's air in the lungs. Now a tension pneumothorax, at its very mildest level, occurs when there is continuing leakage of air into that space at a faster rate than what is being absorbed or going out. So if I put a cupful of air into that space, over a period of time the body can absorb that air. It may take a couple days. But if I'm putting more air into that space at a rate faster than what the body can absorb that, then the pressure's going to build up. Initially the pressure may be very mild. It could just be slightly above atmospheric. Now, if the pressure is slightly above atmospheric, that would still be enough for air to go from the pleural space into adjacent pulmonary veins, but it would not be enough to cause a change in the lung function itself. It would not be enough to squeeze on the lungs or to squeeze on the heart. Now, as the pressure continues to build and more air continues to leak in, then we get what I would call

a "full-blown tension pneumothorax" where it's obvious that if something isn't done there's going to a catastrophe. So I would say that it's a gradation. And in medical terminology we use the term "tension pneumothorax" for what is potentially going to be a disaster. But any time air is going into the lung at a faster rate then it's -- any time air is going into the pleural space at a faster rate than it's being removed, the air in the pleural space is under increased tension.

Q. But is a tension pneumothorax an x-ray diagnosis?

A. No, sir.

Q. It's clinically diagnosed?

A. Yes, sir. When one puts a chest tube into a regular -- if it's just a regular pneumothorax, one probably would not put a chest tube in. But if one did, the air would not come gushing out. Because the air's not under increased pressure. If one puts a chest tube into a tension pneumothorax, when one puts that initial chest tube in, there's going to be a good rush of air coming out.

Q. Well, is it your testimony that Dr. Nguyenduy says that it was a tension pneumothorax?

A. Well, his report indicated that there was a rush of air -- a good rush of air that came out when he put

the chest tube in. That would be consistent with a tension pneumothorax.

Q. But you read his deposition?

A. It's been a while. Yes, sir; I read his deposition.

Q. And he does not say there was a tension pneumothorax, does he?

A. I think he's got possible tension pneumothorax in his operative note.

Q. And Dr. Kavanagh who did a follow-up portable chest film also -- on June the 5th also says there's no evidence for tension.

A. Right. I agree with that. But that does not exclude the -- let me put it this way, it would be very hard for the air in the pleural space to go up to the eyeballs if the air in the pleural space was not at higher pressure than the air in the eyeballs, which is at atmospheric pressure. So we have to have had increased pressure in the pleural space. My point is that it was not enough to cause visible findings on the chest film. It was not a catastrophic amount of tension in terms of compromising the heart or the lung function. And it was not catastrophic, because it was recognized. If that tube had not put down his windpipe -- if

the tube had been put in his chest space, he might have died.

Q. But you concluded that Mr. Casey suffers permanent neurological deficit which came about most probably as a result of a rigid bronchoscope?

A. Complications of rigid bronchoscopy; yes, sir.

Q. And one of the complications might be a tiny bubble of air that reaches the brain?

A. That gets into the pulmonary vein, and then ultimately goes to a part of brain. Yes, sir.

Q. But as far as to the role of the tiny bubble, you're not prepared to say that, based upon a probability of medical certainty?

A. I would say that -- I would say that the most likely cause, with a reasonable degree of medical certainty, would have been either -- would have been a tiny particle, which could have been a bubble of air or a particle of tissue.

Q. One of those two?

A. Yes, sir.

Q. But so far as excluding one or the other, you cannot say that, based upon a probability?

A. I can't say which one or the -- I can say based on the medical literature that there are far more -- I can't say. I don't have enough information.

Q. And no diagnostic studies, as we know them today, that are used by neurologists are going to diagnose whether or not there was a tiny bubble to the brain?

A. That's correct, sir.

BY MR. KING:

Let's take a break.

BY VIDEOGRAPHER:

Off the record at 1:46 p.m.

(OFF THE RECORD).

BY VIDEOGRAPHER:

On the record at 2:04 p.m.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Doctor, I asked you earlier today, had Mr. Casey seen a neurologist or a neurosurgeon, and I think you said you thought he may have seen a neurologist?

A. Yes, sir. I don't have any specific recollection.

Q. You don't have any records from a neurologist?

A. I haven't reviewed any.

Q. Doctor, when a patient under general anesthesia wakes up, doesn't blood pressure normally increase?

A. It depends on the -- what's happening.

Q. But normally it does?

A. I would concede that; yes, sir.

Q. Doctor, did you participate with Mr. Thompson and Mr. Turner in creating some demonstrative evidence using a screw and an x-ray?
A. The evidence there really resulted from the patient asking how this happened. And so I took a screw and held it in front of a model in the office and that evolved into -- because there is some risk of radiation. That evolved into Mr. Casey asking -- he just did not understand how this happened.
Q. So the answer is "yes"?
A. Yes. Yes, sir.
Q. Have you spent time in preparing questions for other witnesses in this case?
A. I haven't prepared questions. I've reviewed with -- I've been of assistance to Mr. Casey's attorneys in answering specific points or specific questions.
Q. Well, I'm not asking about answering questions. Have you assisted in preparing questions for witnesses?
A. They have provided me with questions that they had. And then I can think of some cases where I've said that this is not -- this is a very complicated case, very complicated problem. And you can ask questions about a lot of things that really aren't

relevant.

Q. So the answer to that is "yes"?

A. Yes, sir.

Q. Okay. Did you say that this case -- when I asked you about having a similar type case, did I understand you to say this case is one in a million, that there's not another one like it in the world? And you didn't ---

A. Well, I'm unaware of any case where a physician deliberately tried to use a laser to vaporize a substantial object, because this would require a substantial radiopaque, metallic, or porcelain object. Because this would require generating temperatures over a thousand degrees centigrade. The melting point of porcelain, the melting point of metal -- most metals is in the thousand degree range. And the potential for damaging adjacent tissue, if you get that temperature that high, the potential for burning adjacent tissue -- not a flame fire, but the potential for a -- basically a black burn of adjacent tissue is real. So while I was aware of the laser being used to cut through a metal sliver of a stent, I was unaware that this had ever been -- that a laser had ever been used in this fashion. And on review of the literature,

while the laser is occasionally used to remove granulation tissue, in general the recommendation is that it not be used to vaporize any substantial -- particularly metallic piece of -- a metallic object.

Q. And Doctor, you have not been able to find any cases where a water cooled laser resulted in an air embolism, have you?

A. No, I have -- there have been cases where a regular laser perforation resulted in an air embolism.

Q. And those are in the articles we borrowed?

A. Not restricted to those.

Q. There are others?

A. Yes, sir.

Q. And you didn't bring those?

A. I can bring them for you.

Q. But there are articles with air embolism injury from a water cooled laser?

A. Well, the issue has nothing to do with the water cooling. It has to do with the perforation.

Q. I understand. But do you have other articles?

A. Yes, sir. And we'll get those for you.

Q. But you didn't bring those?

A. No, sir.

Q. And can you tell me about how many?

A. I might need to clarify when I say "there are other articles." On a Google search, there are a lot of references that I -- I have references that I have not printed out. But I can print them out for you, sir.

BY MR. KING:

Would you -- Chuck, Noel, would you provide us ---

BY MR. THOMPSON:

Yeah.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. You're still treating Mr. Casey?

A. Yes, sir.

Q. And you're still prescribing medication to him?

A. Yes, sir.

Q. And also Dr. Smith, a psychiatrist, is prescribing medication?

A. Yes, sir.

Q. And Dr. Gonda, his primary care physician?

A. Yes, sir.

Q. Any others that you know of?

A. I'd have to look at the medicine list. What I do know is that when I started out he was on -- I was prescribing some Advair and some pulmonary medicines but we concluded that since his lung function was normal, that there really wasn't any

need for me to continue prescribing the pulmonary medicines.

Q. Who is monitoring his medication intake?

A. Well, I would say each physician is responsible for monitoring what he's prescribing and notifying the other physicians. And as I mentioned, I've mentioned particularly now that Mr. Casey's on Adderall, because he wasn't on Adderall when I saw him initially. And that's another controlled substance. And in general our office, while we may prescribe controlled substances, we try to have one physician prescribe all the controlled substances. So, you know, our next step here would be to notify Dr. Smith, I believe the Greenville psychiatrist, and I will defer prescribing the refills on the Lortab so he can coordinate that with what he's seeing him on the Adderall.

Q. So you would agree that one physician, when there are multiple physicians involved giving various medications, that one should be in control?

A. Well, it requires extra vigilance if you're sharing it. And if Rush Limbaugh can get into trouble with inadvertent duel doctors, it can happen to anybody.

Q. There could be reactions?

A. Well, I think, first of all, it's not very

efficient, because you really need to review all the medicines. So when someone comes in our office, we review all the prescription bottles. We call the pharmacy. If we were prescribing all this stuff ourselves, there would be less of a -- incumbent on us to do that. So it's an extra responsibility. And initially when I was seeing him and he was on Advair and pulmonary medicines, it was not a major issue. But now that he's really not on any pulmonary medicines, it's like it would be more appropriate for a psychiatrist or someone else to prescribe the chronic pain medicines.

Q. Because he's on psychotic medications, anxiety, depression, and also pain medications?

A. I'd have to have the medicine list in front of me. That sounds like a quite -- he's on three or four medications.

BY MR. KING:

Let me see your exhibit list. I want the pages where the criticisms of Dr. Feldman and Dr. Boscia, with the cover letter.

WITNESS CONTINUES:

A. He's on a fair amount of medicine in my opinion. And I don't know ---

BY COURT REPORTER:

Number 17.

BY COURT REPORTER:

The one right there.

BY MR. KING:

No. No, it's not that. It's some ---

BY MR. GUNN:

What are you looking for?

BY MR. KING:

The one where you questioned whether you'd seen it or not with the cover letter. It's his criticisms of the three defendants. We marked it as an exhibit.

BY COURT REPORTER:

This is it.

BY MR. KING:

Do we have another copy of this?

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Doctor, we've marked as Exhibit 18 -- it came with a couple -- primary areas that Dr. Fogarty is expected to testify in his deposition. And if I understand, you had input in preparing these?

A. Yes, sir. I submitted a -- that two-page -- I reviewed the chart and submitted a two-page summary that I showed y'all.

BY MR. GUNN:

Where's the two-page summary? I haven't seen that.

BY MR. TURNER:

It's new today.

BY COURT REPORTER:

I don't know if we marked that.

BY MR. KING:

Yeah, we did. It's two pages.

BY THE WITNESS:

It's not a clean copy, probably. Do you guys have a clean copy?

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Doctor, the first -- and I'm looking at Dr. Boscia, the first criticism as to Dr. Boscia, would you read that, please, sir?

A. Yes, sir. "In failing to obtain a complete history and physical examination of Mr. Casey, to include any history of aspirating a radiopaque/metallic foreign body, onset and details of physical problems and symptoms supporting aspiration of metallic foreign body."

Q. And what is deficient in Dr. Boscia's history and physical?

A. Well, for starters, he dictated the history and physical after he had done the bronchoscopy. And he even so did not have any history of any acute

indication for the bronchoscopy, such as shortness of breath, wheezing. He gave a history of cough, but actually there was no acute cough. He mentioned pain as a reason for the bronchoscopy, but there are no pain receptors in the tracheal bronchial tree. You can have a stent -- a metal stent in the tracheal bronchial tree for a long period of time with no pain. So there was no history obtained by him of any aspiration. Could I have a copy of that thing I prepared. Because I'll be a little more coherent if I skim -- no, no, the ---

BY COURT REPORTER:

17.

BY MR. KING:

17, I'm sorry.

BY MR. TURNER:

Can we get some copies of that?

BY MR. KING:

There's 17 back -- you want that?

BY MR. TURNER:

Yeah. I want to make copies of this here.

WITNESS CONTINUES:

A. I can be a little more coherent. So let's see. It's -- are we still on the record?

Q. Yes, sir.
A. It's very rare for an adult that's conscious to aspirate a foreign body. The overwhelming majority of aspirations occur in infants and older, essentially geriatric subjects. So right off the bat you're talking about less than five -- one out of twenty folks in Mr. Casey's age range would aspirate. He had no history of ever having aspirated anything at work. He had no evidence in his oral pharyngeal exam of any absent crown or problem there. On his physical exam he didn't have any acute respiratory distress. And actually the pain went away with the nitroglycerin. If the metallic foreign body was causing the pain, and we say there are no pain receptors, you might expect the pain to still be there. And then in terms of -- I'm kind of going into the next one, the only -- if Mr. Casey had never had a chest film. If he had just come into the emergency room with a complaint of chest pain, there never would have been a pulmonary consult. So the only reason for all this was this chest film that showed an apparent metallic foreign body projecting over the aortopulmonary window. Now, the aortopulmonary window is a totally separate location from the left

main stem bronchus. And the statement that the foreign body appeared to be in the left main stem bronchus is a clear cut misinterpretation of the chest film. If we pretend -- do you want me to have a pen or something. If we pretend that this is the bronchus (indicating), and this is a foreign body ---

Q. Is the cup the bronchus?

A. Yes. The cup -- this hole. This hole, and this is a foreign body that's in the bronchus. No matter what angle I shoot this from, no matter whether I'm leaning forward or backwards or sideways, this foreign body is always going to stay with the bronchus. Now, if the foreign body's outside the bronchus, in a certain projection it could look like it's overlying the bronchus, for projecting head on. Now, for projecting sideways, it's not going to be overlying the bronchus. So the minute that you get a foreign body that's not overlying the bronchus, it cannot be in the bronchus. So it was a misinterpretation of the chest film. And ---

Q. So help me with this, the chest film, you've reviewed it?

A. Yes, sir.

Q. And where does the chest film show the foreign

body?

BY MR. THOMPSON:

We can pull up the ---

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Is that it?

BY MR. THOMPSON:

I believe it is.

WITNESS ANSWERS:

A. So this is the aorta coming down like this (indicating). The pulmonary vein is right underneath the aortas. And this metallic object, which looks like a screw, is basically just under the aortic knob and above the pulmonary artery, which would put it in a projection over the aortic pulmonary window. Now, the bronchus -- the trachea is coming down like this (indicating). And the left main bronchus is coming out like this (indicating). It's a little hard to see, but it looks like this here is the bifurcation of the left upper and left lower. Well, the bronchus -- so if we're going to look down the windpipe with this bronchoscope in the hopes of seeing this, it's not going to happen, because this -- this screw -- for us to see the bronchus, needs to be sitting over here. And even if it had projected over here, it

could still have been outside the chest. But we can tell -- look at this chest film ahead of time, that there's no way that we're going to see anything looking down the trachea where the left main bronchus -- because this is outside.

Q. I'm confused.

A. Okay. This here is the trachea.

Q. I've got you. Isn't the left side of that x-ray the right side of the anatomy?

A. Right. We can put this -- the way we usually do x-rays is that we put the -- like we're facing the patient.

Q. Okay. So that's like -- the way you've turned it now, you're facing ---

A. This is the left (indicating). No, right now we're behind the patient.

Q. You're behind the patient?

A. Right. We're behind the patient. And this -- if we were bronchoscoping him, then this is the way it would look. But we're saying that -- if we put the bronchoscope down the trachea, you're -- we're not going to be able to see that, because it's not in the trachea. And in terms of the bronchus, this is a bifurcation, or we can't really see the left main bifurcating, but it's happening here. And this is

left upper, left lower.

Q. Help me with this, where is the left upper bronchus?

A. Well, you can't tell for sure, but what -- let me take a step -- what I can say unequivocally, because this is not -- this film is rotated. This is a portable film. What you can say for sure, is you can say that this is the heart. You can say for sure that that is not in the chest, because we know what leads look like. And we know that you'd have to have surgically implanted that. And so without a history -- but if we didn't have this wire here, if we didn't have that little button sitting over here, you know, without our common sense, you know, who's to say that that little button wasn't put in the chest, left there. That's a whole other story. I don't know if you ever saw the curiosity box at Mary Black, where Dr. -- the original Dr. Black had a collection of things that he had found in people. What we can say clearly is that this is the aortic arch, aortic knob. What we see right under the aortic knob that we have this little indentation here and we've got overlapping rib, but we can say that this is pulmonary vascular, pulmonary artery coming in. So this is

the aorta pulmonary window. This is the space in between the aorta and the pulmonary artery.

Q. So the metallic -- I'm sorry.

A. I'm sorry.

Q. The metallic object that is shown on that film is in the pulmonary window?

A. But it projects over the aorta pulmonary window.

Q. And it is not in the bronchus?

A. No. Because the bronchus is sitting over the trachea. The trachea is sitting over here (indicating). And the bronchus does not bifurcate until a couple of inches below the aorta. So that normal bifurcation of the trachea -- that's why I showed those pictures before. In fact, that would help.

Q. Stay with me just a minute.

A. Okay.

Q. Where is the left upper lobe?

A. The left upper lobe on the chest film?

Q. Yes.

A. The left upper lobe would be over here (indicating. But again, in the projection, it's hard to say just where it starts and stops. But it's -- simplistically, it would be projecting here (indicating). Now, the left lower lobe can

actually be there too. But simplistically we'll say that the left upper lobe is here. There's some overlap.

Q. And where is the left bronchus?

A. The left bronchus is very hard to see. But what we can say is that if this is the trachea here, and it is rotated, that this bifurcation -- this is a smidgeon of air here (indicating). And this looks like the bifurcation between the left upper and the left lower lobe.

Q. Is that ---

A. Again, I'm not a radiologist, so I would defer to Dr. Ryan.

Q. If I say "left upper lobe of the bronchus," is that correct anatomically?

A. Left upper lobe bronchus; yes, sir.

Q. Where is that?

A. The left upper lobe bronchus you really can't see. All you can see is that the left main -- that the trachea is coming here (indicating). And this -- you see this little air shadow there (indicating)? It takes some imagination.

Q. Okay. At the aortic knob?

A. No, no. This right here (indicating).

Q. Okay.

A. These are air shadows that may be created by the left upper lobe bronchi, but it takes some imagination to do that. So to recap, the main you could say is that this is the trachea, this is the aorta, and the trachea does not bifurcate until a significant distance below the aorta, which would mean that the left bifurcation would be here (indicating).

Q. So your criticism of Dr. Boscia's H&P was first that it was done after the procedure; secondarily that it did not contain any history of aspiration?

A. Yes, sir.

Q. That was also Dr. Leshman and Dr. Paladuga also did H&Ps, didn't they?

A. Yes, sir.

Q. Do you have the same criticism of theirs?

A. Not a criticism. It's a finding. They weren't making the decision to do a bronchoscopy. Now, they did not find any history of aspirating.

Q. And the fact they didn't include that in their H&P, is that a criticism of them also?

A. No.

Q. Now ---

A. But if you're doing a bronchoscopy for an aspirated foreign body, then it would be appropriate to say

that the patient recalls having inhaled a fork or a pen or choked on this or that. Or that he doesn't recall it. He has no recollection of having aspirated.

Q. Let's -- do you -- have we discussed Number 1?

A. Yes.

Q. Do you want to go to Number 2?

A. Now, what did we say Number 2 -- Number 2, failure -- I've covered failure to interpret the x-ray.

Q. By the discussion that we just had ---

A. Right.

Q. --- that's in the pulmonary window?

A. Right. Right. Again, personally, I'm not a radiologist and although I interpret chest films and CT scans, I know my limitations. And if there's anything unusual, I know to check with a radiologist because he's the final arbiter. That's all he does all day is look at films. And that keeps me from making -- we all make mistakes -- that keeps me from making mistakes. So looking at this film, I've got a gentleman that has absolutely no history to support getting something in his lungs. He's the wrong age. And on top of it, this thing doesn't communicate with any of the large

airways. So to me that's a tip off to talk with the radiologist and review the radiology report.

Q. Paragraph Number 2 in the Exhibit 18 says, "Failure to discuss with radiologist." And my question is, is it the standard of care to discuss radiographic reports with the radiologist?

A. If there's any question about it. Let me put it this way, if your interpretation is correct, nobody's going to say, you should have talked to the radiologist. If your interpretation is incorrect and it's not an emergency and the whole scenario is atypical, that's what the radiologist is there for.

Q. So is that the reasoning for ---

A. Yes, sir.

Q. And "failing to obtain clinical correlation supporting ingestion of a metallic foreign body as recommended by the radiologist." Do you take it that Dr. Ryan is suggesting to the clinicians that additional x-ray -- diagnostic x-rays be taken?

A. Well, I take it that Dr. Ryan is saying, unless this guy has a history of aspirating. Unless he has a history of a surgeon having previously left a screw in his aorta pulmonary window, that we need to get additional x-ray views because this is

probably a mistake. He's saying "artifact," which is a way of saying it's a mistake.

Q. Well, let's go also to 3, because I think we're going to probably -- I think 3 and 2 are going to kind of tie in together.

A. Yes, sir.

Q. If you look at 3, if I understand the criticism, it's a failure to obtain additional views -- x-ray views?

A. Right. The chest -- this chest film was obtained as part of the chest pain protocol. The patient's scared to death of having a heart attack. We've got an hour to get heart attack medicine going. So the minute he hits the door we get the chest film. It's an emergency film. It's a portable film and the main goal is to show that the patient does not have some catastrophe with his heart or his lungs. Now we know it's not an emergency and we have time to repeat the film. And ideally go to the x-ray department and stand up and -- because this film, being a portable film, is taken in a fashion -- that you get different details if you're taking the x-ray from front to back or back to front. So taking a conventional x-ray where the PA -- so the film is sitting here, so that you get the heart and

the structures you're interested in as close to the x-ray. See in this case the bone -- we can see the spine here, but that's because it's sitting next to the x-ray. We'd like the heart sitting next to the x-ray film. And the trachea and these tubes will be a little easier to see if they were sitting next to the x-ray. So a PA projection and then a lateral or a side projection would be very low risk to the patient, just the risk of the radiation, and would resolve the issue of whether this is sitting in the aorta pulmonary window or whether it's an artifact.

Q. Well, didn't the flexible bronchoscope accomplish the same thing as doing additional diagnostic studies?

A. No, sir.

Q. Tell me why not.

A. Well, the bronchoscope procedure did not show a foreign body.

Q. And the CT that is done -- that is done did not show a foreign body; correct?

A. That's correct. Yes, sir.

Q. Still again, when you have the plain film that we see, when it shows a foreign body, is not the standard of care to go look with a bronchoscope?

A. No, sir.
Q. And what is the standard of care?
A. The standard of care would be to say the odds are 999 out of 1,000 that this is a mistake and to get -- and the patient's not in an emergency. He's not choking to death. And we had like three or four -- we had time to get a conventional x-ray.
Q. So your testimony is that additional x-rays should have been obtained ---
A. Before proceeding to a -- non-invasive tests, such as a chest film, which is a lot less costly and a lot less risky, should have been obtained before proceeding to an invasion -- an invasive test such as a bronchoscopy that requires putting the patient into a light sleep.
Q. But a flexible bronchoscopy is a minimally invasive test; is it not, Doctor?
A. Yes, sir.
Q. Have we discussed 3?
A. Yeah, I think that we said that and/or CT scans which would have eliminated the need for subjecting the patient to the bronchoscopy.
Q. And then 4, "Failure to obtain proper informed consent"?
A. Yes, sir. In explaining the need for the

bronchoscopy, it's my understanding from reviewing the records and talking to Mr. Casey, that he was led to believe that there was definitely something in his chest and that that was somehow connected to his chest pain and that he wasn't going to get any better until they took a look to get it out. And a proper informed consent would have said, you know, this could be real, this could be a mistake. We can give you a choice. We can send you down to the x-ray department and get another x-ray or we can put you to sleep, give you these medicines and put this tube down your windpipe, knowing that we're probably not going to see anything, because this spot doesn't connect here anyway. So the alternative -- there was no documentation in the informed consent that -- the alternatives to the bronchoscopy were explained. And there was no documentation and informed consent that it'd be highly unlikely that the bronchoscopy would visualize metallic -- visualize this metallic foreign body.

Q. You reviewed Dr. Boscia's deposition?

A. Yes, sir.

Q. And didn't Dr. Boscia testify that he told Mr. Casey one of the options was to do nothing?

A. I would submit that that is different -- that is saying like, put up with this foreign body in your chest that could kill you. Doing nothing was -- I would submit is not -- particularly in the scary environment of the emergency room, is not an option. What you want to do is -- because that's not resolving the problem. The problem is what's going on. Doing nothing is not resolving the problem.

Q. Did he not also say that he discussed doing other diagnostic studies?

A. To my knowledge, he did not discuss and Mr. -- he did not state that he offered Mr. Casey -- specifically state that he offered Mr. Casey a lateral and VA chest film and Mr. Casey refused.

Q. But putting the language on the consent form that additional diagnostic studies were considered, that's not standard of care; is it, Doctor?

A. Well, first of all, it wasn't -- there was nothing -- that's a pre-printed consent form which is only -- at the time was only available in the endoscopy suite rather than in the emergency room. So that form would have been completed in the endoscopy suite. Hence, standard of care would be that you document specifically that you had

discussed some of the risks and alternatives. And see, there's no mention that we're going in -- there's no mention on that consent -- that's a generic consent form. There's nothing about it that says specifically we're going to look for a foreign body.

Q. So this form would not be in the emergency room?

A. No, sir.

Q. It would only be in the endoscopic suite?

A. Well, they might have gone up to endoscopy and retrieved it, but that form -- it's my understanding from the depositions that that form was signed in endoscopy because it was witnessed by an endoscopy nurse.

Q. Five? Would you comment on 5 for me?

A. Yes. The bronchoscopy -- let's say that we -- by some fluke that there is a foreign body and that we do want to look at it and retrieve it. This is not an emergency. And I've been through this lots and lots of times. I had a kid come in with a tooth that did project and was in a large airway. But if you're going to perform this procedure appropriately, you would let endoscopy know and you'd plan ahead of time with them. And you'd have the staffing. And you would have a large channel

bronchoscope. You'd have the regular channel scope. You'd have a variety of instruments. You would have a metallic -- a instrument that has a magnet on this, since this appears to be metallic. You would have a variety -- there's several brands of forces. A basket for -- there's several little wire mesh basket devices. There is a catheter named by an unrelated Fogarty that you can insert and use to pull this back. There is a camera, in case you find something that you can't pull out that you would have to take -- either to connect to the scope or you would ask for the video scope. So it sounds like that this procedure was unnecessary and doomed to little success for several reasons. One is that there never was a foreign body in the bronchus to see. And secondly, if there had been a foreign body to see, we did not have the equipment on hand and the staff prepared. Because that conscious sedation is wearing off and you've got ten, fifteen minutes and then --then it's time to either get more sedation. So the fact that the bronchoscopy was a three-minute procedure -- the other -- the big thing is, if you're going to retrieve a foreign body with a fiber optic scope successfully, you can't go through the nose. So in

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the cases that I've reported on with -- when I retreated a foreign body, you get a bite block which keeps the patient from biting into the bronchoscope. Because if you put it through his mouth and he bites into the bronchoscopy, then the endoscopy nurses in the hospital are mad at you; you've got a $20,000 bite because that destroys a 10,000 to 20,000 dollar fiberscope. So you'd have a bite block. You put the fiberscope through the bite block into the mouth. Then you go into the trachea so that when you go to pull that foreign body out, you can pull it out en masse behind the fiberscope. Now, if you put it down through the nose, you can't pull it out through the nose. It's going to fall back into the -- into the -- above the -- it runs the risk of falling back into the windpipe. So the fact that we inserted the scope trans nasally, the fact that we didn't have any of this equipment on hand, the fact that there never was any chance of even seeing this foreign body to start with, would make this an unnecessary bronchoscopy, in my opinion. And the fact that we only spent three minutes. Now, we did see an area of erythematis friable mucosa. I went back and looked at some bronchoscopy reports, keeping HIPAA

in mind. There are dozens of bronchoscopy reports out there that mention erythema and friability and there's no foreign body. They're not -- they're not sending those patients off for a rigid bronchoscopy with a laser.

Q. Is this the same thing as granulation tissue?

A. Well, he had question mark granulation tissue. Now, the reason that I think Dr. Boscia had question mark granulation tissue is that if there really was granulation tissue he would have described it. See, erythematis just means red. So if I rub my skin it's going to be red. And if I rub it long enough, it's going to bruise. It's going to be friable. If I cough long enough. If there's granulation tissue, the surface is going to be irregular. There's going to be something projecting from it. And to have a granuloma that is -- I think we said five or six millimeters in diameter. To have something that is that big and not to describe a projection outward, I think is why we had question mark granuloma. And if there had been a projection, then it would be something to take a picture of. There'd be something to biopsy. If there's only friable erythema, when you go to take a picture, there's not really a whole

bunch that's going to show up. So I think the -- let me put it this way, if we had really seen something, since this is an incredibly rare case to start with, most physicians would have said, "wow." They would have stopped a second or two, gotten the camera, taken a picture. Particularly if they felt they couldn't get it out, so that they would have a picture to show the next doctor. If they saw -- now, let's take another scenario. This screw was not in the chest -- not in the bronchi. But we did see something that was red and friable. Well, that could have been -- and it could have been tuberculosis. It could have been cancer. It could have been sarcoid. There are lots of things that can look like granulomas. And it takes about one minute flat to take a biopsy. And the chances of dislodging anything that's embedded there are virtually nil. So again, the fact that we didn't take a biopsy or even brushings. Again, if you're prepared ahead of time, you have topical epinephrine. Make a solution of that and you put that in the area. And a lot of times that will get rid of the erythema. If you have an area that looks red, it could be nothing and you just squirt it with some epinephrine and the redness goes away.

Q. So is 6 alternatives, either washings, biopsies or photographs of the area?
A. Yes, I think we've covered that.
Q. All right, 7?
A. I think there's a chapter in the book that I gave you that highlights what happened here. If you're in a hurry and you make an initial mistake, mistakes can beget mistakes. So having made an initial mistake of misdiagnosing the foreign body as being in the chest, we're now making subsequent mistakes and we're failing to properly interpret the flexible bronchoscopy results as no foreign body. We're saying no foreign body, but it must be hidden somewhere.
Q. So the criticism on 7 is that Dr. Boscia should have interpreted -- in not finding a foreign body, he should have interpreted that there was not one there?
A. That's right.
Q. That the tissue ---
A. Because all the evidence pointed that way. I'm sorry, sir.
Q. That the tissue that he found -- the tissue of concern would not be explained by a foreign body?
A. It would have lots of other explanations. And a

biopsy -- if he had properly interpreted those findings, a biopsy should have been done and photographs taken.

Q. The next one is "Failure to properly interpret CT scan that he ordered." And I'm going to combine that with 9, and "Failure to follow-up/review CT scan report." Now, is one of them talking about the actual scan and one of them talking about the CT scan report?

A. Yes, sir.

Q. Can you elaborate on those for me?

A. Yes, sir. Dr. Paladuga's note -- let's see, I got -- we wrote -- the next day after the patient left the floor, we wrote a note in the chart, Dr. Boscia did, that said the patient would need a rigid bronchoscopy. This implied to Dr. Paladuga, to the rest of the staff, that indeed there was evidence of a metallic foreign body on the CT scan and on the flexible bronchoscopy. So if we had properly interpreted that CT scan, we would have said, I don't see a metallic foreign body. And if we had read the report, we would have said the radiologist doesn't see a metallic foreign body. And I didn't see one on the bronchoscopy. And we wouldn't have written a note in the chart, which

apparently was written after the patient left the floor, that said the patient's going to need a rigid bronchoscopy.

Q. So ---

A. I mean, as the depositions indicated, until the deposition, Dr. Paladuga was under the impression that there was a foreign body on the CT scan.

Q. So your interpretation of Dr. Boscia's op note ---

A. No, not his op note, his note the next day. He wrote a note in the chart the next day which was misleading, at the very least. It was written after the patient left the floor which, of course, makes it very hard to communicate with the patient's doctors, because you usually communicate with them about their care while they're still on the floor. And it makes it very hard to communicate with the patient. And that note did not allow for any communication with the patient, that there's no -- that the radiologist said that this thing is not in the trachea or left main bronchus. He says it's over the aorta. The CT scan is negative. The flexible scan doesn't show anything. See, none of that was communicated to the patient and the tone of the note -- I mean, why would you write a note saying that someone's going

to need a rigid bronchoscopy. So the tone of that note implies just the exact opposite. That these tests were all positive.

Q. Wouldn't the CT -- Dr. Ryan's CT report, would that not have been in the chart?

A. Not necessarily.

Q. And why not?

A. Particularly when patients are in and out of the hospital, it may not -- it may be a day. Let me put it this way, if I saw a note like that in the chart, I would not feel the need to go look up the CT report or to talk with Dr. Ryan.

Q. Well, we would anticipate that by the time Mr. Casey was discharged that the CT report -- Dr. Ryan's report was in the chart?

A. I don't know that it was or was not. For the sake of argument, it was not.

Q. Then the next one is "Failure to follow up/review the CT scan report."

A. That would relate to -- I think we've covered -- the first one is failure to interpret the scan and the second one is the failure to review the scan report. So we really covered both of those.

Q. But Boscia did review the actual CT?

A. Right. But I -- he says he did, but he did not

properly interpret the CT, because again, as I said when you showed me that CT, I can spot obvious things on the CT. Like I could spot a piece of metal that shouldn't be there. But if I'm not spotting a piece of metal, then I should be getting some help from the radiologist. So failure to see that there wasn't any metallic foreign body on the CT scan was a problem. And at that point we should have reviewed the scanned report, or if there wasn't a report we should have called Dr. Ryan and said, I can't see this foreign body. What gives?

Q. But the fact that Dr. Boscia saw, in doing his flexible bronchoscopy, that he saw abnormal tissue, that wasn't -- that was not appropriately put in his report? In his note?

A. That was not appropriate, again to skip to something that we can identify with. If you have a false assumption, you know, there are people in prison based on a false diagnosis. So once you make a false assumption, you can compound that mistake. And the fact is that we didn't see the foreign body. And that does not mean that the area of erythema represents a foreign body. It may be a non-finding. In fact, as we said, out of a hundred bronchoscopy notes, you're going to find a dozen

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that refer to erythema and friability.

Q. Have we discussed 8 and 9?

A. Well, 9, I think we've covered. And that Mr. Casey, I think, had already left the floor when Dr. Boscia wrote the note, and he did not communicate to him either on the floor or subsequently with a phone call that the -- there wasn't any foreign body.

Q. Isn't that part 10?

A. Yeah, ten, I think we've -- we've pretty much covered 10. And I think we've covered 11.

Q. Well, didn't Dr. Boscia testify that he -- following the flexible procedure that he -- that Mr. Casey was still coming out -- coming out from under sedation, that he discussed with Carol, Mr. Casey's sister, that they did not find a foreign body?

A. My understanding -- I'd have to see the exact deposition since it's been a while. But my understanding is that Carol and Mr. Casey were left with the impression that there was still something there that the foreign body was still there and that it needed to come out.

Q. Let me ask you to read page 430 and 431 of Dr. Boscia's deposition.

A. Okay. Want me to start at the top question?
Q. Yeah. You don't have to read it aloud.
A. Oh, okay.
Q. Just read it to yourself. And my question again, isn't Dr. Boscia testifying that he explained to Carol that he found tissue that was of concern, that he did not find a metallic object?
A. Right, he says, "This is what I saw, you know, there's something there."
Q. So again, he did explain that he did not find a foreign object but he had tissue that he felt like needed to be explored?
A. I would take issue with that, because if there was something significant there, he would have biopsied it. And the something there is something that you're going to find on virtually all of the -- not all of it. You're going to find on easily ten percent of everybody's bronchoscopy notes. So the erythema -- the friable erythematis tissue itself is not a significant finding.
Q. And also Dr. Feldman, in -- I believe it was testified to by both Dr. Boscia and Dr. Feldmen, actually visited with Mr. Casey in his room the afternoon following that procedure; correct?
A. Yes, sir.

Q. And discussed the fact that he was going to be doing a rigid bronchoscopy at some subsequent date?
A. Yes, sir.
Q. And that that was to explore what was in the bronchus?
A. Right. But see there wasn't anything in the bronchus. There never could have been anything. Because it was -- the metallic foreign body was never there.
Q. Have we discussed 10 and 11?
A. I believe so.
Q. Do you want to comment about 12?
A. Yes, sir. We partially covered it. If I am scheduling a procedure for my partner, then I have a duty of extra diligence to the partner to provide him all of the proper information. So to schedule the rigid bronchoscopy with YAG laser without a -- some sort of confirmation that the area that was red and friable was not cancer, was not tuberculosis, was not a fungal infection, and I've -- of course, you kind of see what you expect to see. So since I'm not there, I can't comment. But if you tell me -- if I believe that something's there, I'm going to see it. But to prove it, I better take a biopsy. So whether that the

tissue -- this area of erythema and friability was totally smooth or whether it projected outward, you know, I can't comment. All I can say is there wasn't any description and this patient's getting set up to have a laser and destruction of this area. So with the screw sitting here, and we're going to blast the dickens out of something over here, which either could be nothing -- it could be a total mistake, or it could be something serious. We could be spreading TB germs around.

Q. But is there any ---

A. Fungus germs.

Q. Is there anything that Dr. Feldman has testified to that he was not told or was told that would have caused him to alter his decision to proceed with the rigid bronchoscopy?

A. Well, Dr. Feldman is a very intelligent, rational person. And I believe that if he had been told up front, you know, this patient came into the emergency room. We got all excited and we oohed and aahed, but we really didn't look at it carefully. And now that we're looking at it carefully, here's the trachea and here's the spot and I did see something red down here, but the bottom line is, I didn't see this spot down here.

The bottom line is, this spot's not on the CT scan. Dr. Ryan is saying it's probably an artifact. Are you sure we still want to do a rigid bronchoscopy and, you know, charge away at this area down here. And I suspect that if that information had been conveyed to Dr. Feldman he would have said, this is not an emergency. This is not why Mr. Casey came into the emergency room. He came in for chest pain. Dr. Feldman knows that there aren't any chest pain receptors here. There are irritant receptors, but he wasn't coughing. So Dr. Feldman probably would have said, whoa, let's think about this.

Q. First off, Dr. Ryan didn't say, I think it's an artifact. Didn't he say, question artifact ---

A. Yes, sir.

Q. --- versus a foreign body?

A. Yes, sir.

Q. Clinical correlation suggested?

A. Yes, sir.

Q. And so what Dr. Ryan is saying, I don't know whether it's an artifact or foreign body. I'm just the radiologist. I'm lattering (phonetic) the ball back to the clinician?

A. Yes, sir.

Q. Is 13 -- we discussed 13?
A. Thirteen is more a matter of self-reporting. And I think that for me the bigger problem is -- so if you have someone that's submitted for a procedure that you learn could have been done differently, there is a standard that you report this, just so that other folks don't make the same mistake.
Q. Doctor, I'm sorry. I said 13 and I think you're telling me 15.
A. I'm looking at 14.
Q. I asked you about 13.
A. I'm sorry.
Q. Did we discuss 13?
A. Oh, no, 13.
Q. We discussed 13?
A. No. No.
Q. Tell me about 13.
A. Well, I think that note -- see, we have made a mistake. We now have a situation where one error's perpetuating another. Because there was still a final last chance prior to discharge to say we're not going to do this bronchoscopy. We're going to take a breather and rethink things.
Q. And 14?
A. Fourteen is -- in an ideal world -- I'm going to

digress. If there's something wrong with the needle and the syringe and I accidentally stick myself, I kind of have a duty to report that misadventure so that the same thing doesn't happen to other people. So insofar as there was a misadventure here with the bronchoscopy being done because we were -- kind of made a quick diagnosis and were kind of in a -- we made up our mind we were treating the x-ray, that it would have been appropriate to share this information with the physicians in the emergency room, just to kind of keep the same thing from happening again. But I don't feel that -- like I say, that's an ideal -- an ideal world.

Q. Not the standard of care?

A. It's standard of care, but it's perfection.

Q. Is that a deviation below -- beneath the standard of care?

A. If you have a misadventure, you should report it. Yes, sir.

Q. I understand you said you should in a perfect world. But I'm asking you, is that a deviation from the standard of care?

A. It's a deviation.

Q. And 15?

A. Fifteen is that Mr. Casey should have been informed and even after this initial bronchoscopy and even after the rigid bronchoscopy, he was not aware, according to my understanding from the chart, he was not aware, even on discharge from the second admission that there was a never a foreign body on the CT scan. So it would have been appropriate to communicate to the patient that there'd been an error.

BY MR. KING:

I'm told we have a limited amount of time on this tape. So this would be a proper time to take another recess.

BY VIDEOGRAPHER:

This marks the end of tape number two in the deposition of Dr. Charles Fogarty. We're off the record at 3:07 p.m.

(OFF THE RECORD).

BY VIDEOGRAPHER:

This is continuation of the deposition of Dr. Charles Fogarty. This is tape number three. We're on the record at 3:18 p.m.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. Doctor, is there anything about Dr. Boscia's care and treatment that you're critical of that we have

not discussed?

A. Not that I'm aware of at this time, sir.

Q. Let's move to Dr. Feldman.

A. Yes, sir.

Q. You have criticisms of Dr. Feldman also, I believe?

A. Yes, sir.

Q. And the first criticism you have of Dr. Feldman is what, please, sir?

A. I'm reading from this list here?

Q. Sure. Yes, sir.

A. "Failure to properly communicate with Dr. Boscia, who is the physician ordering the bronchoscopy." Particularly if you do not have all the -- if you're handing off a procedure from -- if you're handing off -- signing out a patient from one doctor to another or a procedure for one doctor scheduling for another, it's appropriate to double check with the doctor on basic reasons like why we're doing the procedure? What's the evidence to support the need for the procedure? What are the alternatives for the procedure? What are the results of any findings since we last spoke. And it doesn't sound like Dr. Boscia had communicated fully to Dr. Feldman that there really was not a foreign body documented in the left main bronchus

on either the chest film, CT scan, or bronchoscopy.
Q. If Dr. Feldman understood from Dr. Boscia that Dr. Boscia had not observed a foreign body in doing the flexible and that the CT that he reviewed did not show a foreign body, if Dr. -- if Dr. Boscia did, in fact, communicate that to Dr. Feldman, would that criticism fall away?
A. Well, I don't know that he did is the problem.
Q. I'm asking if he ---
A. If he had?
Q. If he did, would that fall away?
A. Yes, sir. I'll accept that.
Q. And the second criticism?
A. "Failure to review the May 28 and 29 medical records including history, physical, bronchoscopy, portable chest and CT scan results prior to the rigid bronchoscopy procedure."
Q. Now, you've read Dr. Feldman's deposition, have you not?
A. Yes, sir.
Q. And did he not testify that he reviewed Dr. Boscia's H&P before doing the rigid?
A. Yes. The concern I have there is that we were operating on a very tight timeline, since he had not refreshed himself talking to Dr. Boschia. The

H&P, the transcription folks were still typing away on that at 11:25, 11:30. So that really there was a very limited time window. We're talking about 20 minutes to review the history. We don't even know that the history made it to the floor. If they're typing away, it's still got to get typed up and sent up to the floor, printed out on the floor printer, put in the chart. And that's a very tight time window to review the records, talk with the patient, exam them, do all that stuff.

Q. Didn't Dr. Feldman testify that in fact they waited on the H&P before moving forward with the rigid?

A. Again, it's been a while since I've looked at that, but I will accept that, that they waited. Which mean that they had even less time, since they were still typing away at 11:25 or so.

Q. But Dr. Feldman did testify that he reviewed -- before he did the rigid he did review Dr. Boscia. I think he did say that he reviewed Dr. Paladuga. And then corrected, that he was in error saying Paladuga and it would be -- he meant to say Boscia's H&P?

A. Well, I want to put the words properly, because we clearly did not review the portable chest film report and the CT scan report prior to the

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bronchoscopy.

Q. Well, didn't Dr. Paladuga say that he showed Dr. Feldman the portable chest and that he ---

A. No, we're talking about the report.

Q. No, the -- I think the film.

A. I'm talking about the portable chest ---

Q. You're talking about the report.

A. --- report.

Q. Okay. You're not talking about the film. But he ---

A. Right.

Q. --- Dr. Feldman had seen, even before Dr. Boscia's involvement, had seen the portable chest film?

A. Right. The problem, as you know with -- you make a case of mistaken identity in the lineup is that once you've made a mistake, unless you have a system to double check -- if you show me this chest film and I'm convinced that there's a foreign body, then I'm not going to look at it again carefully, because I've already got up my -- my mind made up. So what I need to prevent the perpetuation of that error is a safeguard such as reviewing the report of someone else who is not bringing any biases. And that would be the report of Dr. Ryan on the portable film and Dr. Ryan's CT report. And it

doesn't look like those things were -- it looks like we were kind of blindsided. We didn't have much time to prepare for the -- we've got an office full of patients. We get called. We've got to get over there and get this done. We didn't have a lot of time to review this stuff with Mr. Casey.

Q. And then the fourth one, you said "In failing to obtain and review CT scan and report"?

A. Well, let's look at 3.

Q. I'm sorry.

A. We have a saying if it's not documented it's not done. And while we may have looked at the history and physical or perform one and we may have updated Dr. Boscia's history and physical, if I'm handing a case off to my partner, I may dictate the -- so I may see someone in the office and since I've cut back on procedures, may say to the patient, you need a bronchoscopy. And I may dictate a history and physical on them and go over the case with Dr. Smith. But then when Dr. Smith sees the patient a few days later, he needs to do more than just sign at the bottom. He needs to have some documentation that he's actually reviewed and gotten the same results. That is, there's been no change in the interval, particularly if it's more than a day or

two. There's been no change in his findings and my findings. See and there was a change in that at the time the patient went home, particularly if the chest CT scan results were not in the chart, there was some updating to do to document as part of that history/physical. When I say "history/physical," that's the document, and that includes supporting laboratory data. You don't just stop with the history. You have the blood count and you have the x-ray reports. So it was failure on Dr. Boscia's history and physical, which was dictated after the first bronchoscopy, but before the CT. So somewhere on that history/physical it would have been appropriate to update it by saying the history/physical part hadn't changed, but we got this CT scan that doesn't show a foreign body.

Q. Any other changes other than the negative CT that should have been included on the update?

A. Well, I think that's the main thing. Of course, the patient was not having any -- his chest pain issue had resolved. There was no urgency to the procedure but that's the main thing.

Q. And then are we on 4?

A. Yes, sir. And I think the key thing there is -- and it's a lead up to 5, is failure to advise the

patient that indeed there is no foreign body documented, metallic foreign body documented on the CT scan as being the chest. And particularly -- you could say, well, maybe it's moved around, but particularly if Dr. Boscia was correct and somehow this whole thing is a mistake and somehow it really is sitting down here and somehow it's imbedded, if it's really imbedded under the tissues at 2:30, then it should still be there on the CT scan at 6:00 o'clock. So the fact that the CT scan obtained a few hours later is really just overwhelming evidence that there really was never anything there. Because if there was something there, then it couldn't have just disappeared. And so when -- so leading into 5, when we are getting the informed consent from Mr. Casey and -- I'm aware as a doctor that -- and particularly since we do clinical trials, that the whole informed consent process is very tough. If the patient is on the table, you're in scrubs, and he's geared up to go for this procedure, it's very hard to shift gears and say, you know, maybe we don't need this procedure. Maybe we don't want to do this at all. So we have the informed consent form that says that we're going to do -- get consent to do a rigid

bronchoscopy plus YAG laser to remove this foreign body. If that's the consent we're getting from the patient, clearly we've not communicated to the patient that there isn't any foreign body there on the CT scan and probably an artifact on the portable chest. Because if we communicated that to him, then a rational patient would not have consented. And if the patient's irrational, we've still got the same problem; he's not competent to give a consent. So that in my opinion there was a failure to obtain informed consent. And the main problem is just that there wasn't enough time and we're -- everything's in gear. We're on the launch pad and everything's in gear to do this procedure.

Q. So the informed consent form should have had verbage regarding abnormal tissue?

A. It should have had there wasn't any foreign -- see there wasn't any foreign body to remove. There was no metallic foreign body.

Q. Okay.

A. This whole thing was triggered by -- if there had never been that portable chest film, none of this would have happened. Now, for the sake of argument, if there had been proper communication and Dr. Boscia had said, you know, there isn't any

foreign body on the CT scan, but there is this piece of red area and I was just scared to death to do anything with it. Then it would have been appropriate for Dr. Feldman to perhaps do a totally different procedure. He might have said, well, let's just do a flexible bronchoscope, which won't be as difficult on the patient and let's just go back in the environ of the OR and see what's going on and get a biopsy of that before we go lasering it.

Q. Doctor, is it your conclusion that there was never a metallic object?

A. Yes, sir.

Q. So if the plain film x-ray is either -- shows an artifact or has an erroneous object ---

A. If that -- if that screw was in the chest, the only way it could have been there would have been to have been surgically implanted. Because it's outside of the trachea and it's sitting in between the aorta and the pulmonary artery.

Q. So if I aspirated ---

A. There's no way that could get there.

Q. It wouldn't be there?

A. No way. To take a jump, if this screw had been sitting in the middle of your heart, you'd go back

and say, you know, did you ever get a gunshot wound or someone hit you with a BB 20 years ago, because we've got to explain a piece of metal sitting in your heart. And you go back and get additional history. But you wouldn't go looking for a piece of metal with a fiber optic bronchoscope if the screw had projected in the middle of the heart.

Q. Have we discussed the informed consent?

A. Yes, sir. There's some small points. Really to protect the physician, there should be a time on the informed consent and that's particularly since we talked about clinical research earlier. It's important to document that you actually got that informed consent in a timely but unrushed environment. And so if the time of that consent -- the time that that was signed was 11:30, that would be one thing. But if it was signed at 11:57 as you're being wheeled into the operative suite, one could argue that the patient was under some subtle pressure to sign that.

Q. But Doctor, there's no requirement that the informed consents be done a day before or longer before a procedure's done, is there?

A. Not to my knowledge, sir.

Q. We've discussed informed consent now?

A. Yes, sir.
Q. Now, what's 6, "Time Out"?
A. Well, hospital procedure too -- because mistakes do happen, because surgeons do operate on the wrong whatever, at the start of a procedure, as well as any time a procedure is not going as planned, there should be a preliminary session where everybody says, you know, why are we doing this and what's the plan? And had that been done -- we had a scenario where the anesthesiologist knew that there was no foreign body. But again, maybe because we were under time constraints, it does not sound like there was a planning session and that we got going without the patient or the doctor. And I would submit that some of the staff -- I don't know, I haven't talked with them, but I would submit that the endoscopy staff that is dialing up the wattage probably did not know that there was no metallic foreign body on the CT scan.
Q. But that would not have been a judgment call for the staff to ---
A. Well, it's the entire surgical team. And I have had the experience personally of being stopped. I've had the experience of being in a hurry and saying, trust me, and having an endoscopy nurse

say, you're not going anywhere. You're not doing anything until you get X, Y and Z done. So the surgical team does have the authority to insist that hospital procedures be followed. Now, we're not saying that they should have been done, but we're just saying that it's -- that I would submit that an additional safeguard -- that the "Time Out," if it had been conducted -- the point of the "Time Out" is to get away from, I'm the captain of the ship and do what I say to, we're a team effort and let's all look out for each other. And if the entire team had known that there was no foreign body on the CT scan, then particularly as this procedure went on and on and on, they might have made some comments.

Q. But Doctor, isn't "Time Out" accomplished when we look and we say, okay, this is Mark Casey, he's having a rigid bronchoscope and his physician is Dr. Greg Feldman. Doesn't that comply with "Time Out"?

A. As a patient, that's not the "Time Out" that I experienced. The time I had a corneal transplant, and the "Time Out" that I experienced was a little bit more than that. Do you know why you're having this? Do you know what the alternatives are? Do

you really know what's -- that's at the patient end. And I had already signed the consent.

Q. Have we discussed "Time Out"?

A. Yes, sir.

Q. And the next one is "unnecessary procedure"?

A. Well, the rigid bronchoscopy was performed to remove a foreign body with the assistance of YAG laser from an area where there was no metallic foreign body. Now, that -- and again, as Dr. Mehta says in his chapter on removing foreign bodies, "Bronchoscopies performed for the wrong reason will often lead to complications and mistakes. Mistakes beget mistakes. And the reason for the mistakes is often that we're in a hurry and we don't follow the procedures, like taking a 'Time Out.'" But getting to the ---

Q. Let me stop you just a minute, Doctor.

A. Yes, sir.

Q. Help me again with what the quotes you just read.

A. This is from this reference that we gave you on the ---

Q. Flexible bronch ---

A. Dr. Mehta's chapter on flexible bronchoscopy.

Q. What page are you reading from?

A. That is page 202. And you have this chapter. And

he goes on to say, "The preparation is the key to success. Problems and complications generally arise when one takes shortcuts. Most unsuccessful bronchoscopies occur because the clinician has other commitments and is in a hurry to finish the case. A failed bronchoscopic procedure," and that would be Dr. Boscia's, "increases the risk of the patient having to undergo another procedure. Know your limitations. Adult airway obstruction is very uncommon." I could go on. But this is -- to me these things are all interrelated and unfortunately predictable.

Q. Now, have we discussed 7?

A. Yes. I think that if -- I honestly believe that if Dr. Feldman had really -- let me -- let me start over and just talk personally. There are times when folks tell me things and it doesn't sink in. I'm not listening. I don't get it. And I truly believe that if Dr. Feldman had understood in a way that had sunk in, that there wasn't a foreign body on the CT scan, that the area that Dr. Boscia was worried about was a totally different area then the apparent artifact, that he would have re-thought what he was doing and would either have cancelled the procedure or altered the procedure. But not

having done that, we ended up with an unnecessary procedure.

Q. Have we discussed 8 and 9, or are they separate?

A. Well, I think the problem with -- again, this is mistakes begetting mistakes. If you go in looking for something and you don't see it, and I've done probably 50 bronchoscopies with laser -- flexible bronchoscopy, before turning the baton over to Dr. Feldman, I can tell you that the longer the procedure goes, the more likely it is to go poorly. So the continued use of the scope and instrumentation, particularly when we didn't find what we expected initially because we were expecting to see a metallic foreign body that looked like a screw. A dental crown in general is porcelain. In general those are white. The patient didn't have any history of having lost a crown or having lost any teeth. In fact, he had lost a filling three years ago, but his oral exam was normal at the time of the procedure. So getting in there and not finding what we're expecting, it would have been appropriate at that point to again call -- and I've done this, I've called my partner and says, I'm going to take a -- if there's a cancer or something in the left upper

lobe and I've called him and I've said, "Are you sure we've got the right side? Is it the left upper lobe? Let's just -- I'm not seeing what you're -- told me I was going to see. Let's just double check this." So it sounds like -- again, because the area that Dr. Boscia described with the X sounds a little different than the area that -- they're both in the same area, but the X that Dr. Boscia made is really at the take off of the left upper lobe bronchus. Whereas the are that Dr. Feldman described is more in a subsegment -- in a segment. It sounds like it's a little bit further out. So right off the bat we're not totally seeing what Dr. Boscia described. We don't have the pictures. So I think continuing to use the scope, continuing to do the biopsies, continuing to do the lasers, then set the stage for increased tissue damage and perforation.

Q. But Doctor, the truth is, porcelain restorations -- dental restorations are a fairly recent vintage and older restorations are generally amalgams which are metallic?

A. Crowns -- the crowns -- the patient did not have a missing crown, number one. Number two, the crowns that -- my dentist just went on vacation here,

thanks to me. The crowns that I've had going back ten years have all been porcelain. So unless we're talking about a crown -- this individual is only -- at the time is in his forties.

Q. Restorations are, up until -- as I said, recent years, have been amalgams?

A. What we're saying is we're describing something that's white. So if it's a crown -- if it's a white crown, then the likelihood is that it's porcelain. And that's not what we were expecting to see, looking at that and the description. And again, it should have shown up on the CT scan.

Q. Ten and 11 we have discussed with respect to Dr. Boscia?

A. Let me go a little -- the problem with 9 is that if we honestly thought that there was a crown or a substantial amalgam, that that is a lot different than vaporizing a sliver of metal. So we are into -- it just takes one pulse too many to perforate a hole. And I actually reported on five consecutive cases of laser bronchoscopy that had complications at Pontevidra, a couple of years before Dr. Feldman joined us. So I'm in a position to know about the one pulse too many that causes a complication. So I think attempting to ---

Q. Complication being in the pneumothorax?
A. Pneumothorax, bleeding, stroke, death. Those are all complications that can happen from one pulse too many. So it can -- of course, if you're vaporizing a substantial piece of metal or amalgam, the amount of energy there, you're talking more -- you're talking a couple thousand jewels. I think in his deposition Dr. Feldman -- we don't have the tape and it's not clear, but it would be hard to vaporize. You could get the chemists and the physicists in here and they would tell you that if you were truly vaporizing a crown or an amalgam that that would be impossible without using several thousand jewels. And you've got a melting temperature that's over a thousand degrees. So there's no way that you're not going to damage, burn, adjacent tissue. So I think that's the -- and it's -- and it's -- you get going and you're looking for something and you keep looking and it's not there, so you look harder and you look harder and then you've got more problems.
Q. So a laser would not be used to vaporize a dental restoration?
A. To my knowledge, in removing foreign bodies, the use of the laser would be to fragment something or

to free it up. But if you actually saw something, then you would use the forceps or other instrument to retrieve it. If you could not retrieve it, then you'd say, well maybe this is cartilage that's attached to the cartilage ring and that's when I go yanking on it, it won't come out. You get a -- I've gotten portable chest films in the OR. Of course, the current OR they've -- it's a little bit easier, but if things are not going smoothly, and you want to take that "Time Out" -- stop the procedure, I don't want to say perform a -- you would want to stop the procedure because it's not life or death to start with, and just say, the Lord didn't mean for us to do this procedure today -- to complete this procedure today.

Q. So have we discussed 9?

A. Yes, sir.

Q. Ten and 11, I think that that was the same criticisms that you rendered against Dr. Boscia?

A. Yes, sir. Now particularly with an operative procedure, if the result is that the patient ends up being admitted as a complication of the operative procedure, and I don't -- and this may have been done. I don't know. I just don't have any documentation. I know that when I

bronchoscoped somebody with a flexible scope and then they had a complication, they didn't wake up, they needed intubation, they bled, and they needed admission, that that was an unexpected admission and that was reported to the hospital and there was an explanation of why it happened, how it happened and what we could do to keep it from happening again.

Q. That may have been done here?

A. Yeah, I don't know.

Q. Doctor, the two pages which we've marked as Exhibit 19, did I understand that you generated those?

A. Yes, sir.

Q. And the corrections, additions, changes made did you ---

A. Some of -- I sat down with the -- I think with both -- both of the attorneys. At this ---

Q. Mr. Thompson and Mr. Turner?

A. --- point, I don't remember -- I don't remember who I sat down with when I went over this.

BY MR. TURNER:

Spencer, I'll address that.

BY THE WITNESS:

Yeah.

BY MR. TURNER:

I recognize my writing.

BY THE WITNESS:

Is that your writing? Yeah.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. So these were corrections made by Mr. Turner?

BY MR. TURNER:

Yeah. My understanding was that was elaborated into the much longer sheet you're going through.

BY THE WITNESS:

Yeah.

BY MR. TURNER:

And if we look at it again -- when we referenced it earlier, I did not realize that was the two pages.

DIRECT EXAMINATION RESUMED BY MR. KING:

Q. But the actual original bullets or the original preparation of the report, you generated?

A. Right. Those are points that -- because this goes back a couple years. And frankly I never -- I started out as a fact witness and I never expected that it would progress to this point where I would end up as a expert witness. So when the -- Mr. Turner advised me that that would be useful, I said, let's -- let me look again at the chart and look at with an eye with what I think could have been improved on.

Q. So these are corrections made after review of the chart?
A. The typewritten is what I did.
Q. Right.
A. And then I brought that to Mr. Turner and then as a joint effort we're going over that. Although some of the corrections may have been -- I'd say most of those were done after I left. And then you prepared this sheet here (indicating).
Q. But these corrections were made to conform to the chart?
A. Yes and no, so.
Q. Elaborate then.
A. Yeah. But I'd have to look at the corrections here.

BY MR. TURNER:

Can we go off the record for one minute?

BY MR. KING:

Let him finish.

WITNESS CONTINUES:

A. Well, I don't know if they were made to conform to the chart. "Failure to inform patient of chest CT results, risks and alternatives." That's all stuff that we discussed. This is basically stuff that I generated that we discussed and then -- because I

really don't see -- I'm obviously talking about -- I've got Dr. Feldman. And so you've inserted the word "Feldman" there. Your note -- written note changes the note from "operative" to "informed." I don't think -- this is just semantics. I remember we talked about the oximeter and that we talked about -- I remember talking about the failure to monitor for cerebral hypoxemia, but the reality is that that's not standard of care. And that's getting under Dr. Shantha. So you can -- but that's my -- is that a fair -- really don't want to get too specific, but that's my recollection.

Q. Doctor, did Mr. Casey, during either of the procedures done by Drs. Boscia or Feldman, did he ever suffer a coma?

A. I don't know if he was comatose. He had a period of delirium and confusion, but I don't -- he was heavily sedated, so I don't know that you can -- I don't know that you could answer that. I am not in a position to answer that question.

Q. How about respiratory arrest?

A. No, because he was intubated to prevent a respiratory arrest.

Q. Did he suffer anoxia?

A. No, sir. Anoxia would be total circulatory

collapse. Well, let me take a step back. The hallmark of a pulmonary -- the hallmark of an embolus is for that one little area that the embolus bocks there's lack of oxygen to that particular area. So he did not suffer global anoxia, but he may well have suffered a localized anoxia to a small area of tissue.

BY MR. KING:

I'm going to stop. I may have some questions after Mr. Gunn's examination and after Mr. Thompson and Mr. Turner, if they chose to ask you questions.

EXAMINATION BY MR. GUNN:

Q. Dr. Fogarty, I represent Dr. Shantha in this litigation. Let me ask you, sir, I saw where you made some notes about Dr. Shantha. And I saw that he was not included on the a little bit more formal report that you brought today, the December 20th report. And here's my question to you, sir, are you going to express any opinions under oath regarding deviations from the standard of care by Dr. Shantha as a anesthesiologist in this case?

A. On reflection, the outline from 1 to 7, I feel is overly broad. And given my understanding now of how the operating room -- how things actually happen, I would submit that there are only two

concerns that I have with Dr. Shantha. And they really -- they overlap. And the two concerns are that we did not -- we had knowledge that the CT scan was negative for metallic foreign body and that that was not communicated to the other team. And that -- of course, that overlaps with the "Time Out" concept where everybody says, why are we doing this and is this the right procedure for this patient?

Q. All right, sir. So ---

A. I think the other -- so the "Time Out," for -- Number 1, I would say -- I don't know if there's any documentation that we had that -- what I -- the type of "Time Out" that I've experienced is a patient at the Regional and at other hospitals. And I -- in terms of reporting the extent of the areas of deviations, I don't know that he was aware of all this stuff. So I think that -- 1 and 4 -- in his note, he had that the CT scan was negative for radiopaque foreign body.

Q. All right, sir. Well, let me see if I can try -- what I want to try to do is kind of cut to the chase and I appreciate your answer there. What I'm trying to find out is -- and I know that you've learned some more about the case since you did your

original two-page Exhibit 19?

A. Yes, sir.

Q. I understand that you -- well, let me go back and ask you. The two-page set of notes that you did that are Exhibit 19, I presume you did those somewhere early on compared to where we are now?

A. Yes, sir.

Q. And I assume in fairness to you and to all the parties, you've learned a good bit more about the case since then; have you not, sir?

A. Yes, sir.

Q. Now, having acquired all that information and understanding what you just told me, what I need to know in order to adequately protect the interests of Dr. Shantha is this, and I understand you have concerns. From the standpoint of actual sworn testimony that I can expect on his behalf, and from the standpoint of actual expected sworn testimony, do you anticipate or have you formed any definitive opinions regarding actual deviations from the standard of care by Dr. Shantha, as opposed to any concerns and questions you might have?

A. Yes, sir.

Q. Now, do I understand that -- is that what you just told me, that is that you feel like he deviated

from standard of care by failing to communicate the fact that the CT scan was negative for a foreign body?

A. Yes, sir. Particularly if we are aware -- and I realize that he was not in the operating room the whole time.

Q. Right.

A. But from my initial standpoint, if you're in the operating room for the whole time and you know that there's no foreign body and the surgeon says, I can't find this foreign body, what's this, what's that? Give me the laser. It's not a crown. Maybe it's a filling or something. And so if I'm in the OR and I hear this kind of stuff, of course, I've got initially that I thought I told him there's no foreign body, but if you're there for the duration, you kind of know, even if I did tell him there's no foreign body, it didn't sink in. He doesn't know that there's no foreign body there. And he's continuing to do this two-hour procedure with a laser which in science fiction movies is a potentially lethal weapon. I mean, you can -- so from my standpoint, had Dr. Shantha been there and been aware, then he would have said, you know, we need to stop this procedure. There is no foreign

body. You're going after something that's not there. So the failure to communicate the absence of a foreign body, while I can appreciate how that might have happened, still was another check that might have kept this misadventure from happening.

Q. Well, what I'm trying to find out, and I hear you on all that, is we -- Dr. -- the record shows that Dr. Shantha was not indeed there through the whole procedure; is that correct?

A. That's right, sir.

Q. And there's nothing wrong with that is there, sir?

A. No, sir.

Q. Now, given the fact that he wasn't there, is it still your feeling and your judgment that he had an obligation to go behind the wisdom of the procedure and to point out to Dr. Feldman at some point that, Dr. Feldman, you need to turn back on this procedure or re-evaluate it?

A. Well, let me take a step back. Did Dr. Shantha -- I don't know. Did Dr. Shantha tell the nurse there, the nurse anesthetist, did he make her aware that there is no foreign body? See, I don't know that she knew that or not. But if he's not there, then it's kind of incumbent on whoever he delegates to be there to know there is no foreign body. And

I realize when a nurse goes telling a doctor, you sure you want to do this, that creates a problem. I do have to say that as a doctor I have had nurses tell me, we need to quit.

Q. Sure. Well, I understand a nurse has an obligation to exercise independent judgment skill and to step in to exercise the chain of command. I assume that's what you're talking about?

A. Right.

Q. There's no question but that on Dr. Shantha's handwritten note that was made prior -- well prior to the commencement of the procedure, he noted that there was no foreign body present on CT; did he not?

A. Yes, sir.

Q. And that was on the chart available for anybody to see; was it not, sir?

A. Yes, sir.

Q. So that, indeed, is at least a form of communicating that ---

A. Yes, sir.

Q. --- fact; is it not, sir?

A. Yes, sir.

Q. Now -- and the record indicates to you that Dr. Shantha was not actually present throughout the

procedure, and you're okay with that?

A. Yes, sir.

Q. And nonetheless it's your opinion -- you feel like to a reasonable degree of medical certainty that as an anesthesiologist he departed from the standard of care expected of an anesthesiologist by failing to communicate in some fashion that the procedure ought not go forward?

A. Well, I don't know that he needed to communicate the procedure ought not go forward. I just don't know that while we've got it written in the pre-op notes, I also know that there's no guarantee that the surgeon's going to look at that. I mean, maybe he should. And it's my opinion that Dr. Shantha should have figured out some way to -- because that's a real red flag. If the informed consent says "remove foreign body," and there is no foreign body, it's like, do we have the right patient here? So -- but right now it would be my testimony that Dr. Shantha -- the standard at the hospital is now that not only you tell -- if you're giving an order, you give the order and it's repeated back to you so that you know the message has been received. So what I don't know is did Dr. Shantha give a message that was received. Because there's no

documentation that the message was received. There's no documentation that the nurse anesthetist received the message, that Dr. Feldman received the message, and that the endoscopy team received the message.

Q. All right, sir. Let me -- but you will agree with me that it was conveyed in a timely fashion ---

A. Yes, sir.

Q. --- at least in writing?

A. Yes, sir.

Q. Now, let me ask you, insofar as this entire line about the potential deviation from the standard of care by Dr. Shantha, I note that -- or at least my observation that you have some questions about what is the actual procedure about the way an anesthesiologist would do it; is that a fair statement?

A. Yes, sir.

Q. To make it easier then, would you agree or would you defer, Dr. Fogarty, to a good, well-qualified board-certified South Carolina anesthesiologist from a South Carolina teaching institution on that question?

A. Yes, sir.

Q. If I'm hearing you correctly, in fairness you would

not -- now, I know you're not going to defer to some jack leg that's barely hanging onto his or her license by a thread, but you -- a good, qualified anesthesiologist from a teaching institution, you'd defer to him or her?

A. As far as what the standard of care is ---

Q. Yes, sir.

A. --- for the anesthesiologist communicating the findings; yes, sir.

Q. Yes, sir. Okay.

A. I can't comment as a pulmonologist on the standard of care for an anesthesiologist.

Q. Okay.

A. I mean, that's ---

Q. Well, that may be the short answer to it. I just want to make sure that you feel like a -- that you don't feel qualified as a pulmonologist to really address under oath to a court the standard of care expected of an anesthesiologist?

A. Yes, sir.

Q. All right, sir.

BY MR. GUNN:

I believe that's all I have. Thank you, sir.

BY MR. KING:

Chuck, Noel?

EXAMINATION BY MR. THOMPSON:

Q. Dr. Fogarty, let me follow up on what Mr. Gunn just asked you. Now, as to Dr. Shantha, who I believe the report of the pre -- the pre-surgery workup that he did on Mr. Casey, if I'm not mistaken I believe it is indicated that it looks like it was completed around 11:00 a.m. on 6/3/04.

A. Yes, sir.

Q. One hour prior to the beginning of the surgery. And Dr. Shantha had written down on that page which appears to be in his handwriting that the CT scan was negative for the chest foreign body. And on the same page it has the surgical procedure that was to be done which was removal of the chest foreign body. And my question then may be a little bit broader than Mr. Gunn's is, wouldn't there be a basic standard of care duty that would be applicable to any physician in a similar situation when they are aware of something -- some fact, some finding as such as here by the CT scan that would be totally inconsistent with the removal of a chest foreign body; that when you have two physicians working together for the benefit of a patient, that there is a duty to communicate between those two physicians and that there are some checks and

balances in that regard?

BY MR. GUNN:

Let me object to the form of the question on at least five bases, but I don't want to butt in with the witness. If you are able to answer that, go ahead, sir.

WITNESS ANSWERS:

A. I was thinking of the movie -- there's a movie where there's a line and what we have here is a failure to communicate. My understanding of the question is that there is documentation that Dr. Shantha communicated in writing. But the written note also documents the existence of a discrepancy. The fact that the procedure preceded, raises the question of was the communication received. He's communicated it and it should have been received. And again, I don't know the standard of care for how far an anesthesiologist needs to go, short of a padlock on the operating room.

BY MR. GUNN:

Wait. Wait. We've got -- we've just got a complete volley of activity here that -- why don't we just let all -- let me know when you're ready for the witness to answer. We had total chaos. Go ahead, sir.

BY MR. THOMPSON:

I would ask that the exhibit that I think that's been marked that I've referenced, prepared by Dr. Shantha.

BY THE WITNESS:

Are you talking about this here?

BY MR. THOMPSON:

Yes. That's what I'm looking for. It is missing from my note.

BY MR. KING:

That's not -- that's not -- that's not a marked exhibit. There is one that's ---

BY MR. GUNN:

It's the pre-op -- it's the pre-op -- it's not the anesthesia sheet. It's the pre-op anesthesia evaluation. And I can get my copy. So let's have an authorized flurry of activity and find it.

BY MR. THOMPSON:

All right. I think we have found it. Could I have this marked as an exhibit for Plaintiff. And we'll have this subsequently marked as the next.

BY COURT REPORTER:

So you want to start with 1 Plaintiff? 1 as Plaintiff or do you want to ---

BY MR. THOMPSON:

That would be appropriate, I think.

BY COURT REPORTER:

This one as the first one? Okay.

(COURT REPORTER MARKS ONE-PAGE DOCUMENT AS PLAINTIFF'S EXHIBIT NO. 1; ATTACHED TO DEPOSITION).

BY COURT REPORTER:

This one is marked as 21.

BY MR. THOMPSON:

That's already marked?

BY COURT REPORTER:

Yes.

EXAMINATION RESUMED BY MR. THOMPSON:

Q. Dr. Fogarty, I'm going to show you Plaintiff's Exhibit Number 1. And I removed it from a notebook. Bates stamped page 129. And it has captioned at the top, "Anesthesia Preoperative Evaluation." And as I had communicated in just discussions prior to my asking this question, on Plaintiff's Exhibit 1, there where it has the time and date and the signature, would you agree that's ---

A. Yes, sir.

Q. --- 6/3/04, 11:00 o'clock, Dr. Shantha? And where it has midway -- on Plaintiff's Exhibit Number 1, to the right, it has "CXR," and I believe that

would stand for chest x-ray?
A. Yes, sir.
Q. And it has "metallic FB," metallic foreign body?
A. Yes, sir.
Q. Underneath that in handwriting it has "CT of chest, negative"?
A. Yes, sir.
Q. And then we have Defense Exhibit Number 1, for purposes of this deposition, which is -- it has "Anesthesia Record." And the surgery there, if you will -- I'm reading it as bronchoscopy laser removal foreign body?
A. Yes, sir.
Q. And looking at those two together and knowing that Dr. Shantha and Dr. Feldman are going to be working together, Dr. Feldman as the surgeon, Dr. Shantha as the anesthesiologist in carrying out the proposed surgery, the standard of care, where you have such a inconsistency which appears to be present in these two exhibits, do you not believe that that creates an obligation under the standard of care for there to be a communication from the physician that made this note?
BY MR. GUNN:
Which note?

EXAMINATION RESUMED BY MR. THOMPSON:

Q. Chest x-ray, metallic foreign body, and then a CT scan negative to the surgeon, Dr. Feldman, who is about to do the surgery for the removal of a chest foreign body.

BY MR. GUNN:

Let me object to the form of the question. Go ahead.

WITNESS ANSWERS:

A. I like examples. And to me it's a little like problem: lesion on right hand; plan: remove left hand. So, you know, there certainly is a discrepancy there. And certainly if I was Dr. Feldman, I would have wanted Dr. Shantha to grab me by the collarbone and shake me over the head, do whatever it took, to make sure that I, Charlie Fogarty, really understood that there was no foreign body. Now, whether that's ideal care or standard of care for anesthesiology, I would defer to -- since I'm not an anesthesiologist, to anesthesiology. But I would say that it looks suboptimal and it creates the potential -- it's like the anesthesiologist has recognized the potential for an error. And he's not communicating in a fail safe fashion.

Q. You are aware that Dr. Shantha, and Mr. Gunn will correct me if I'm misstating here, indicated in his deposition that he did not attend a pre-surgical "Time Out" on 6/3/04 as to Mr. Casey ---

BY MR. GUNN:

Object to -- go ahead. Excuse me. I didn't mean to interrupt you.

EXAMINATION RESUMED BY MR. THOMPSON:

Q And I don't believe that he was aware of such.

A. Well, again ---

Q. Isn't it incumbent on the physicians involved in a surgical procedure to see that there is a "Time Out" that's carried out immediately prior to the surgical procedure? I believe it's usually done in the OR, where issues such as this are brought to everyone's attention?

BY MR. GUNN:

Object to the form of the question.

WITNESS ANSWERS:

A. I'll give an equally complicated answer to you. First, my knowledge of what was the standard of care at the time this happened and what the current standard of care is, is incomplete. I am aware that the -- the expectations for standard of care, precisely because of errors like the ones that

occurred here, has gone up. And that at least at the hospital there is a push for fail safe communication where not only is the message given, it is expected that the respondent will repeat back that the message has been received. But again, I'm not an anesthesiologist and I do not know if that standard of care was in place at the time of this unfortunate occurrence.

Q. Doctor, would you agree that that obligation to communicate such an essential fact, such an essential diagnostic finding before this potentially life threatening, invasive surgery involving general anesthesia, that that duty of communication, it would apply to all of the members of the surgical team, all of the healthcare professionals involved?

BY MR. GUNN:

Let me object to the form of the question in that the witness has already testified that he did not -- was not aware of the standard of care of a anesthesiologist.

WITNESS ANSWERS:

A. I believe, I ---

BY MR. GUNN:

For the record.

WITNESS CONTINUES:

A. All I can say is that if the problem says "cancer on right hand" and the plan is to operate on the left hand, and that's on the anesthesiology note, and the consent is to operate on the left hand note, my belief is that the current standard of care would -- but I don't have any proof of it, because I'm not an anesthesiologist. I'm not in the OR. That the current standard of care would require that this discrepancy be communicated in a fail safe fashion to all the members of the team during a "Time Out."

Q. And Dr. Fogarty ---

A. And I do believe that the "Time Out" policy was in place at the time this happened. I don't know of any -- the only thing I know of in the last couple of years is that there's been an increased move to have the staff repeat back to you what you've said. But that really goes with verbal orders. I don't know of any move where they repeat back what you've written.

Q. And would you agree that you don't have to be a board-certified anesthesiologist to recognize that duty of communication under these circumstances, required by the standard of care?

BY MR. GUNN:

Object to the form of the question.

WITNESS ANSWERS:

A. I believe that. I believe there's an obligation.

Q. Now, Dr. Fogarty, in listening to Mr. King, as attorney for Dr. Feldman and Dr. Boscia, ask you questions and listening to your responses, was I correct in understanding that you opine that Dr. Boscia should have consulted -- or should have obtained and reviewed the radiology report from the 5/28 portable x-ray prior to going forward with any invasive procedure? And if he had questions after reviewing that, that he should consult with the radiologist who rendered the report?

BY MR. KING:

Objection to the form of the question.

WITNESS ANSWERS:

A. It's my opinion that to prevent errors, the hospital requires an independent person such as the radiologist to review and interpret radiology films and that in a non-emergency situation if there is any concern at all for anything out of the ordinary or potential for misinterpretation, that either the verbal or written opinion of the radiologist should be obtained. And I think this case kind of

demonstrates the importance of getting that opinion. Because had it been obtained, the outcome might have been different.

Q. And Dr. Fogarty, I would also ask, would the standard of care also have required Dr. Feldman to obtain and review the radiology report from 5/28/04?

A. Yes, sir.

BY MR. THOMPSON:

I want to have this marked as an exhibit and I believe it is the operative note of Dr. Boscia, Bates stamp page 67 from the procedure of 5/28/04.

(COURT REPORTER MARKS ONE-PAGE DOCUMENT AS PLAINTIFF'S EXHIBIT NO. 2; ATTACHED TO DEPOSITION).

EXAMINATION RESUMED BY MR. THOMPSON:

Q. And Dr. Fogarty, in that -- the procedure carried out, the flexible bronchoscopy carried out by Dr. Boschia on Mr. Casey on 5/28/04, did that occur some five days before the procedure carried out on 6/3/04 for removal of a chest foreign body? I'm going to show you Plaintiff's Exhibit Number 2, the operative report of Dr. Boscia as to the first procedure?

A. Yes, sir.

Q. Is that something that the standard of care would

have required Dr. Feldman to have reviewed prior to his procedure?

A. The -- I believe the standard of care would require that the -- in terms of the handoff, that if a written report is available that it would be reviewed in a non-emergency situation. If the written report is not available, that the substance of that report should be communicated. And the reason I believe that is if we look at pathology and the surgeon in breast biopsies, even though the surgeon is told something, he wants to see that in writing before he proceeds with his operative procedure. Something -- if something's available in writing, to reduce the chances of verbal miscommunication, the standard of care that should be reviewed. If it's not available, the substance should be reviewed in a non-emergency situation.

Q. And if you will continue to look at that operative report, Plaintiff's Exhibit Number 2, Dr. Boscia. Can you tell us the transcription time and date on that?

A. The transcription -- time dictated was 2:37 p.m. on May 28th. The time that it was actually typed up was at 21:43. I'm going to embarrass myself in front of these Citadel folks. But that would be

like 9:43 p.m. on June 3rd.

Q. So that operative report, it would not have been ---

A. It was not available in writing.

Q. All right. So it was not available in writing. Do you opine that Dr. Feldman had some obligation to locate and approach Dr. Boscia to learn as much specific information as he could about the 5/28 procedure, in that it would provide him guidance as to any subsequent procedure addressing the same issue as to the foreign body and the removal of a metallic foreign body from Mr. Casey's chest?

A. Yes, sir.

Q. And a failure to do so on that part, would you consider that a breach of the standard of care?

A. Yes, sir.

Q. And did you note on Plaintiff's Exhibit Number 2, and this can be substituted because it has highlighted in yellow exactly what I'm about to ask, Dr. Fogarty. But Dr. Boscia, in his operative note, he has there "no observable foreign body was noted," period. Am I reading that correct?

A. Yes, sir.

Q. Would that be an important fact? Do you think that Dr. Feldman would want to know and should know?

A. Yes, sir.
Q. Now, you addressed informed consent as to the flexible bronch procedure of Dr. Boscia on Mr. Casey, 5/28/04 and also the rigid bronch with YAG laser on 6/3/04. When a YAG laser is being utilized by bronchologists in a flexible -- excuse me, in a rigid bronchoscopy procedure in the main OR where the patient is going to be under general anesthesia, does that create a risk of potential fire?
A. Not ordinarily. If the scope -- the rigid scope is metallic, the risk of fire would be low. However, if one is vaporizing a substantial, and we're talking several milligrams -- a lot more than several milligrams. A substantial metallic object, then one is talking about generating -- first of all, it's never been done in the literature in humans. But in animal models, one is talking about generating a substantial amount of heat with the potential for a local fire, if you will, a local burn of the adjacent tissue.
Q. And a ---
A. You're talking about melting metal. You're talking about the red glow of the porcelain on the shuttle that keeps it from catching on fire as it comes in

from outer space. You're talking about a lot of heat.

Q. And is that also an oxygen-rich environment?

A. Yes. But, again, the anesthesiologist would generally keep the oxygen concentration at 40 percent. But I believe that given the unusual nature of this case and the unusual nature of the foreign body that -- even if the foreign body really was there, and there was going to be a deliberate attempt to vaporize this foreign body, that it would have -- that would have been an unusual occurrence. And the standard of care for explaining risks is -- and there was a nice review on informed consent, which we may want to introduce from the Mayo clinic earlier this year. The current standard of care for informed consent is that one mentions risks that are very rare but potentially lethal. And that one also mention risks that are fairly common. So given the -- if the metallic foreign body really had been there and it really had been vaporized and metal had been melted, the potential for a lethal occurrence, in my opinion, was there. And that risk would fit the criteria for mentioning to the patient.

Q. And the risks created there, would one of those be

spontaneous fire?
A. A local fire in the -- in the -- not like the whole trachea's going to catch on fire. But if you're melting metal, then you have the risk of a local -- the area could immediately just all turn to charcoal.
Q. And before Dr. Boscia engaged in the flexible bronchoscopy on 5/28/04 with the note for removal of a chest foreign body, is it your opinion that he should have completed a PA and lateral x-ray first, ---
A. Yes, sir.
Q. --- to get a confirmation of the presence of the foreign body?
A. Yes, sir.
Q. And a PA and lateral x-ray, that doesn't require an informed consent, does it?
A. No, sir.
Q. Typically the more at risk and potential danger involved in the procedure, that determines whether or not an informed consent is required, doesn't it?
A. Yes, sir.
Q. And when you compare that flexible and lateral x-ray to the -- or excuse me, the PA and lateral x-ray to the flexible bronchoscopy, the flexible

bronch, it requires an informed consent, doesn't it?

A. Yes, sir.

Q. And if a PA and lateral had been done by Dr. Boscia prior to the flexible bronch, based on your review of all of the records, what do you think would have happened?

A. We wouldn't be sitting here today.

Q. Do you think Mr. Casey would have likely been discharged from the emergency room to leave without coming back or any surgery?

A. He still had some ongoing cardiac concerns. But I believe that he would either have been observed for a very brief overnight stay with reference to his heart because there was still some concerns there or discharged with outpatient follow-up aimed at his heart.

BY MR. THOMPSON:

This is a copy of the consult and history and physical conducted by Dr. Boscia as to Mr. Casey on 5/28/04. And if I could, I'd like to get this marked as Plaintiff's exhibit.

BY COURT REPORTER:

Number 3.

(COURT REPORTER MARKS TWO-PAGE DOCUMENT AS PLAINTIFF'S

EXHIBIT NO. 3; ATTACHED TO DEPOSITION).

EXAMINATION RESUMED BY MR. THOMPSON:

Q. Dr. Fogarty, Plaintiff's Exhibit Number 3, which I have just identified, could you take that, please?

A. Yes, sir.

Q. And did I characterize that properly as the consult of Dr. Boscia which includes his H&P, which I believe is indicated as having been carried out on the afternoon of 5/28/04 ---

A. Yes, sir.

Q. --- just before, sometime before the procedure?

A. Yes, sir.

Q. And when I say, "carried out sometime before the procedure" ---

A. Oh, your question is what now?

Q. First, just let me ask you a simple question. Does that appear to be Dr. Boscia's consult and H&P from his consultation ---

A. Yes, sir.

Q. --- with Mr. Casey on 5/28/04?

A. Yes, sir. Dictated at a little after 2:30. Dictated 14:26.

Q. And do you know whether the procedure itself, the flexible bronchoscopy procedure for removal of this metallic body by Dr. Boscia, whether that procedure

had already taken place when this was dictated by him?

A. Yes, sir. It's my understanding both from the time lines, although there may be plus or minus a minute and from Dr. Boscia's deposition, that he did the bronchoscopy and then dictated the history.

Q. Is that problematic to you?

A. Not if there's total disclosure. It would be acceptable in an emergency situation to handwrite a brief note in the chart with the reason for the bronchoscopy, to go ahead and get the informed consent, to then do the bronchoscopy, and then while you're in the area -- this is if you're in a hurry and it's a very tight day. And while you're in the area to dictate the history and physical. But it would be inappropriate to make it sound like you had not yet done the bronchoscopy. So the appropriate thing would have been to have this -- all this one note with two headings and then one would not make it sound like at the time of the history -- at the time that you're dictating this, that you really don't know what the bronchoscopy's going to show. Because at the time you're actually dictating this, you do know what the bronchoscopy's going to show. So transparency might be that I saw

the patient at 2:00 o'clock. At the time I saw him I thought this, this and that. I went ahead and bronchoscoped him. Now that I'm dictating this, here's what I -- here's what I think's going on.

Q. All right. And ---

A. Beause this note could be misconstrued without some detective work.

Q. Look -- continue to look at that, if you will. On the first page of the two-page consult and H&P of Dr. Boscia, do you see some handwriting down on the first page?

A. Yes, sir.

Q. Can you read that?

A. I see something that looks like "LUL," left upper lobe. I'm not sure. There is some handwriting. It's -- it's probably better than mine, but I still am not -- this looks like -- do you know what this is here? LUL -- I see, LUL dash B-U-R ---

Q. Do you want me to attempt to help you?

A. Yes, sir.

Q. Does it look like LUL, then bronchus "FB," question mark?

A. Yes, sir. Yes. Bronchus foreign mark -- foreign body question mark.

Q. And under that "dental"?

A. Dental; yes, sir.
Q. And I take it you're having a hard time reading that handwriting?
A. Yes, sir.
Q. And do you recognize whose handwriting that might be?
A. This is probably Dr. Feldman's handwriting.
Q. And where it's got "LUL bronchus FB," question mark, how do you interpret the meaning of that? With the question mark.
A. Well, it gets back -- it gets back to what the intent of the writing is. If the intent of the writing is to update this history and physical for the chart, then one would write, "history and physical," and we do this a lot when we're on with physician extenders, we would write, "agree with above, no significant change." Or "agree with above," ta da da da has changed. And then we would sign, date and time it. And that would -- if the intent was to provide an updated history and physical, this note with the handwriting, "agree with above," with the addition that the "chest CT that was ordered in the five days in between this H&P and today is negative for foreign body." And then sign and date it would be an -- I think an

acceptable history and physical. So again, it's not clear what the intent of this notation is or when it was written.

Q. When you're attempting to update a history and physical, in essence to use it as your own for purposes of procedure, does the standard of care require that you put the date and the time and also the changes since the earlier history and physical?

A. Yes, sir.

Q. Are there anything such as that indicated on that first page of the two pages?

A. Not that I can see here, sir.

Q. And if we go to the second page of this, it also has handwriting at the bottom. If you could, read that to us.

A. I don't know what -- this looks like "2 cc by 2:00 o'clock"? I don't know what that -- that is. But this here says, "procedure," and I can't read the next word, but it says, "explained," and then this looks like "the risks, sore throat, bleeding, pneumothorax." And "rigid bronchoscopy." And this looks like "agrees," although I'm not -- is that what it's supposed to say?

Q. I'm not sure. Do you recognize that also as Dr. Feldman's handwriting?

A. Yes, sir. The thing that I would say that's unusual is that ordinarily on the consent form, which has the time and the date, is where you would explain the risks and the procedures because it's key to document that you've really done that before the procedure's started. Particularly in research, they're making a big deal over even drawing a tube of blood, unless you've already obtained the consent. So it would be important to have on one sheet of paper the time and the date of the discussion.

Q. And the same document, Plaintiff's Exhibit Number 3, the consult note and history and physical prepared by Dr. Boscia, tell us on the second page when it was transcribed.

A. This was transcribed at 11:00 p.m. on June the 3rd, 2004. So that would mean that this writing would have to have occurred after the procedure was done.

Q. All right. Let me see that. When you say after the procedure was done ---

A. The rigid bronchoscopy.

Q. The transcription time ---

A. Is 9:00 p.m.

Q. --- 6/3/04 at 11:25?

A. Oh, I'm sorry. That's a different -- I'm sorry. I

beg your pardon. I'm -- that's not correct. Thank you very much. This was -- this was -- and I deeply apologize. This was typed up at 11:30 in the morning. Again, I did not go to the Citadel and this military time -- and so this would have been done before the procedure because the procedure was not done until approximately noon. So this could have -- this means that during the half hour before the procedure that this -- that these notations could have been done. It would be ideal if a date and time had been here, but this could have been done before the procedure. And I apologize for that error.

Q. All right. But it has transcribed 6/3/04 at 11:25. That's when it first becomes available to be printed off?

A. Yes, sir. Well, frankly, I'm not sure if that's when they start typing or when they finish typing. That would be a separate -- so anyway, it wouldn't take them more than five minutes. It's a moot point.

Q. Assuming it's when they finished ---

A. It still would have been available at 11:30, well before the procedure started.

Q. And I believe the operative records indicate that

Dr. Feldman, and you correct me if you think I'm wrong, entered the OR suite to begin the procedure at 11:57 a.m., which would have been some 32 minutes after the time typed on this document as to when it was transcribed?

A. Yes, sir.

BY MR. GUNN:

What is that document, Chuck?

BY MR. THOMPSON:

It's Dr. Boscia's -- his consult note and his H&P.

BY MR. GUNN:

Okay.

EXAMINATION RESUMED BY MR. THOMPSON:

Q. Dr. Fogarty, would you expect Dr. Feldman to be able to carry out an adequate history and physical and have a comprehensive and acceptable informed consent discussion with Mr. Casey and also have a properly drafted informed consent form itself completed by Mr. Casey done within this period of some 25 minutes, especially considering that Mr. Casey had never been to his office?

A. Doing a history and physical, I think a reasonable amount of -- and reviewing the records, a reasonable amount of time -- pushing -- particularly for a healthy individual, that could

be done in 15 minutes. The informed consent for the rigid bronchoscopy with the YAG laser, to explain that in lay terms would probably take another five to ten minutes. So -- and to give the appearance of doing this without pressuring the patient, to appear to be in an unhurried fashion where the patient is truly free to decline. So it would be pushing to do that. I would not testify that it would be impossible. I would just say it would be very, very difficult to do that. And I think one evidence -- one bit of evidence that there was difficulty is that it does not appear that Dr. Feldman had time to review the CT scan. And that he did not know -- he did not have time to review the anesthesiology part of the chart. So if I'm doing an interval history, then I'm going to review Dr. Smith's notes, but I'm also going to review everything else that's available to cover what's happened in that interval. And part of that's just to cover myself. If a nurse or somebody has written down something that conflicts with what is in one of my partner's notes, I need to address any discrepancies prior to the procedure. So I think the fact that the anesthesia note was available and does not appear to have been

reviewed and the discrepancies addressed would indicate that we were in a hurry, that we were pushing.

BY MR. THOMPSON:

Have one more marked.

(COURT REPORTER MARKS ONE-PAGE DOCUMENT AS PLAINTIFF'S EXHIBIT NO. 4; ATTACHED TO DEPOSITION).

BY MR. THOMPSON:

Again, gentlemen, I have marked in yellow on this sheet so it can be replaced with a redacted sheet.

EXAMINATION RESUMED BY MR. THOMPSON:

Q. I've got Plaintiff's Exhibit Number 4, and it appears to be a consent form for -- I'm looking at the date at the top, 6/3/04, and I'm looking at the patient, William M. Casey, signed. So I'm handing it to you suggesting that is the informed consent form that Dr. Feldman completed and had -- presented to Mr. Casey to obtain his signature.

A. Yes, sir.

Q. It doesn't have the time, does it?

A. No, sir.

Q. And it doesn't tell who is going to actually do the surgical procedure, does it?

A. No, sir.

Q. And you've already testified to some extent

concerning this. But where you have handwriting on that form, "Description of operation in language of laymen," can you read that and ---

A. It says, "rigid bronchoscopy plus laser, plus removal of foreign body."

Q. Now, it says that that is where you are to put in laymen's terms, such that the patient can understand it, a lay patient. Does that meet the requirement, in your opinion, of explaining in laymen terms what's about to be done as far as the invasive surgical procedure by Dr. Feldman?

BY MR. KING:

Objection to the form of the question.

WITNESS ANSWERS:

A. What this form says to me, as a patient, is the doctor is saying to me, I'm going to do a rigid bronchoscopy and use a laser to remove a foreign body that's in your lungs. And what this form does not document is that for the average layperson, they may or may not know that a rigid bronchoscope is a metal tube about two feet long and that there is some risk of chipping a tooth or having a problem there. As a physician, I still have to remind myself what the acronym "laser" stands for. And the average lay person may not understand that

the laser can be a very safe tool, but it can also be a lethal weapon. And it implies that we're going to remove a foreign body. So it suggests that the patient has not been told that there isn't any foreign body. So it raises the serious questions as to whether there was truly an informed consent. And whether the patient was given the options of not doing any procedure or getting another film or whatever.

Q. Number two on the consent form, where it has "Dr." blank "has explained to me my condition." I'm not going to read the complete paragraph.

A. Yes, sir.

Q. Can you read the handwriting in there identifying the doctor?

A. It says -- it looks to me like Dr. Feldman.

Q. All right. And I note that you seem to be able to read that without apparent difficulty. Have you read and been exposed to Dr. Feldman's handwriting frequently in the past?

A. We need to be careful in talking about handwriting. What goes around comes around. And -- but I think this is legible to me. It's -- particularly if Dr. Feldman had explained this procedure to Mr. Casey on a previous day, that it's not documented, not

done, particularly with our research experience, it would have been a simple matter to have a line in here on such and such a date spent 30 minutes going over the procedure with the patient. Because once it's after the fact, then it's self-serving. You're kind of stuck. So I think that the thing that's lacking here are some additional statements to document what was done and when.

Q. And look for ---

A. And it implies that Dr. Feldman is unaware that there's no foreign body. Because if Dr. Feldman knew that there was a foreign body, he's a very sophisticated physician, I doubt that he would have proceeded along the lines that he did.

Q. And with your total knowledge of the case, do you find that this informed consent form is adequate or defective as required by the standard of care?

A. That form, as it stands, would not meet the current standard of care.

BY MR. THOMPSON:

Thank you. I think that's all.

RE-DIRECT EXAMINATION BY MR. KING:

Q. Doctor, have you read Mr. Casey's deposition?

A. I've not read Mr. Casey's deposition.

Q. And how about his sister, Carol Hyslop, have you

read her deposition?
A. No, sir.
Q. Have you ever been employed as an expert witness in another matter before?
A. Yes, sir. I haven't been employed. I've been -- I've been an expert witness.
Q. How many times?
A. Approximately a dozen times.
Q. And what fields have you been qualified as an expert witness in?
A. Matters relating to pulmonary problems. Some specific cases would be causation and etiology of respiratory problems following an accident with a permanently paralyzed diaphragm. Problems following inhalation of mold. Problems with exposure to poisonous gases in a fumigation plant. While I've been a fact witness in other medical malpractice cases, this is the first malpractice case, to my knowledge, that I've been an expert witness.
Q. So insofar as opining as to breach of the standard of care by a physician, you have never done that previously?
A. No, sir.
Q. How much time did you spend on this case, so far as

the litigation? I'm not asking about Mr. Casey's care and treatment as a patient. I'm asking about how much time have you spent as an expert witness?

A. I've spent a lot more than I planned on. When I initially saw Mr. Casey, I was -- my intellectually -- my curiosity went up, since I'd seen several patients and I did a literature review. And I became aware that I might be called on as a fact witness. And it was only in the last -- oh, I guess year or so, I'd have to look, that I was requested to become an expert witness. And I've ended up -- frankly, I never thought it would get this far. I thought things would be settled. But I have probably spent the equivalent of several weekends -- we're talking over a three-year period. Maybe a couple -- and generally been weekend time, but maybe a couple hours here and there. I would say between 40 and -- these depositions, the ones I read, that was a weekend. I'd say -- I didn't keep track of the time. But I would say probably 40 hours.

Q. And how are you billing for this time?

A. I'm not billing. In general, on all of the depositions I've done, as far as actual deposition, I've not submitted any bills. I do have some

aggressive billing clerks at the Lung and Chest office. And they have -- and I wouldn't known which ones, but they have submitted bills for written reports for independent medical evaluations, which would be a little different. I mean, the first step's an IME and that would be a little bit different than a deposition.

Q. But you have not billed and do not intend to bill for your expert time in this case?

A. No, sir.

Q. Doctor, this Exhibit 19, which you prepared and we've talked about this.

A. Yes, sir.

Q. Was that prepared after this lawsuit was commenced or before?

A. That was prepared after the suit was commenced, sir.

Q. There was an article that appeared in the Spartanburg Herald Journal within days after this lawsuit. The article is dated May 31st, 2006. And it's by staff writer, Rachel Leonard. Have you seen that article?

A. I don't recall this. That's got a -- I probably did see this, because it's got a -- the "botched" word is kind of inflammatory. Yes, sir; I believe

that I saw this.

Q. Did you discuss this -- the contents of this article with Ms. Leonard before it was published?

A. Before it was -- no, I don't even know who Ms. Leonard is.

Q. You've never -- you did not -- to your knowledge, you did not meet with Ms. Leonard ---

A. No.

Q. --- in preparation ---

A. I have no idea.

BY MR. KING:

I believe that's it.

BY MR. GUNN:

It's 5:10 civilian time now. I have some more questions, given the state of the testimony.

EXAMINATION BY MR. GUNN:

Q. Dr. Fogarty, I've got a -- and I may be mistaken, but I gathered from your testimony earlier when you were testifying about your background and what you did these days in practice, do you still do procedures that require patients to undergo general anesthesia?

A. Not generally. I do do bronchoscopies with conscious sedation. I'm hitting 65. I've had a corneal transplant. I'm looking -- there are guys

out there that have got more energy, better eyesight. I'm looking -- I mean, in a pinch I feel very comfortable doing them. But, you know, why not pass it on to someone that's got a little more energy and use.

Q. I'm hitting 65 too, so if I quite handling lawsuits, you tell me. And I'm just having a little fun with you there. Let me -- but I am ---

A. Well, I'll go to law school and you go to medical school.

Q. Let me ask you, when did you -- the conscious sedation procedures that you use -- or that you do, you don't utilize the services of an anesthesiologist there, do you?

A. No, sir.

Q. When did you cease doing -- routinely doing procedures that require the use of an anesthesiologist?

A. I really haven't done procedures requiring an anesthesiologist. I mean, that would have been very rare by special arrangement where I really -- in the OR, probably with somebody else, like a -- for a while there was a push by pulmonologists to do thorcoscopic procedures. And, you know, you go to a course, you get back and you do it under

supervision and you decide that you really don't want to do it. So I have not done -- the only time that I would have been in the OR would have been if anesthesia called me to assist with a difficult intubation. And there have been times when, even though they've got expertise, I know the patient or something like that, and you assist, usually with a fiber optic scope and a difficult intubation.

Q. Well, the state of your relationship with the anesthesiologist that you just described to me, has that been throughout the course of your career here at Spartanburg Regional?

A. Yes, sir. My main time with the anesthesiologist is discussing cases before the case or after or in the physicians lounge when we're both on call for the night or whatever.

Q. Well, let me see if I can sort of fairly capsule what you just told me about your relationship in the operating room or in procedures with an anesthesiologist. As I understand it, over the years, since you've been on staff at -- in all the years that you've been on staff at Spartanburg Regional, your interplay with anesthesiologists has been that: one, sometimes you are called -- have been called by anesthesiologists to assist ---

A. Let me take a step back, sir.
Q. Yeah.
A. Prior to Dr. Feldman's joining our practice in, I think, 1992, ---
Q. Yeah.
A. --- I did a fair amount of laser bronchoscopy. And even though it was with the large channel fiber scope, a fair number of these were done in the operating room. Some of these were done with the anesthesiologist placing a relatively fire resistant tracheal tube with a double lumen catheter. So that prior to 1992, I would have been in the OR with anesthesia, still not -- maybe 25 times in my lifetime. Not that much.
Q. Okay. That's fair enough. Let's talk about just since 1992 then.
A. Then the answer would be very rarely.
Q. Since 1992, your interaction with anesthesiologists has been, number one: when an anesthesiologist called you to come to the OR for a difficult intubation. That's happened from time to time. Number two: to discuss either prior to or subsequent to a procedure some medical situation with an anesthesiologist; is that correct?
A. That's correct, sir. And in the last -- since I

developed my corneal problems, and to explain to the court here, if you will, my current vision is analogous to someone that most of the time is totally sober but now and then has a drink. So there are times when I appreciate that all of my vision is 20/40 and I'm okay to drive, but it's not what it should be. And because that is intermittent and unpredictable, I have elected to just take myself out of a scenario where I might not have a choice of saying, I don't want to do this. So my contact in the OR and critical care for, I would say, the last five years has been minimal. Just true emergencies.

Q. Where did you have your corneal transplant, by the way?

A. I had it in Charleston.

Q. The "Time Out" that you told us about, was the "Time Out" conducted by the nursing staff there?

A. It was actually conducted by the anesthesiologist. I've had other procedures in Spartanburg with anesthesia, and I should shut up, but the anesthesiologists started out with asking me if I had any objection if we had a word of prayer. That got my attention.

Q. At Spartanburg Regional?

A. No, at Charleston.
Q. Was it Charlie Wallace?
A. I don't know who it was, but he got my attention. And it was generic. It was not anything offensive about it. But it got my attention that this guy was serious about what he was doing. Anyway ---
Q. Well, you're not critical of Dr. Shantha because there was no word of prayer here?
A. For all I know, maybe there was.
BY MR. GUNN:
You might want to go ahead and change the tape.
BY VIDEOGRAPHER:
This marks the end of tape number three in the deposition of Dr. Charles Fogarty. Off the record at 5:19 p.m.
(OFF THE RECORD).
BY VIDEOGRAPHER:
This is the continuation of the deposition of Dr. Charles Fogarty. It's tape number four. On the record at 5:22 p.m.
EXAMINATION RESUMED BY MR. GUNN:
Q. Let me ask you a question or two about some questions that were asked early on today about any neurological impairment you feel that Mr. Casey may have as a result of the June 3rd, 2004 procedure.

If I'm hearing you correctly, Dr. Fogarty, that although you feel like it's more probable than not that Mr. Casey did suffer some degree of neurological impairment as a result of that procedure, you can't point to any changes -- any anatomical changes that are supportive of that; would that be a fair statement?

A. The anatomic changes would be too small to detect. If we wanted to biopsy his brain, we could find areas in the forebrain. The act of proving it would be destructive itself.

Q. And I'm not sure the rules of court would permit us to do that, so I guess we'll have to waive that. We won't request it. So if there are any anatomic changes, they are so microscopic that we couldn't detect them at this point?

A. That's correct, sir.

Q. And if I'm hearing you correctly, there are no -- there's no CT scan, MRI, plain film, or EEG evidence which supports such a neurological impairment either?

A. That's correct. Although neurocognitive impairment affects probably 20, 30 percent of the patients having procedures like open heart surgery. It is very difficult to detect with current technology,

before the fact. After the fact, you can test for it and establish that it's happened. But you cannot ahead of time predict who it's going to happen to. And you have some overlap, you can say that the longer the procedure, the older the patient, the more intervention you do with the vascular system, the dialysis, open heart surgery, the more likely that you're going to have a neurocognitive impairment.

Q. And if I heard you correctly and understood you correctly, the standard methodology for trying to find out whether there's that neurocognitive -- or neurological impairment is to rely upon psychological testing of some type?

A. Yes, sir.

Q. And in this instance you have simply reviewed in summary the data of that kind that's been provided on the plaintiff and seem to agree with it?

A. Yes, sir.

Q. At least in your area of expertise, don't find anything inconsistent with it?

A. Yes, sir.

Q. Now, let me make sure that I, as a lawyer, understand what you will say in so far as what you believe to be the mechanism of injury, if I can.

A. Well, I don't know that medical science has established the exact mechanism in all cases.
Q. All right. Well, let me see if I can understand what you said your best information is on that earlier today. You feel like what happened physically to -- more probably than not to Mr. Casey on June 3rd, 2004 is one or more of the following things: either a tiny bubble theory, that a tiny bubble -- one or more tiny bubbles migrated to his brain and left a tiny, tiny lesion. I think you characterized it as a black spec perhaps, and you were using the analogy of the fingertip there. But what I would -- what I would call in shorthand sort of a tiny bubble theory; is that one of them?
A. Yes, sir. The correct term would be small, microscopic air emboli.
Q. Gotcha.
A. Small enough to block the blood flow in a capillary, but not big enough to block the blood flow in an artery.
Q. That's one potential mechanism for Mr. Casey's injury, that ---
A. Yes, sir.
Q. --- you feel like could be a possibility or a probability? Okay. Number two, would be during

the actual procedure itself, some damage to an adjacent or nearby body structure?

A. A blood vessel.

Q. A blood vessel? Okay.

A. Could have allowed the same size embolus. But instead of being an air bubble, it would be a particle. A little fleck of cartilage or a little fleck of blood cells or dead tissue.

Q. There's no -- there's no -- not -- I don't suggest that there should be or ought to be, or has to be, but there's no detectible physical evidence of that phenomenon, is there?

A. There's no way in humans to monitor that at the time -- currently that it's happening. You can demonstrate this in animal models but not in people.

Q. The third possibility or probability is that simply by undergoing the anesthesia for a period of time that it just relates to just the anesthesia, like an open-heart patient?

A. Yes, sir.

Q. What are the other possibilities now, besides those three?

A. Again, I'm not an expert in psychology, but to my knowledge, those would be the main ones. There are

theories around. There are certainly inflammatory byproducts, things called cytokines, inflammatory mediators that may get into the system and stir up inflammation.

Q. Right. Well, there's no evidence of that here. That's kind of remote, isn't it?

A. Where we stand with neurocognitive impairment is that we -- to use the Charleston example, we know that the town is tore up, but we really do not have the tools to establish whether it was a tornado or a hurricane. All we know is that the buildings are tore up.

Q. I looked back and I made a note or two and I noted that you said that you felt like the impairment ---

A. To be fair in that example, it would not be the whole town of Charleston. It would be just like one little -- couple of houses, to be consistent with our example for a neurocognitive impairment.

Q. Between Trade and Broad.

A. Somebody else's house.

Q. Now, the note I made was that the potential phenomena that could cause the neurocognitive impairment would be the piece of tissue, the damage to adjoining structures, the anesthesia, just the -- I'll call that the open heart similarity ---

A. Yeah.
Q. --- the air -- microscopic air emboli ---
A. Well, the anesthesia is really non-open heart. So folks that have shoulder surgery. Just anybody that has longer surgery. Now, if you're going to blame something strictly on anesthesia, most of that happens in the geriatric population. It happens in the 40, 50, but the vast majority, where you don't have anything except anesthesia, is a Medicare -- I hate to say it, someone my age and older. The open heart is the tiny air bubbles, which can still get in, versus the particular material which can get in and how much of what. And the thought was that there'd be less of it if they didn't do it on pump. And depending on the surgeon, you know, there may be less of it, if you don't go on bypass. But it's still there.
Q. And I think another thing you mentioned potentially was the transient changes in hemodynamics?
A. Yes, sir.
Q. In fairness, would any transient change in hemodynamics you would expect some sort of evidence to be left, would you not? Other than just the impairment itself?
A. The problem is that the anesthesiologist currently

does not have a way to -- we're measuring things at very -- we're measuring what's going on at the trunk of the tree, and then a month later we're being asked what went on in that fifth branch limb. But we don't have a way to measure that right now.

Q. Okay. And you said that's not a deviation from standard of care?

A. No, sir.

Q. All right. And you're unable, as I understand it, Dr. Fogarty, to say which of those potential methods or injury or any combination of them took place here?

A. Yes, sir. I would say statistically the air bubbles is the most likely. But any one of them in any given individual could account for the problem.

Q. And the air bubble theory that you advance would be referred to in the literature that you gave Mr. King earlier today?

A. Yes, sir. But I mentioned -- the reason I mentioned the air bubbles is simply he had such a massive volume of air to get out. And we know that there was a tension pneumothorax from Dr. Nguyenduy. And we know that this air was under higher pressure than the pressure in the veins. And we know that even if you don't actually poke a hole, that there

are pores in these blood vessels, and we know that it's possible for air to get in.

Q. All of these potential mechanisms, potential sources for mechanism of injury, any one of those can, of itself occur even in the exercise of good medicine, can they not?

A. Yes, sir.

Q. Your whole theory here, as I understand it, is the fact that you feel like it was an unnecessary procedure? With all those ---

A. Yes, sir. If ---

Q. --- sub-criticisms talked about.

A. If the procedure is inappropriate and the risks have been explained, then, you know, the patient would have been prepared to -- would have given a proper, informed consent and been prepared to accept those risks.

Q. The technical manner in which the procedure was performed you're not critical of?

A. I'm not sure what you mean by that, sir.

Q. I'm talking about the way the hands were manipulated by the people performing the procedure and that nature, just that it -- it was not proper informed consent and it was an unnecessary procedure?

A. I'm not in a position to critique the way the patient's arms were held on the table, if that's what you mean.
Q. Right. Sure.
A. Now, as far as the actual use of the laser and the forceps and --those things may have played a role. So that would be a different story.
Q. Let me understand then, with regard to understanding, you said that you're not familiar with the standard of care expected of an anesthesiologist. Let me make sure -- your observation that you make about Dr. Shantha is that he failed to communicate to the remainder of the surgical team, primarily Dr. Feldmen on June 3rd, that the CT scan in fact was negative when -- for a foreign body when the chest film had been suggestive of one; is that correct?
A. No. No. The CT, which is the gold standard, showed there was no foreign body.
Q. Correct.
A. And yet we're doing a rigid bronchoscopy to remove a foreign body.
Q. Okay, all right. Let me make sure I understand the scenario as it was on Mr. Casey's medical chart when this procedure commenced on June the 3rd. We

know that -- we know that the CT -- the written CT scan report was on the chart, was it not?

A. I really don't know what was on the chart and what was not.

Q. Well, it had been transcribed and was available as of the time the patient was discharged back still in May, wasn't it?

A. Yes, sir. But I don't know that -- again, I do not know what was on the chart and what was not.

Q. Well, would it be available on the computer?

A. Yes, sir. Well, I don't know what the computer status was at that time. But it would have been available, certainly with a phone call.

Q. The notes of the Dr. Boscia, the op note or consultation note from the 5/31 procedure additionally would have been available if not on the chart, by way of a phone call?

A. Yes, sir. That was -- but that was not in the chart at the time that Dr. Shantha -- he wrote his note at 11:00, I think.

Q. Correct.

A. And Dr. Boscia's note was not typed up until 11:25, 11:30. So Dr. Shantha would not have had access to Dr. Boscia's consult note.

Q. No, sir. I think I misled you there. I'm talking

about at the time the procedure commenced at noon.
A. Yes, sir. At noon -- yeah, at noon, Dr. Boscia's H&P would have been available to be in the chart.
Q. The discharge summary from the prior hospitalization would have been on the -- would have been available, would it not have?
A. It should have been. Again, I don't know if it was or not.
Q. Which would have shown no negative foreign body?
A. Yes, sir. Well, the problem is that Dr. Paladuga didn't dictate that in the discharge summary, because he had the misleading note. And Dr. Paladuga didn't know that there was no foreign body.
Q. Well, in ---
(Dr. Fogarty receives phone call).
BY WITNESS: (ON PHONE)
I'm still deposing.
EXAMINATION RESUMED BY MR. GUNN:
Q. In any event, I think we can agree, can we not, Dr. Fogarty, that at the time the procedure of June 3rd, 2004 commenced there was significant valid -- or significant, at least, information on Mr. Casey's chart and available -- even more information probably available that the CT scan had

been negative for a foreign body. Is that not correct, sir?

A. I'm not really sure. I mean, the scary thought that occurred to me that maybe there wasn't anything in the chart. And because Dr. Shantha's a very diligent anesthesiologist, he'd called to get those records. And that he knew the results of those records because he had called the x-ray department. It's -- I mean, I don't know, it's possible that the only indication in the chart that the CT was negative was Dr. Shanta's note.

Q. Well, wasn't the CT -- the written CT scan report available?

A. It was available, but I don't know that it was in the chart. Let me take a step back. I don't know. Do we have the time that was typed up. It's a little tougher with radiology stuff. But I don't know that that was in the chart at the time the procedure commenced.

Q. Well, let me ask you, and I don't want to ---

A. It was typed up. Okay.

Q. I'm not going to go back ---

A. Okay. Well, I'll concede that it should have been available.

Q. Okay. I mean, there was a good -- there was a good

body ---
A. Yes, sir.
Q. At the time this procedure started on June the 3rd, 2004, there was in addition to Dr. Shantha's note that the CT scan was negative for a foreign body? In addition to that, there was a significant body of data available showing that same thing on the chart or available by telephone. Is that -- would you agree?
A. I believe that's a fair statement.
Q. Good enough. And did you -- and you said you read Dr. Feldman's deposition?
A. Yes, sir.
Q. From reading that deposition ---
A. I mean, we need to be -- it's been a while. I read it awhile back, and then I skimmed it briefly last night, so you have to refresh me.
Q. In reading Dr. Feldman's deposition, did it appear clear to you that utilizing his judgment as a critical care and chest position, that regardless of what the CT scan had shown, he felt like the patient needed this procedure?
A. He may have felt that way. I'll take his word for it that he felt that way.
Q. But, I mean, that's the state of the record in this

case. He so indicated it, didn't he? And I realized you differ sharply with that. Even I've figured that out.

A. Well, no, what I'm saying there are times when I feel very strongly about something.

Q. Right.

A. And a word from somebody -- I mean, I kind of believe in angels, so a word from somebody to me kind of changes the way I feel about things.

Q. Sure. I understand that.

A. And so I'm just raising the possibility that if somebody had put a buzz in Dr. Feldman's ear that the way he felt about it might have changed. But that didn't happen.

Q. I understand that is your reasoning or that is your qualification, but let me see if I can get you -- let me see if I can get you ---

A. Who can get me?

Q. --- to answer a question. Dr. Fogarty, understanding all that, nonetheless, after you've read Dr. Feldman's deposition, he testified that it was his feeling that this procedure should go forward, irrespective of the negative CT scan?

A. Yes, sir.

Q. Now, in fairness, I understand your qualification

of that. So the state of the affairs at the time this procedure started on June the 3rd, 2004 that -- was that there was a significant body of written data either on the chart or available to the effect that the prior CT scan had been negative to a -- for a foreign body; right?

A. Yes, sir. I'm not supposed -- if I may interrupt?

Q. Sure.

A. If the chart says cancer on the left hand and the surgeon is determined to operate on the right hand, and he says he's determined to operate on the right hand, to me that's analogous to the situation that we had going on with this misadventure.

Q. Well, that's a matter -- I don't want to quibble with you, but I think that's a matter we really need an expert for.

A. Yeah.

Q. And you're here as an expert, so, you know, I'm not ---

A. But we're just saying that there's a very striking discrepancy ---

Q. Right.

A. Between no foreign body and a procedure to remove a foreign body.

Q. We'll -- other reasonable men and woman may differ

with you, ---

A. Yes, sir.

Q. But I recognize that you have the right to say that. But none the less -- none the less, at the time this procedure commenced there was a significant amount of data available on the chart or by telephone, including Dr. Shantha's note that the CT scan had been negative ---

A. Yes, sir.

Q. --- for a foreign body? And Dr. Feldman's considered judgment as a board-certified chest doctor, and I understand you differ sharply with this, ---

A. Yes, sir.

Q. --- was that the procedure, nevertheless, should go forward; correct?

A. Yes, sir.

Q. So in order to change that state of affairs, Dr. Shantha would have needed to step in and essentially substitute his judgment as an anesthesiologist for the judgment of a board-certified chest physician on whether the procedure needed to go forward; is that a fair statement?

A. I don't know that he'd need to substitute his judgment as an anesthesiologist. But he'd need to

substitute his judgment as a physician, as the patient's advocate. His -- said that the -- tell the anesthesiologist, I'm not worried about them putting me to sleep. I just want them to wake me up. They're my advocate in the operating room.

BY MR. GUNN:

Thank you, sir.

BY THE WITNESS:

You're welcome.

EXAMINATION BY MR. THOMPSON:

Q. Dr. Fogarty, going back to Dr. Tuan Nguyenduy, ---

A. Yes, sir.

Q. --- who I believe is a board-certified thoracic surgeon. And I think the records indicate that when Mr. Casey was in medical distress, following the complication from this procedure on 6/3/04, that he was consulted by Dr. Feldman and assisted Dr. Feldman in Mr. Casey's treatment, which I believe is placement of a ---

A. Thoracostomy.

Q. --- thoracostomy tube into Mr. Casey's chest; why is that typically done?

A. Well, the chest tub in this case would be done to prevent progression of a pneumothorax, particularly if there's evidence of any kind of distress from a

mild problem to that of a full blown tension pneumothorax with the potential for arrest.

Q. And I think in answering some of Mr. King's questions earlier concerning Dr. Nguyenduy, he asked you about a tension pneumothorax. Was there any indication that Dr. Nguyenduy had diagnosed Mr. Casey with a tension pneumothorax as a result of the perforation from the surgery?

A. Yes, sir. His operative note says it all. On one end he has, I think, questioned tension pneumothorax. On the other hand he has -- when he put the tube in, a good rush of air came out. And for a rush of air to come out, that means that the air in the pleural space where the tube is has to be under higher pressure than atmospheric air. If you have a pneumothorax and you put a chest tube there and air goes in, you know that there's no -- which has happened, you know that that's not under any tension.

Q. And thinking back now in your review of Dr. Nguyenduy's deposition, do you recall that he did, in fact, diagnose Mr. Casey with a ---

A. I believe that he said there a tension pneumothorax in his deposition.

Q. And that he treated him for that with the

thoracostomy tube?
A. Yes, sir.
Q. Now, Mr. Gunn had asked you about what he was referring to as mechanism of injury and going through multiple scenarios. One scenario that wasn't mentioned was hypoxia cognitive problems. Are you aware of any evidence in this case that Mr. Casey suffered from hypoxia?
A. Well, the patient did have a period where he appeared blue. Again, these things are very hard, because you could be measuring oxygen saturation on your finger and you'd have lots of oxygen in the blood going to your finger, but you may not have oxygen in the blood going to part of the brain. So I would say that there's some evidence, but it's not more probable than not. Leave it at that. I'd say -- I would put it in a category of possible -- a possible mechanism. But there would be other mechanisms that would be more likely.
Q. And could you have one mechanism ---
A. Well, they could all be working together.
Q. --- working with another?
A. Yeah, they could all -- they could all be working together.
Q. And that would include hypoxia?

A. Yes, sir.

BY MR. THOMPSON:

I think that's all.

RE-DIRECT EXAMINATION BY MR. KING:

Q. Doctor, what are the clinical signs of a tension pneumothorax?

A. Of course, early on -- it's like, what are the signs of a car using up gas. Early on there aren't any, but at some point the car quits. So a tension pneumothorax, early on there might be very little signs except that the blood pressure and pulse might go up. The patient might appear restless. At some point he would start working harder to breath because the air in the pleural space is impacting more on the lung, which is relatively pliable. So when you go to take the breath, then that lung is going to feel that there's compression there, as opposed to the heart. As the amount of air increases, and the lung gets more and more scrunched up, then the increased pressure is impacting on the blood vessels returning to the heart and you would progress from an elevated blood pressure and a rapid heart rate to low blood pressure. But early on -- the whole key is to intervene at a time when the patient is restless

and maybe mildly uncomfortable, mildly gasping for breath. The problem is -- and I've seen one death, is that if you don't intervene and that air continues to build up, it can block off -- it can make intubation very difficult. So I've seen one death where a tension pneumothorax is suspected. The surgeon had some problems in getting there and by the time he got there the patient needed intubation and anesthesia couldn't intubate the patient.

Q. Have you answered the question? Does that answer the question?

A. Oh, don't encourage me to talk more.

BY MR. KING:

That concludes my side.

BY VIDEOGRAPHER:

This concludes today's deposition of Dr. Charles Fogarty. Off the record at 5:53 p.m.

(There being no further questions, this deposition was concluded at approximately 5:53 p.m.)

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DATE OF BIRTH [redacted], 1944

PLACE OF BIRTH Sioux City, Iowa

MARITAL STATUS Married 1968-*Jane Carol*

Children: *Charles Dervin, 1970- Thomas Franklin, 1973- John Wells, 1977*

EDUCATION

- 1961-66, B.S.-Providence College, Providence, Rhode Island
- 1966-70, MD, University of Rochester, Rochester, New York

POSTGRADUATE TRAINING AND FELLOWSHIP APPOINTMENTS

- 1970-71 Intern in Medicine, Strong Memorial Hospital, Rochester, New York
- 1973-75 Resident in Medicine, Strong Memorial Hospital, Rochester, New York
- 1975-77 Fellow in Pulmonary Diseases University of Pennsylvania Philadelphia, Pennsylvania

EXHIBIT # 1 Dr. Fogarty 12/22/08

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MILITARY SERVICE

•1971-73 Chief, Preventive Medicine Section,
U.S. Army General Hospital Fort Gordon,
Augusta, Georgia

PROFESSIONAL SERVICES

•Partner, Spartanburg Lung and Chest Medical Associates 1978- Present

• Medical Director, Spartanburg Medical Research
1994- Present

• Medical Director, Spartanburg Bone Density Center
1996- Present

• Medical Director, Respiratory Therapy, Spartanburg Tech College
1988

HOSPITAL AFFILIATIONS

•Spartanburg Regional Medical Center
101 East Wood Street
Spartanburg, SC 29303
1978- Present

•Mary Black Memorial Hospital
1700 Skylyn Drive
Spartanburg, SC 29307
1978- Present

HOSPITAL APPOINTMENTS

•1976-1978, Staff Medicine, Philadelphia General Hospital, Philadelphia, Pennsylvania

•1977-78 Associate in Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

•1978-Present Director, Pulmonary Function Laboratory, Spartanburg, SC

•1979-Present Medical Staff, Member Mary Black Memorial Hospital
Spartanburg, SC

•1980-Present Clinical Associate Professor, Medical University of SC Spartanburg Regional Medical Center, Spartanburg, SC

•1980-2001 Medical Director, Respiratory Therapy,
Spartanburg Regional Medical Center Spartanburg, SC

•1985-Present Medical Director, Respiratory Therapy Program,
Spartanburg Technical College Spartanburg, SC

•1994-2000 Chairman, Dept of Medicine
Spartanburg Regional Medical Center
Spartanburg, SC

•1996-1999 Member IRB, Spartanburg Regional Medical Center
Spartanburg, SC 29303

•1996-2001 Member P & T Committee
Spartanburg Regional Medical Center
Spartanburg, SC 29303

SOCIETY APPOINTMENTS

•1991-1992 President, Spartanburg County Medical Society

•2001-Present Program Chairman of 2002, International Society of Clinical Densitometry Atlanta Meeting

•2001-Present Certification Course Instructor, International Society of Clinical Densitometry

SPECIALTY CERTIFICATIONS

•1975 Internal Medicine, American Board of Internal Medicine Certificate # 52798

•1978 Pulmonary Medicine, American Board of Internal Medicine Certificate # 52798

•1989-1999 Critical Care, American Board of Internal Medicine Certificate # 52798

•1999 Certified Clinical Densitometry (CCD), Internation Society Clinical Densitometry (ISCD)

•2002 Certified Clinical Research Investigator

•2002 Association of Clinical Research Professionals (ACRP) - Clinical Investigator

•2005 Certified Principal Investigator (CPI) Academy of Pharmaceutical Physicians and Investigators

LICENSURE

•South Carolina, SC08691
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AWARDS, HONORS, MEMBERSHIPS, HONORARY SOCIETIES

- 1966 Alpha Epsilon Delta
- 1966 Delta Epsilon Sigma
- 1998 Selected for The Best Doctors in America
- 2003 Marquis-Who's Who in Medicine and Healthcare
- 2005 Award for Excellence in Human Research Protection

MEMBERSHIPS IN PROFESSIONAL AND SCIENTIFIC SOCIETIES

•American College of Physicians
•American Thoracic Society
•European Respiratory Society
•International Society for Clinical Densitometry
•American Society of Bone and Mineral Research

•Infectious Disease Society of America
•Southern Medical Association
•Association of Clinical Research Professionals
•Academy of Pharmaceutical Physicians and Investigators
•SOCRA (Society of Clinical Research Associates)

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3. Fleegler B, Fogarty C, Owens G, Cohen E, Cassileth PA. Pathologic Flail Chest Complicating Multiple myeloma. *Arch Intern Med* 1980; 140: 414.

4. Caston, CJ, Utley JR, Fleming HE, Harper MJ, Story JR, Fogarty CM. Endocrine marker for L-Tryptophan response in postcardiopulmonary bypass delirium patients. *Adv in Ther;* 6: 161-179, July/August 1989.

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8. Fogarty CM. Levofloxacin in the treatment of community acquired pneumonia. *Penetration* 1997; 5-9.

9. Fogarty CM, Sullivan JG, Chattham MS, Williams RR, Kojak C, Ruben A. Once a day levofloxacin in the treatment of mild to moderate to severe community- acquired pneumonia in adults. *Inf Dis In Clin Prac* 1998; 7: 400-407.

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11. Fogarty C, McAdoo MA, Paster RZ, Martel AY, Macko AC, and Breen J. Gatifloxacin vs. clarithromycin in the management of acute sinusitis. *J Res Dis*;1999; 20: S17-S22.

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13. Fogarty C, Dowell ME, Ellison T, Vrooman PS, White BJ, and Mayer H. Treating community-acquired pneumonia in hospitalized patients: gatifloxacin vs. ceftriaxone/clarithromycin. *J Res Dis;* 1999; 20: S60-S69.

14. Fogarty, C, Goldschmidt, R, and Bush, K. Bacteremic multidrug-resistant pneumococcal pneumonia in three patients treated unsuccessfully with azithro mycin and successfully with levofloxacin. *Clin Infect Dis*; 2000; 31: 613-615.

15. Fogarty CM, Bettis RB, Griffin TJ, Keyserling CH, Nemeth MA, Tack KJ. Comparison of a 5-day regimen of cefdinir with a 10-day Regimen of cefprozil for treatment of acute exacerbations of chronic bronchitis. *J Antimicrobial Chemotherapy*, 2000; 45: 851-858.

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18. File TM, Larsen LS, Fogarty CM, Schechter RB, Peloquin S, Choudri SH, Haverstock D, Jackson P, Gnjidic ZH, Church D. Safety and Efficacy of Sequential (IV to PO) Moxifloxacin for the Treatment of Community-Acquired Pneumonia in Hospitalized Patients. *Today's Therapeutic Trend s*2001; 250-270.

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Chapters

1. Dauber J, Fogarty C. Immune Deficiency States and Recurrent Pulmonary Infections: Chap. 89 in Fishman, A.P. (ed.), Pulmonary Diseases and Disorders, McGraw Hill, Philadelphia, 1980.

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Abstracts

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3. Murphy DM, Fogarty C, Metzger L, Heyer R. Comparison of dynamic compliance methods: spontaneous versus respirator controlled breathing. *Amer Rev Resp Dis* 1978: 117; 161. American Thoracic Society Meeting, Boston, May 1978.

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6. Heyer R, Epstein P, Metzger L, Fogarty C, Murphy D. Abnormalities of volume of isoflow in non-smoking asbestos-talc workers, *Amer Rev Resp Dis* 1978; 117: 241.

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9. Katz AS, Ochs RH, Fogarty CM. Carcinoma of the lung in young adults: a case control clinical-pathological study. *Amer Rev Resp Dis* 1979; 119: 136.

10. Koffler H, Fogarty C, Singer A, Geib J, Friedland I, Ertapenem study group (sellersville, PA; Spartanburg, SC; Merck Res. Lab, Blue Bell, PA). A Double-Blind, Multicenter Clinical Trial of Ertapenem (ERTA) V. Ceftriaxone (CRO) for Treatment of Community-Acquired Pneumonia (CAP). *American Journal of Respiratory and Critical Care Medicine* 2001; 163(5): A930.

11. Fogarty CM, Peloquin S, Choudri SH, Haverstock D, Weinstein DM, Jackson P,Church D. Efficacy and safety of sequential (IV/PO) moxifloxacin for the treatment of community-acquired pneumonia in hospitalized patients. *International Journal of Antimicrobial Agents* 2001; 17: S73.

12. Fogarty CM, Peloquin S, Choudri SH, Haverstock D, Weinstein DM, Jackson P, Church DA. Efficacy and Safety of Sequential (IV/PO) Moxifloxacin for the Treatment of Community-Acquired Pneumonia in Hospitalized Patients. *International Journal of Antimicrobial Agents* Supplement 1 2001; 17: S73.

13. Fogarty C, Patel TC, Sidarous E, Leroy B. Telithromycin is an Effective Treatment in High-Risk Patients with Community- Acquired Pneumonia. *Amer Ger Soc* 2002; 50(4): S1-S204.

14. Fogarty CM, Cyganowski M, Palo WA, Hom RC, Craig WA. A Comparison of Cefditoren Pivoxil and Amoxicillin/Clavulate in the Treatment of Community-Acquired Pneumonia: A Multicenter, Prospective, Randomized, Investigator-Blinded, Parallel-Group Study. *Clin Ther* 2002; 24(11): 1854-1870.

15. West M, Boulanger BR, Fogarty C, Tennenberg A, Wiesinger B, Oross M, Wu, SC, Fowler C, Morgan N, Kahn JB. Levofloxacin Compared with Imipenem/Cilastatin Followed by Ciprofloxacin in Adult Patients with Nosocomial Pneumonia: A Multicenter, Prospective, Randomized, Open-Label Study. *Clin Ther* 2003; 25(2): 485-506.

16. Van Rensburg D, Fogarty CM, Rangaraju M, Jenkins S, Nusrat R. Telithromycin is Clinically Effective in Patients with Community-Acquired Pneumonia(CAP) Irrespective of Age. American Geriatrics Society 2003 Annual Scientific Meeting, Baltimore, Maryland, May 16, 2003.

PRESENTATIONS

1. Fogarty C, Patel T, Haverstock MS, Church D, and Williams J. Community-acquired pneumonia: efficacy and safety of moxofloxacin. American College of Chest Physicians 1999, Chicago, Illinois, November 2, 1999.

THOMPSON 017963

2. Slama, TG, Fogarty, CM, Medeiros, AA. Grand rounds: clinical challenges in the management of respiratory tract infections. Anti-Infective Imperatives-LEVAQUIN^R National Consultants Meeting, Arizona, February 4, 2000

3. Fogarty CM. Achieving clinical success in the face of today's changing microorganisms. American College of Chest Physicians, San Francisco, California October 23, 2000.

4. Fogarty CM. Bone Densitometry for Diagnosis of Osteoporosis. International Society for Clinical Densitometry (ISCD), Raleigh, North Carolina, September 8, 2001.

POSTER PRESENTATIONS

1. Fogarty CM. A Noncomparative Study to Evaluate the Safety and Efficacy of Levofloxacin in the Treatment of Community-Acquired Pneumonia in adults. 19th International Congress of Chemotherapy, Montreal, Quebec, Canada, July 17, 1995.

2. Fogarty CM, Fogarty CD, Nodine K. Does BMD disconcordance decrease in older, more *osteoporotic* subjects? International Society for Clinical Densitometry (ISCD), Orlando, Florida January 16, 1998.

3. Fogarty CM, Fogarty CD, Nodine K. Is dexa scanning additional sites worth doing in a clinical setting? International Society for Clinical Densitometry, Orlando, Florida, January 16, 1998.

4. Murray JJ, Friedman B, Chervinsky P, Fogarty C, Baker JD, Rogenes PR, Edwards L, Lincourt WR and Clinical Study Group. Asthma severity as a determinant for selecting appropriate doses of fluticasone propionate (FP) or beclomethasone dipropionate (BDP). AAAAI, Washington, DC March 1998.

5. Fogarty CM. Bacterium treatment failure with azithromycin in community-acquired pneumonia: a report of 3 patients infected with erythromycin- resistant and penicillin-and cephalosporin-nonsusceptible strains, treated successfully with levofloxacin. Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), San Diego, California September 26, 1998.

6. Williams RR, Fogarty CM, Dunbar L, Greenberg R, Kojak C, Bahal N, Eschle R, Morgan N. Efficacy of levofloxacin in the treatment of community- acquired pneumonia due to *mycoplasma pneumonia* and *chlamydia pneumonia*. Infectious Diseases Society of America (IDSA), Denver, Colorado. November 15-17, 1998.

7. Fogarty CM, Nodine K, Fogarty CD. Peripheral screening: 50% decrease in false negative rate using two sites. International Society for Clinical Densitometry (ISCD), New Orleans, Louisiana, January 15, 1999.

8. Fogarty CM, Nodine K, Fogarty CD. Right and left hip discordance rarely results in mis- classification of patients. International Society for Clinical Densitometry (ISCD), New Orleans, Louisiana, January 15, 1999.

9. Fogarty CD, Nodine K, Fogarty CM. Combined right and left hip BMD has better precision than just a single hip measurement. International Society for Clinical Densitometry (ISCD), New Orleans, Louisiana, January 15, 1999.

10. Fogarty CM, McAdoo M, Paster RZ, Audet MC, Breen J, Macko A. Comparison of once daily gatifloxacin (GAT), 400 mg PO for 10 Days with twice daily clarithromycin (CLA), 500 mg PO for 14 Days, in patients with acute maxillary sinusitis: a multicenter phase III study. Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), San Francisco, California, September 26, 1999.

11. Fogarty CM, Williams J, Haverstock D, Church D. Efficacy and safety of moxifloxacin versus clarithromycin for the treatment of community- acquired pneumonia. ICAAC, San Francisco, California, September 29, 1999.

12. Dowell ME, Mayer H, and Fogarty CM. A randomized, double-blind, multicenter, comparative study of gatifloxacin (GAT) 400 mg IV and PO versus ceftriaxone +/- erythromycin in the treatment of community-acquired pneumonia requiring hospitalization. ICAAC, San Francisco, California, September 29, 1999.

THOMPSON 017964

13. Fogarty C, Garber G, Greenberg RN, Weaver L, Huang X, Tack KJ. Randomized comparison of clinafloxacin and a ceftazidime-based regimen (TAZ) in the treatment of nosocomial pneumonia. ICAAC, San Francisco, California, September 29, 1999.

14. Fogarty CM, Fogarty CD, Nodine K, and Homuth J. A comparison of two fan-beam densitometers: the LUNAR PRODIGY and the hologic QDR-4500SL. American Society for Bone and Mineral Research (ASBMR), St. Louis, Missouri, October 3, 1999.

15. Fogarty CD, Woods S, Kirkland J, Fogarty CM. Using a Gauge with Red, Yellow, and Green Intervals to Display a T-Score Helps Physicians and Patients Better Understand a Bone Density Report. ISCD Dallas, Texas, March 16, 2001.

16. Koffler H, Fogarty C, Singer A, Geib J, Friedland I, Ertapenem study group (Sellersville, PA; Spartanburg, SC; Merck Res. Lab, Blue Bell, PA). A Double-Blind, Multicenter Clinical Trial of Ertapenem (ERTA) V. Ceftriaxone (CRO) for Treatment of Community -Acquired Pneumonia (CAP). 2001 International Conference of the American Thoracic Society, San Francisco, May 2001.

17. Fogarty C, Patel TC, Sidarous E, Leroy B. Telithromycin is an Effective Treatment in High-Risk Patients with Community-Acquired Pneumonia.Washington, DC, June 11, 2001.

18. Fogarty CM, Peloquin S, Choudri SH, Haverstock D, Weinstein DM, Jackson P, Church DA. Efficacy and Safety of Sequential (IV/PO) Moxifloxacin for the Treatment of Community-Acquired Pneumonia in Hospitalized Patients. Abstracts of the 22nd International Congress of Chemotherapy (ICC), Amsterdam, The Netherlands, June 30-July 3, 2001(Presented July 2,2001).

19. Fogarty C, Milanowski J, Heyder A, Verbeeck F, Yang J, Mayer H. A Randomized, Double Blind, Multicenter Study of 5 Day and 10 Day Therapy with Oral BMS-284756 in the Treatment of Acute Exacerbation of Chronic Bronchitis (AECB). 41st Annual ICAAC, Chicago, Illinois, December 16-19, 2001.

20. Fogarty C, Patel TC, Galbraith H, Zuberbuhler GA, Leroy B. Efficacy of the First Ketolide Antibacterial, Telithromycin, in the Treatment of Community-Acquired Pneumonia Caused by *Streptococcus pneumonia*. 41st Annual ICAAC, Chicago, Illinois, December 16-19, 2001.

21. Fogarty C, Choudri SH, Haverstock D, Perroncel R, Jackson P, Church D. Efficacy of Moxifloxacin for Treatment of Community-Acquired Due to Penicillin- Resistant Streptococcus pneumonia. 41st Annual ICAAC, Chicago, Illinois, December 16-19, 2001

22. Hassman J, Fogarty C. Clinical and Bacterial Efficacy of Telithromycin in Patients with Community-Acquired Pneumonia. *Ann Emer Med* 2002; 40 (4): S102. American College of Emergency Physicians (ACEP) Annual Meeting Research Forum Seattle, October 8, 2002 and American Osteopathic Association (AOA) meeting Las Vegas, October 9, 2002.

23. Fogarty C, Larsen S, Jackson T, Hamed K, Song J, Church D. Sequential IV to PO Moxifloxacin Monotherapy for Community-Acquired Pneumonia. 40th Annual Meeting of IDSA Chicago, Illinois, October 25, 2002.

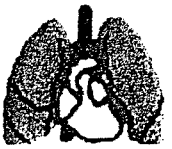
24. Fogarty C, Zervos M, Nusrat R. Efficacy of Telithromycin in the Treatment of Community- Acquired Respiratory Tract Infections in Patients at Increased Risk of Morbidity and Mortality. 41st Annual Meeting of IDSA San Diego, California, October 9-12, 2003.

MISCELLANEOUS

- 2002 Health Improvement Institute Applications Judge
- 2002 Clinical Therapeutics Editorial Advisory Board, Editorial Consultant (Peer Review)
- 2001 International Society for Clinical Densitometry Consensus Forum, Panel Member Denver, CO

(Updated 22Dec2008)

THOMPSON 017965



CASEY, WILLIAM M

50 Y old Male, DOB: [redacted]/1958
419 QUAIL RIDGE CIRCLE, BOILING SPRINGS, SC-29316-6119
Home: 864-814-2617
Guarantor: CASEY, WILLIAM M Insurance: BCBS PPC
PCP: FRANK F GONDA

12/08/2008

Charles M. Fogarty, MD

Current Medications

Tricor 145 mg 1 tab(s) qd by Dr. Ganda has not taking any latly
Vytorin 10 mg-40 mg 1 tab(s) qd not taking
mirtazapine 45 mg 1 tab(s) once a day (at bedtime)
Adderall XR 20 mg 1 cap(s) tid
Lortab 10 500 mg-10 mg 1 tab(s) Q6H
Ambien 10 mg 1 tab q/hs/prn

Past Medical History

Chest wall pain
Back pain
Hyperlipidemia
Difficulty with multitasking, concentrating, s/post pneumomediastinum/pneumothorax

Social History

Marital status: Divorced.
Education level: College one year.
Occupation: disabled from his Lungs.
Alcohol: reports, socially.
Other MDs: Primary care Dr. Ganda.

Allergies

NKMA

Review of Systems

CONSTITUTIONAL:
no Fever/Chills. no Night sweats.
ENT:
no Nasal discharge. no Sore throat.
RESPIRATORY:
no Shortness of breath. no Cough, Dry. no Wheezing. c/o Pleuritic Chest Pain, left chest wall.
CARDIOLOGY:
no Leg edema. no Dizziness.
GASTROENTEROLOGY:
c/o Nausea. no Vomiting.
Reviewed by: Theresia Meyers

CC

1. States still feelling the same, chest wall pain with exertion and back pain

HPI

Interim History:

Mr. Casey he reports no significant change in his chest wall pain or back pain. This is mainly related to movement or exertion. It is relieved by Lortab.

He continues to have difficulty in concentrating. He has to take notes to remember what is going to do later in the day. He is followed by a psychiatrist in Greenville and is on Adderall but still has difficulties with staying focused. He continues his regular followup with Dr. Gonda who is his primary care doctor.

Vital Signs

Wt: 182.6, BP: 124/80, HR: 99, O2 sat: 96%, FIO2: .21, FVC: 3.97, FEV1: 3.23, FEV1/FVC%: 81%, Ht: 68, BMI: 27.76.

Physical Examination

on exam the patient is no acute distress. The patient has not been paying as much attention by his own admission to oral hygiene and he has teeth are in only fair repair On exam today. The pupils are symmetric. Next her wrist pain. Trachea midline. No wheezes rales or rhonchi. The patient's chest wall pain increases with anterior-posterior compression suggesting a mass a skilled etiology. Fremitus is symmetric. Heart tones regular. No murmur or gallop. No abdominal organomegaly. No cyanosis edema or clubbing. Coordination normal range..

Assessments

the patient appears stable in terms of his lung function. He needs to followup with a dentist; The deterioration in his oral hygiene and condition of his teeth over the last year is rather striking but consistent with his lack of attention.. His overall functional status does not appear any worse or any better than on his last visit and we deferred his continued treatment to his primary care doctors..

Treatment

1. Others

Continue Lortab 10 tablet, 500 mg-10 mg, orally, 120, 1 tab(s), Q6H, 30 days, Refills 5
he continues with chronic chest wall and back pain. He does not appear to

EXHIBIT #2 Dr. Fogarty

THOMPSON 017966

be overusing or misusing his Lortab and we will continue to write refills as indicated.

Labs
Spirometry FVC - 3.97/86%, FEV1 - 3.23/86%, %FEV1 - 81%, Gaffney,Jamie12/8/2008 1:16:45 PM > The vital capacity is lower normal range crit is down slightly from the June value of 4.2 but stillin the lower normal range. FEV1 is 3.23. 6% of predicted also normal range. This

Procedure Codes
SPIROMETRY

Follow Up
6 Months

Electronically signed by CHARLES FOGARTY,MD PA on 12/22/2008 at 08:10 AM EST

Sign off status: Pending

Lung and Chest Medical Associates
2030 North Church Place
Spartanburg, SC 29303-2799
Tel: 864-582-6858
Fax: 864-542-9043

Patient: CASEY, WILLIAM M DOB: [redacted]1958 Progress Note: Charles M. Fogarty, MD 12/08/2008

Note generated by eClinicalWorks EMR/PM Software (www.eClinicalWorks.com)

Lung and Chest Medical Associates
MultiSpiro A

77168 Casey, William Mark
nic: CAUCASIAN Height: 68.0 in. Sex: MALE Age: 50 Weight: 182.0 lb

COMMENTS:
PRE-BD COMMENTS:

LAST CALIBRATED: Mon Dec 8,2008 7:33:27 am

TYPE	Test Date and Time	Exp.Time	Normals	Test#
Pre-BD:	Mon Dec 8,2008 1:16:40 pm	3.7 secs	KNUDSON/IMTS	1

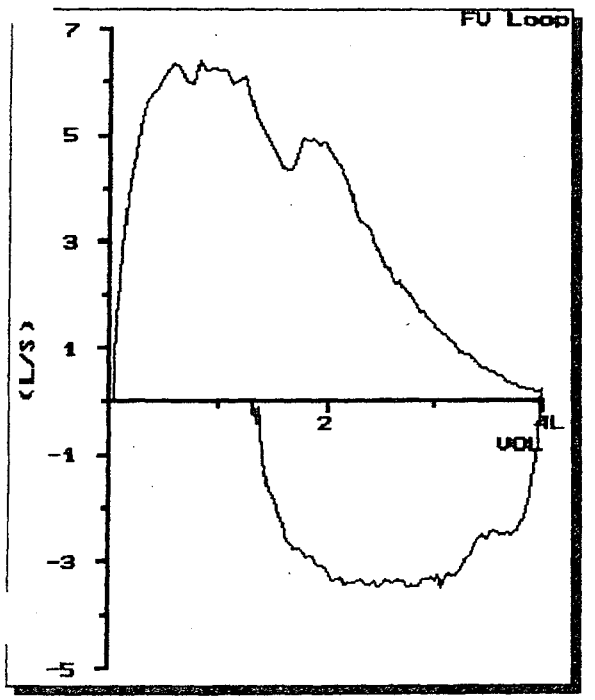
Expiratory	Actual	Predicted	% of pred
FVC	3.97 L	4.64 L	85.59 %
FEV 0.5	2.49 L	2.98 L	83.63 %
FEV 1.0	3.23 L	3.74 L	86.32 %
FEV 3.0	3.90 L	4.37 L	89.19 %
FEV 0.5/FVC	62.64 %	64.11 %	97.71 %
FEV 1.0/FVC	81.31 %	80.63 %	100.85 %
FEV 3.0/FVC	98.17 %	94.21 %	104.20 %
PEF	6.35 L/S	8.50 L/S	74.70 %
FEF 25-75%	3.31 L/S	3.76 L/S	88.14 %
FEF 75-85%	0.92 L/S	0.94 L/S	97.96 %
FEF 25	6.17 L/S	7.87 L/S	78.35 %
FEF 50	4.66 L/S	4.44 L/S	105.00 %
FEF 75	1.31 L/S	1.72 L/S	76.02 %
FEF .2-1.2	5.98 L/S	7.07 L/S	84.53 %

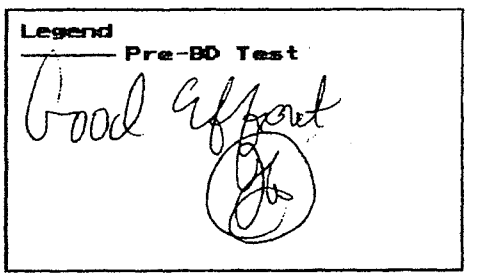
Inspiratory	Actual
IVC	2.67 L
FIV1	2.59 L
PIF	3.60 L/S
FIF50	3.47 L/S
FEF50/FIF50	134.34 %

Interpretation:

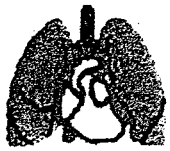
NORMAL

MAX FVC = 3.97L TEST # 1
MAX FEV-1 = 3.23L TEST # 1





THOMPSON 017968



CASEY, WILLIAM M

49 Y old Male, DOB: [redacted]/1958
419 QUAIL RIDGE CIRCLE, BOILING SPRINGS, SC-29316-6119
Home: 864-814-2617
Guarantor: CASEY, WILLIAM M Insurance: BCBS PPO
PCP: FRANK E GONDA

06/11/2008

Charles M. Fogarty, MD

Current Medications
Tricor 145 mg 1 tab(s) qd by Dr. Ganda has not taking any lathy
Vytorin 10 mg-40 mg 1 tab(s) once a day
Adderall XR 20 mg 1 cap(s) QAM
diazepam 10 mg 1 tab(s) TID
Lortab 10 500 mg-10 mg 1 tab(s) Q6H
Ambien 10 mg 1 tab q/hs/prn

Past Medical History
Chest wall pain
Hyperlipidemia
Difficulty with multitasking, concentrating, s/post pneumomediastinum/pneumothorax
Back pain
Neuro cognative impairment

Social History
Marital status: Divorced.
Education level: College one year.
Occupation: disabled from his Lungs.
Alcohol: reports, socially.
Other MDs: Primary care Dr. Ganda.

Allergies
NKMA

Review of Systems
CONSTITUTIONAL:
no Fever/Chills. no Night sweats.
ENT:
no Nasal discharge. no Sore throat.
RESPIRATORY:
no Shortness of breath. no Cough, Dry. no Wheezing. Chest Tightness c/o, Occasional, With activity.
CARDIOLOGY:
no Leg edema. no Dizziness.
GASTROENTEROLOGY:
no Nausea. no Vomiting. no Heartburn.
NEUROLOGY:
c/o Headache, some. Memory loss c/o.
ALLERGY:
no Runny nose. no Sinus congestion.
PSYCHOLOGY:
c/o Depression.
Reviewed by: Theresia Meyers

CC
1. 5-6 MO F/U
2. Some chest tightness with exertion
3. Short term memory loss
4. Back pain

HPI
Interim History:

Mr. Casey reports no major change. He continues to have problems getting through the day. He is easily distracted and has difficulty staying focused. He has difficulty concentrating. He forgets what he is set out to do. He feels that he is doing stupid things. He cuts the speaker on the stereo off and then wonders why the music is off. Occasionally he feels he is doing things that don't make sense when he is thought it through.

Separately,His chest wall discomfort is intermittent. He continues to have back pain.

Vital Signs
Wt: 192.7, BP: 130/100, HR: 116, O2 sat: 95%, FIO2: .21, FVC: 4.20, FEV1: 3.42, FEV1/FVC%: 81%, Ht: 68, BMI: 29.30.

Physical Examination

Appears comfortable at rest. Pupils symmetric. Oropharynx clear. Trachea midline. No wheeze rales or rhonchi. Heart tones regular. No murmur gallop. No organomegaly. No edema clubbing. Coordination normal range..

Assessments
1. Back pain - 724.5 (Primary)
2. Hyperlipidemia - 272.4

Treatment
1. Back pain
Continue Lortab 10 tablet, 500 mg-10 mg, orally, 120, 1 tab(s), Q6H, 30 days, Refills 5

Labs
Spirometry FVC - 4.20/90%, FEV1 - 3.42/91%, %FEV1 - 81%, Gaffney,Jamie 6/11/2008 3:25:28 PM > The vital capacity is stable or slightly improved compared to December value. As in the lower normal range of 4.2 L. The FEV1 is also well preserved at 3.4 L.

Procedure Codes
SPIROMETRY

Follow Up
The patient was given a prescription for Lortab. Dr. Gonda is prescribing his other medications. He will check back with us in 6 months urinne meanwhile he was encouraged to have an outline for how he is going to plan the day in a week and take additional notes. He was advised is unlikely his chest wall pain is related to his heart although he remains concerned about heart disease. He is not smoking at present. He remains unable to return to work.

Electronically signed by CHARLES FOGARTY,MD PA on 12/22/2008 at 08:10 AM EST

Sign off status: Pending

Lung and Chest Medical Associates
2030 North Church Place
Spartanburg, SC 29303-2799
Tel: 864-582-6858
Fax: 864-542-9043

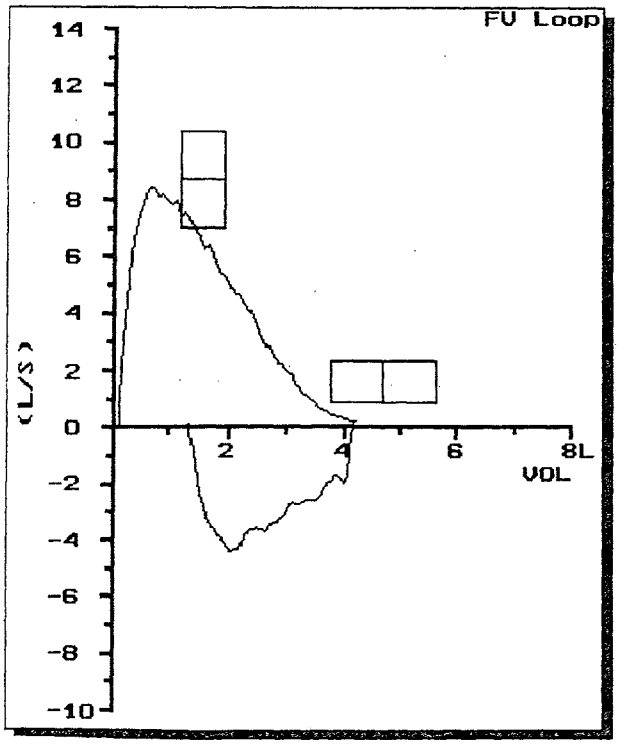
Lung and Chest Medical Associates
MultiSpiro A

I[illegible] 77168 Casey, William Mark
E[illegible]ic: CAUCASIAN Height: 68.0 in. Sex: MALE Age: 49 Weight: 192.0 lb

COMMENTS:
PRE-BD COMMENTS:

LAST CALIBRATED: Wed Jun 11,2008 7:23:22 am

TYPE	Test Date and Time		Exp.Time	Normals	Test#
Pre-BD:	Wed Jun 11,2008 3:20:28 pm		4.5 secs	KNUDSON/IMTS	1
Expiratory	Actual	Predicted	% of pred	Inspiratory	Actual
FVC	4.20 L	4.66 L	90.14 %	IVC	2.89 L
FEV 0.5	2.73 L	2.99 L	91.31 %	FIV1	2.53 L
FEV 1.0	3.42 L	3.77 L	90.83 %	PIF	4.56 L/S
FEV 3.0	4.06 L	4.40 L	92.18 %	FIF50	3.61 L/S
				FEF50/FIF50	127.57 %
FEV 0.5/FVC	64.98 %	64.14 %	101.30 %		
FEV 1.0/FVC	81.40 %	80.78 %	100.77 %	Interpretation:	
FEV 3.0/FVC	96.49 %	94.36 %	102.26 %		
				NORMAL	
PEF	8.34 L/S	8.53 L/S	97.75 %		
FEF 25-75%	3.60 L/S	3.79 L/S	94.81 %	MAX FVC = 4.27L TEST # 2	
FEF 75-85%	0.84 L/S	0.97 L/S	86.56 %	MAX FEV-1 = 3.42L TEST # 1	
FEF 25	7.85 L/S	7.89 L/S	99.48 %		
FEF 50	4.61 L/S	4.48 L/S	102.94 %		
FEF 75	1.35 L/S	1.74 L/S	77.25 %		
FEF .2-1.2	7.63 L/S	7.12 L/S	107.16 %		



Legend
Pre-BD Test

Good Effort
DG

THOMPSON 017971

CASEY, WILLIAM M

49 Y old Male. DOB: [redacted]/1958
419 QUAIL RIDGE CIRCLE. BOILING SPRINGS. SC-29316-6119
Home: 864-814-261-
Guarantor: CASEY, WILLIAM M Insurance: BCBS PPC
PCP: FRANK E GONDA

01/02/2008

Charles M. Fogarty, MD

Current Medications
None

Past Medical History
Chest wall pain
Hyperlipidemia
Difficulty with multitasking, concentrating, s/post pneumomediastinum/pneumothorax; neurocognitive impairment
Back pain

Allergies
NKMA

CC
1. Xrays

HPI
Interim History:
Mr. Casey is here to obtain some x-rays with a piece of metal in front of or in back of his chest per the letter from Mr. Thompson. He is still puzzled as to why the doctors felt there was a metal object in his chest when he does not have any recollection of ever having had anything go down into his windpipe.

Assessments
1. Back pain - 724.5 (Primary)

Treatment
1. Back pain
We showed Mr. Casey the frontal view of the x-ray taken today which shows a metallic object which appears to be overlying the left upper chest. We then showed Mr. Casey the side view which makes it clear that in fact the front to is potentially misleading in so far as a metallic object is actually outside the chest as evident on the lateral view.

Diagnostic Imaging
X ray : Chest PAL Front and side views of the chest were taken with a small metallic object takes to the back of his chest to simulate what might have happened if he had been lying on top of a small metallic object with his portable chest film was taken in May 2004.

Follow Up
Keep Exisitng

Electronically signed by CHARLES FOGARTY,MD PA on 12/22/2008 at 08:10 AM EST

Sign off status: Pending

Lung and Chest Medical Associates

2030 North Church Place
Spartanburg, SC 29303-2799
Tel: 864-582-6858
Fax: 864-542-9043

Patient: CASEY, WILLIAM M DOB: [redacted]/1958 Progress Note: Charles M. Fogarty, MD 01/02/2008

Note generated by eClinicalWorks EMR/PM Software (www.eClinicalWorks.com)

Lung and Chest Medical Associates
MultiSpiro A

ID: 77168 Casey, William Mark
Ethnic: CAUCASIAN Height: 68.0 in. Sex: MALE Age: 49 Weight: 184.0 lb

COMMENTS:
PRE-BD COMMENTS:

LAST CALIBRATED: Wed Dec 19,2007 7:30:36 am

TYPE	Test Date and Time	Exp.Time	Normals	Test#
Pre-BD:	Wed Dec 19,2007 2:12:35 pm	4.5 secs	KNUDSON/IMTS	1

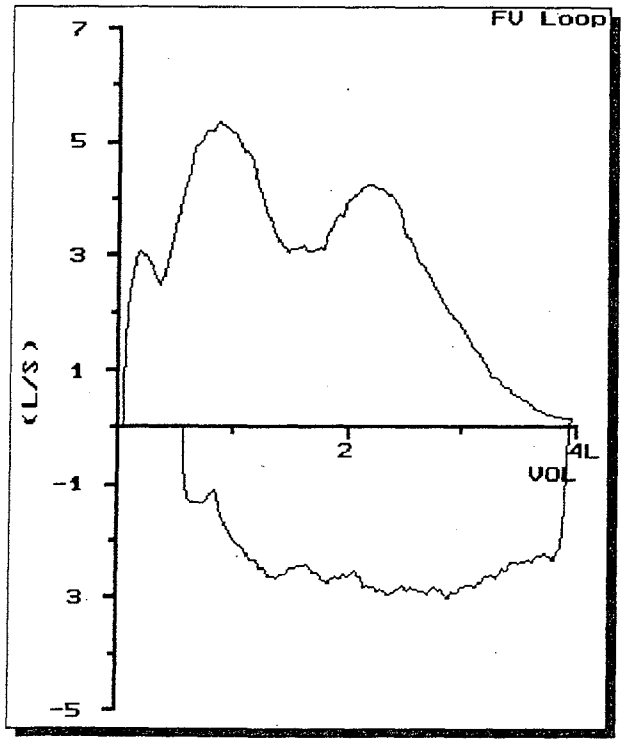
Expiratory	Actual	Predicted	% of pred
FVC	3.95 L	4.66 L	84.58 %
FEV 0.5	2.07 L	2.99 L	69.10 %
FEV 1.0	3.20 L	3.77 L	84.96 %
FEV 3.0	3.82 L	4.40 L	86.89 %
FEV 0.5/FVC	52.40 %	64.14 %	81.70 %
FEV 1.0/FVC	81.14 %	80.78 %	100.44 %
FEV 3.0/FVC	96.93 %	94.36 %	102.73 %
PEF	5.27 L/S	8.53 L/S	61.81 %
FEF 25-75%	3.23 L/S	3.79 L/S	85.05 %
FEF 75-85%	1.02 L/S	0.97 L/S	105.93 %
FEF 25	5.05 L/S	7.89 L/S	64.00 %
FEF 50	3.93 L/S	4.48 L/S	87.87 %
FEF 75	1.68 L/S	1.74 L/S	96.47 %
FEF .2-1.2	3.97 L/S	7.12 L/S	55.81 %

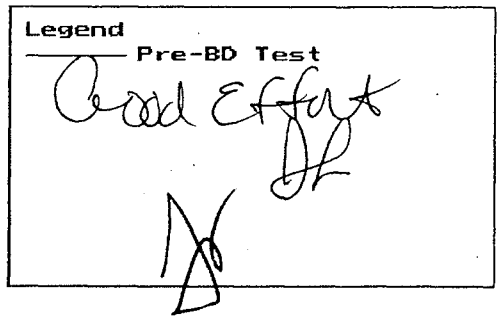
Inspiratory	Actual
IVC	3.39 L
FIV1	2.56 L
PIF	3.08 L/S
FIF50	2.95 L/S
FEF50/FIF50	133.45 %

Interpretation:

NORMAL

MAX FVC = 4.01L TEST # 2
MAX FEV-1 = 3.20L TEST # 1





THOMPSON 017974

BURTS, TURNER, RHODES & THOMPSON
ATTORNEYS AT LAW
260 NORTH CHURCH STREET
SPARTANBURG, S.C. 29306

AM BURTS (1907 - 1982)
NOEL TURNER
RICHARD H. RHODES
RAY E. THOMPSON, JR.
M. NOEL TURNER, III

MAILING ADDRESS
P.O. BOX 3408 29304
PHONE: 864-585-8166
FAX: 864-583-6927

December 27, 2007

VIA HAND DELIVERY

Charles M. Fogarty, MD
Lung and Chest Medical Associates
2030 N. Church Place
Spartanburg, SC 29303

RE: William Mark Casey
DOB: [redacted]/58

Dear Dr. Fogarty:

My client, William Mark Casey, is still trying to understand why Dr. Joseph Boscia and Dr. Gregory Feldman felt there was a metal object in his chest that needed bronchoscopies to get it out. I think it would be helpful to Mr. Casey to understand if you showed him how a piece of metal laying underneath him or on top of him appeared on his plain chest film.

Would you consider taking a front to back x-ray with a piece of metal underneath his body or on top of his body that would give the impression that the piece of metal is actually inside his chest? Also, would you consider taking a side view chest film that shows the metal object is really outside of his body? Although we will probably never know the proper identification of the piece of metal that appears in the May 28, 2004 portable chest x-ray, please presume it is a small screw or the back of an earring. I am enclosing along with this letter the back of an earring that appears to be of similar size to the metal object in the x-ray taken of Mr. Casey on May 28, 2004. Obviously, I do not want to request anything that would create a further health risk to Mr. Casey and I would defer that judgment to you. I think this would help Mr. Casey to understand and visualize what I have been unsuccessful in trying to explain to him.

With warm regards,

I remain,
BURTS, TURNER, RHODES & THOMPSON

2 Jan 08
PT. would like us to proceed c CXR

By: _____
RAY E. THOMPSON, JR.

RET:ar
Enclosure

CASEY, WILLIAM M

49 Y old Male, DOB: [redacted]1958
419 QUAIL RIDGE CIRCLE, BOILING SPRINGS, SC-29316-6119
Home: 864-814-261-
Guarantor: CASEY, WILLIAM M Insurance: BCBS PPO
PCP: FRANK E GONDA

12/19/2007

Charles M. Fogarty, MD

Current Medications
Tricor 145 mg 1 tab(s) once a day
Lortab 10 500 mg-10 mg 1 tab(s) Q6H
Vytorin 10 mg-40 mg 1 tab(s) once a day

Past Medical History
Chest wall pain
Hyperlipidemia
Difficulty with multitasking, concentrating, s/post pneumomediastinum/pneumothorax; neurocognitive impairment
Back pain

Social History
Marital status: Divorced.
Education level: College one year.
Alcohol: reports, socially.
Other MDs: Primary care Dr. Ganda.

Allergies
NKMA

Review of Systems
CONSTITUTIONAL:
no Fever/Chills. no Night sweats.
ENT:
no Sore throat. no Sinus pain.
RESPIRATORY:
no Shortness of breath. no Cough, Dry. Wheezing c/o, Occasional. Chest Tightness c/o, Occasional, With activity.
CARDIOLOGY:
no Heart Trouble. no Leg edema. no Dizziness.
GASTROENTEROLOGY:
c/o Nausea, some. no Vomiting.
ALLERGY:
no Runny nose. no Sinus congestion.

CC
1. Some chest tightness with exertion
2. Back pain

HPI
Interim History:

Mr. Casey reports continued troubles with the organizing his stay and remembering what he is supposed to do unless he takes notes or special effort to concentrate. He finds that his mood fluctuates. He is discouraged in that he does he should be capable of doing more.

Vital Signs
Wt: 184, BP: 120/86, HR: 115, O2 sat: 94%, FIO2: .21, FVC: 3.95, FEV1: 3.20, FEV1/FVC%: 81%, Ht: 68, BMI: 27.97.

Physical Examination

no acute distress at rest. Pupils symmetric. Oropharynx clear. Teeth good repair. Trachea midline. No jugular venous distention. No carotid bruit. Chest expands symmetrically. Heart tones regular no murmur gallop no edema or clubbing coordination normal range.

Assessments
1. Hyperlipidemia - 272.4 (Primary)
2. Back pain - 724.5

Treatment
1. Back pain
Continue Lortab 10 tablet, 500 mg-10 mg, orally, 40, 1 tab(s), Q6H, 10 day(s)

2. Others
With reference to the patient's difficulty concentrating and staying focused he was encouraged too take simple measures such as using a daytime her and less to keep on task. Review this at the start and end of the day. he is followed by Dr. Frank Gonda and we will defer any additional medicine/pharmacologic therapy to Dr. Gonda .He remains worried about his heart although his current chest pain is more consistent with chest wall pain he was encouraged take fish oil capsules on general principles since he does have a hyperlipidemia

Diagnostic Imaging
X ray : Chest PAL Meyer,Theresia 12/19/2007 2:58:27 PM > p.m. b the

chest showed clear lung fields bradycardic contours unremarkable. No localized infiltrates.

Labs
Spirometry FVC - 3.95/85%, FEV1 - 3.20/85%, %FEV1 - 81%,
lawter jamie 12/19/2007 2:20:11 PM > She from a tree shows a vital capacity and the lower normal range. Extraocular rates are normal range.

Preventive Medicine
Immunizations: Influenza , 2007, decline.

Procedure Codes
SPIROMETRY
CHEST X-RAY PAL

Electronically signed by CHARLES FOGARTY,MD PA on 12/22/2008 at 08:09 AM EST

Sign off status: Pending

Lung and Chest Medical Associates
2030 North Church Place
Spartanburg, SC 29303-2799
Tel: 864-582-6858
Fax: 864-542-9043

Patient: CASEY, WILLIAM M **DOB:** [redacted]/1958 **Age:** 48 Y **Sex:** Male **Telephone Encounter**
Phone: 864-814-2617 **Primary Insurance:**
Address: 419 QUAIL RIDGE CIRCLE, BOILING SPRINGS, SC 293166119
Encounter Date:
Provider: SMITH,MD PA, WILSON P

Answered by Thompson, Maria

Date: 09/07/2007
Time: 02:44 PM

Caller Angela- Burts Law Firm

Reason needs med. records after 08-05

Message needs updated medical records on Mark Casey. They have up until August 2005. Double check release expiration, get signed and send updates to Burts Law Firm. MT

Action Taken Thompson,Maria 9/7/2007 2:48:03 PM >

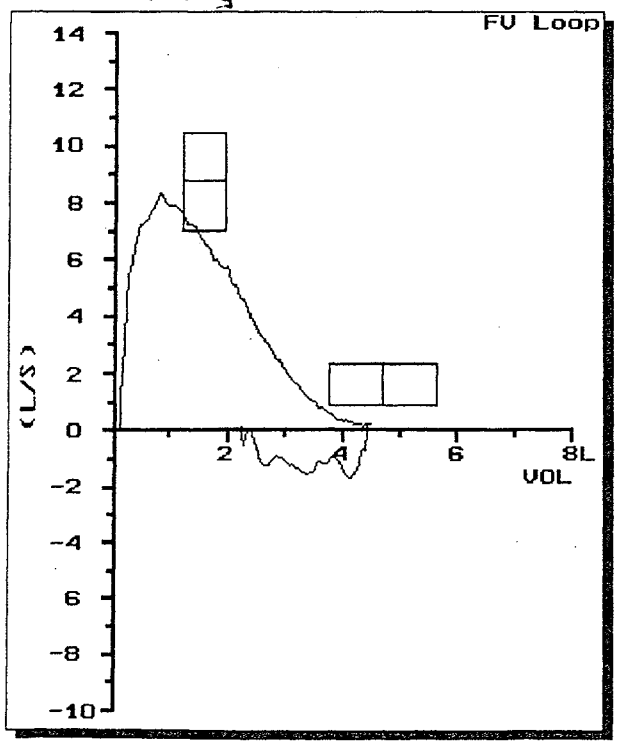
Lung and Chest Medical Associates
MultiSpiro A

ID: 77168 Casey, William Mark
Ethnic: CAUCASIAN Height: 68.0 in. Sex: MALE Age: 48 Weight: 197.0 lb

COMMENTS:
PRE-BD COMMENTS:

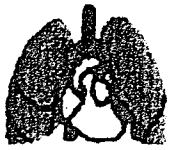
LAST CALIBRATED: Thu Jun 28,2007 7:30:08 am

TYPE	Test Date and Time		Exp.Time	Normals	Test#
Pre-BD:	Thu Jun 28,2007 3:36:49 pm		6.8 secs	KNUDSON/IMTS	2
Expiratory	Actual	Predicted	% of pred	Inspiratory	Actual
FVC	4.47 L	4.69 L	95.43 %	IVC	2.25 L
FEV 0.5	2.78 L	3.01 L	92.50 %	FIV1	1.27 L
FEV 1.0	3.50 L	3.79 L	92.26 %	PIF	1.88 L/S
FEV 3.0	4.14 L	4.43 L	93.41 %	FIF50	1.67 L/S
				FEF50/FIF50	257.76 %
FEV 0.5/FVC	62.21 %	64.17 %	96.94 %		
FEV 1.0/FVC	78.24 %	80.93 %	96.68 %	Interpretation:	
FEV 3.0/FVC	92.50 %	94.50 %	97.88 %		
				NORMAL	
PEF	8.20 L/S	8.57 L/S	95.77 %		
FEF 25-75%	3.17 L/S	3.83 L/S	82.86 %	MAX FVC = 4.47L TEST # 2	
FEF 75-85%	0.66 L/S	0.99 L/S	67.14 %	MAX FEV-1 = 3.51L TEST # 1	
FEF 25	7.52 L/S	7.91 L/S	95.02 %		
FEF 50	4.31 L/S	4.51 L/S	95.47 %		
FEF 75	1.07 L/S	1.76 L/S	60.60 %		
FEF .2-1.2	7.42 L/S	7.17 L/S	103.48 %		



Legend
Pre-BD Test

THOMPSON 017979



CASEY, WILLIAM M

48 Y old Male. DOB: [redacted]/1958
419 QUAIL RIDGE CIRCLE, BOILING SPRINGS, SC-29316-6119
Home: 864-814-2617
Guarantor: CASEY, WILLIAM M Insurance: BCBS PPO
PCP: FRANK E GONDA

06/28/2007

Charles M. Fogarty, MD

Current Medications
Combivent 90 mcg-18 mcg/inh 2 puff(s) QID
Lipitor 20 mg 1 tab(s) once a day (at bedtime)
Tricor ? 1 tab(s) once a day
Lortab 10 500 mg-10 mg 1 tab(s) Q6H

Past Medical History
Chest wall pain
Hyperlipidemia
Difficulty with multitasking, concentrating, s/post pneumomediastinum/pneumothorax

Allergies
N.K.D.A.

CC
1. 6 MO F/U

Labs
Spirometry

Procedure Codes
SPIROMETRY

Electronically signed by CHARLES FOGARTY,MD PA on 12/22/2008 at 08:09 AM EST

Sign off status: Pending

Lung and Chest Medical Associates
2030 North Church Place
Spartanburg, SC 29303-2799
Tel: 864-582-6858
Fax: 864-542-9043

Patient: CASEY, WILLIAM M **DOB:** [redacted]/1958 **Age:** 48Y **Sex:** Male **Telephone Encounter**
Phone: 864-814-2617 **Primary Insurance:**
Address: 419 QUAIL RIDGE CIRCLE, BOILING SPRINGS, SC 293166119
Encounter Date:
Provider: FOGARTY,MD PA, CHARLES M

Answered by Pearson, Nicole

Date: 01/03/2007
Time: 03:04 PM

Refills
Start Lortab 10 500 mg-10 mg, 120, 1 tab(s) QID , Refills=5

Spiro

CMF WPS MLA EBK JDC RVM Beth Darla Lab

...ng and Chest Medical Associates Sptbg. ✓ Greer ____

me: Wm H. Casey Chart#: 7168 Date: 1-3-07

Wt 197.2 Ht ____ B/P 139/100 H/R 120 RR ____ Temp ____ 02Sat 97 FiO2 .21

Cough / Smoking
Sputum / Nausea
Dyspnea / Vomiting
Wheeze / Diarrhea
Edema / Chest Pain
Palpitations / Pain
Oriented / ETOH
New Allergies / Fever/chills

When was your last DEXA
Bone Densometry Testing done?
Seeing new doctors? no For: ____

Present Illness + reason for visit: ____

Wavering. Some Chest tightness. ↑ BP lately
some Lab
Worse w/ exception / worry
refill needed for Lotab
Still unable to organize self, plan
day to day Heart ↓ frustrated

Lotab 10 mg
combined 10 mg
tranxene 50 mg

Hospitalizations or major life changes since last visit: no

Meds. Review based on: ____ in bottle ____ on list ____ from memory

PHYSICAL EXAM: WNL/NEG ABN/POS

*General Appearance___
*Skin Turgor___
*ENT___
*Mouth___
*Sinus___
*Neck___
*Chest/Lungs: Breath Sounds ___
Wheezes___
Rales___
Effort___
Symmetry___
art: Rhythm___
Murmurs___
Gallop___
Tones___
*Abdomen___
*Extremities___
*Mobility: Gait___
Reflexes___
Aides___

(mild) for disorder but not
in basis of severe cognitive impairment

w/ memory, executive function not
tested

*Mental Status___

LAB ORDER: Spirometry___ EKG___ Sinus___ CBC___ Glu___ PT___ INR___ O2Sat Rest___
Lung Vol___ DLCO___ U/A___ CXR___ ABG's___ Bun___ Cre___ K+___ Theo___ 02Sat Exercise___

Office Treatment: ____

Education: Does pt want to quit smoking? Yes/No Other: ____

Materials/counseling given: ____

PFTs WNL

Diagnosis: ____ Plan ____

___Abn CXR(lung fluid),793.1
___Anticoagulant Circulating,28615
___COPD,496
___Cough,786.2
___Dyspnea,786.09
___Fatigue(general),780.79
___Fever,780.6
___ILD,515
___Monitoring(drug name_____),V58.1
___Rhinitis,477.9
___Sleep Apnea/Disorders (nec), 780.53

① Severe cog. relative impairment
S/P basal ganglia & pneumocephalus -
stroke + ? embolic

② Chronic CW Pain - Lortab,
fibrosis help

③ H-HTN - No added salt
diet

scriptions: ____

...ext appt: ___Weeks___Months W/ CMF WPS EBK MLA JDC RVM PA NP Signature ____ Staff ____
Next Visit: Spiro L/V DLCO PA PAL Sinus DEXA BLDWK ____ Other ____

RTO 4 mo

THOMPSON 017982

Lung and Chest Medical Associates
MultiSpiro A

ID: 77168 Casey, William Mark
Ethnic: CAUCASIAN Height: 68.0 in. Sex: MALE Age: 48 Weight: 197.0 lb

COMMENTS:
PRE-BD COMMENTS:

LAST CALIBRATED: Wed Jan 3,2007 7:22:27 am

TYPE	Test Date and Time	Exp.Time	Normals	Test#
Pre-BD:	Wed Jan 3,2007 2:35:55 pm	7.4 secs	KNUDSON/IMTS	1

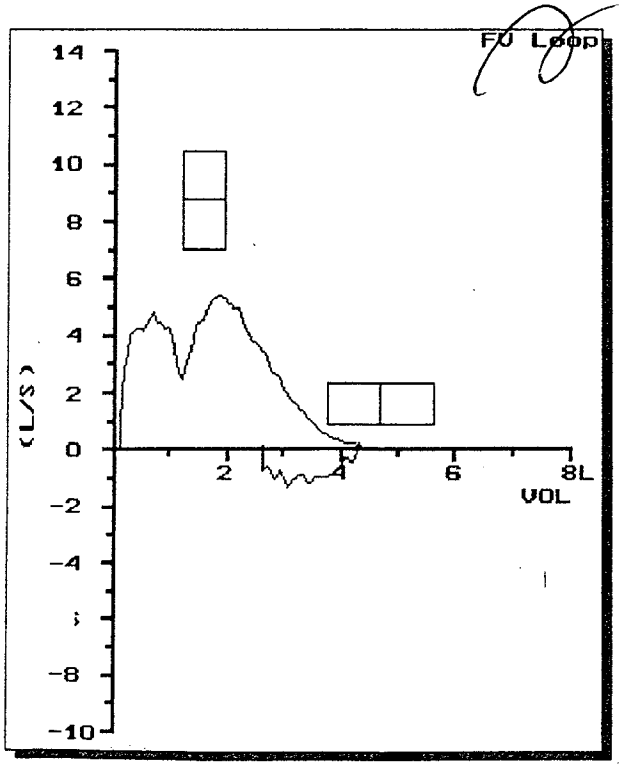
Expiratory	Actual	Predicted	% of pred
FVC	4.35 L	4.69 L	92.75 %
FEV 0.5	2.48 L	3.01 L	82.50 %
FEV 1.0	3.42 L	3.79 L	90.16 %
FEV 3.0	4.04 L	4.43 L	91.23 %
FEV 0.5/FVC	57.08 %	64.17 %	88.95 %
FEV 1.0/FVC	78.68 %	80.93 %	97.22 %
FEV 3.0/FVC	92.96 %	94.50 %	98.37 %
PEF	5.30 L/S	8.57 L/S	61.88 %
FEF 25-75%	3.11 L/S	3.83 L/S	81.22 %
FEF 75-85%	0.77 L/S	0.99 L/S	77.62 %
FEF 25	2.52 L/S	7.91 L/S	31.80 %
FEF 50	4.64 L/S	4.51 L/S	102.75 %
FEF 75	1.33 L/S	1.76 L/S	75.08 %
FEF .2-1.2	3.73 L/S	7.17 L/S	52.09 %

Inspiratory	Actual
IVC	1.73 L
FIV1	0.64 L
PIF	1.52 L/S
FIF50	1.35 L/S
FEF50/FIF50	344.62 %

Interpretation:

NORMAL

MAX FVC = 4.35L TEST # 1
MAX FEV-1 = 3.42L TEST # 1



Legend
Pre-BD Test

good effort

THOMPSON 017983

CASEY, WILLIAM M

48 Y old Male, DOB: [redacted]/1958
419 QUAIL RIDGE CIRCLE, BOILING SPRINGS, SC-29316-6119
Home: 864-814-2617
Guarantor: CASEY, WILLIAM M Insurance: BCBS PPO
PCP: FRANK E GONDA

01/03/2007

Charles M. Fogarty, MD

Current Medications
None

CC
1. 6 MO F/U

Vital Signs
Wt: 197.2, BP: 159/106, HR: 120, O2 sat: 97%, FIO2: .21, FVC: 4.35, FEV1: 3.42, FEV1/FVC%: 78.68%, Ht: 68, BMI: 29.98.

Labs
Spirometry FVC - 4.35/92%, FEV1 - 3.42/90%, %FEV1 - 78.68%, Marce 1/3/2007 2:46:02 PM >

Procedure Codes
SPIROMETRY

Electronically signed by CHARLES FOGARTY,MD PA on 12/22/2008 at 08:09 AM EST

Sign off status: Pending

Lung and Chest Medical Associates
2030 North Church Place
Spartanburg, SC 29303-2799
Tel: 864-582-6858
Fax: 864-542-9043

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M. NOEL TURNER, III

MAILING ADDRESS
P.O. BOX 3408 29304
PHONE: 864-585-8156
FAX: 864-583-6927

December 27, 2007

VIA HAND DELIVERY

Charles M. Fogarty, MD
Lung and Chest Medical Associates
2030 N. Church Place
Spartanburg, SC 29303

RE: William Mark Casey
DOB: [redacted]/58

Dear Dr. Fogarty:

My client, William Mark Casey, is still trying to understand why Dr. Joseph Boscia and Dr. Gregory Feldman felt there was a metal object in his chest that needed bronchoscopies to get it out. I think it would be helpful to Mr. Casey to understand if you showed him how a piece of metal laying underneath him or on top of him appeared on his plain chest film.

Would you consider taking a front to back x-ray with a piece of metal underneath his body or on top of his body that would give the impression that the piece of metal is actually inside his chest? Also, would you consider taking a side view chest film that shows the metal object is really outside of his body? Although we will probably never know the proper identification of the piece of metal that appears in the May 28, 2004 portable chest x-ray, please presume it is a small screw or the back of an earring. I am enclosing along with this letter the back of an earring that appears to be of similar size to the metal object in the x-ray taken of Mr. Casey on May 28, 2004. Obviously, I do not want to request anything that would create a further health risk to Mr. Casey and I would defer that judgment to you. I think this would help Mr. Casey to understand and visualize what I have been unsuccessful in trying to explain to him.

With warm regards,

I remain,
BURTS, TURNER, RHODES & THOMPSON

By: _____
RAY E. THOMPSON, JR.

2 Jan 08
PT. would like us to proceed c CXR

RET:ar
Enclosure

THOMPSON 017985

THE CIBA COLLECTION
OF MEDICAL ILLUSTRATIONS

Volume 7

Respiratory System

A compilation of paintings depicting anatomy and embryology, physiology, pathology, pathophysiology, and clinical features and treatment of diseases

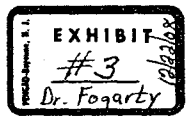
Prepared by

Frank H. Netter, M.D.

Edited by

Matthew B. Divertie, M.D.

Alister Brass, M.D.
Directing Editor



Commissioned and published by

CIBA

THOMPSON 017986

Rupture of Trachea or Major Bronchi

Rupture of the trachea or major bronchi is usually secondary to a nonpenetrating injury of the chest as a result of an automobile accident. It is a serious injury with an estimated overall mortality of 30%. More than 80% of the ruptures are within 2.5 cm of the carina. Injuries to the main bronchi and intrathoracic trachea are more prevalent than those to the cervical trachea because the latter is protected by the mandible and sternum anteriorly and by the vertebrae posteriorly.

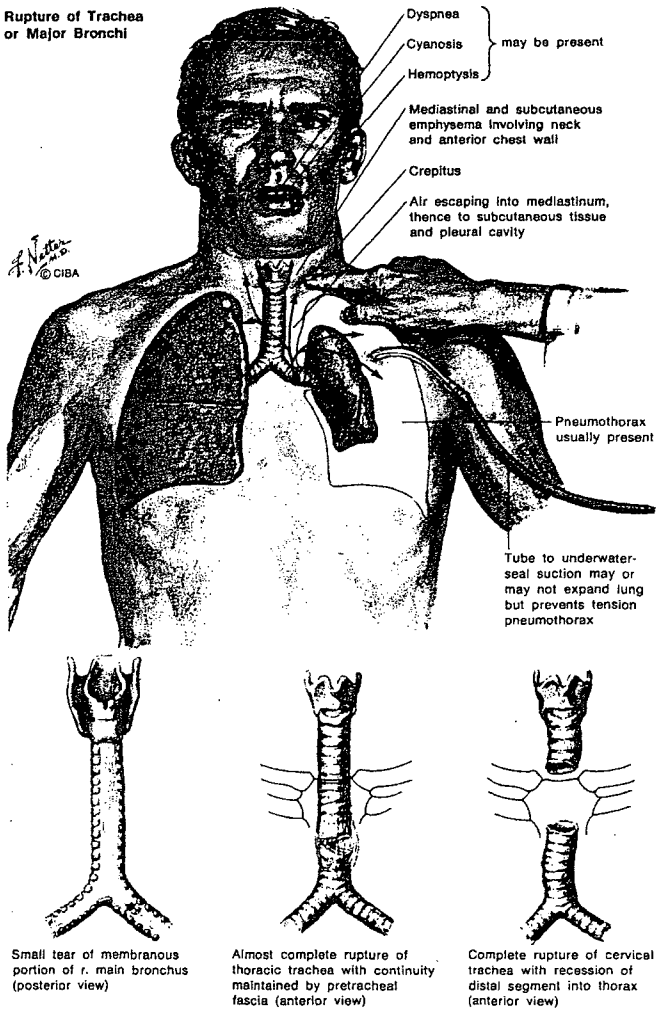
Intrathoracic tracheal lacerations usually occur at the junction of the membranous and cartilaginous trachea within 2.5 cm of the carina. When lesions are vertical, they occur posteriorly, where the cartilage is deficient. The most common site of major bronchial rupture is also within 2.5 cm of the carina. Major bronchial rupture is usually unilateral, and more frequent on the right side. Accompanying important injuries have been reported in only 50% of cases of tracheobronchial rupture, despite the severity of these injuries.

The clinical picture appears in two patterns, depending on whether or not there is free communication between the rupture of the tracheobronchial tree and the pleural cavity. If there is free communication, a large pneumothorax results. Tube thoracostomy causes continuous bubbling of air in the water seal, and suction fails to reexpand the lung. The usual signs of tracheobronchial disruption are hemoptysis, dyspnea, subcutaneous and mediastinal emphysema, and occasionally cyanosis. Subcutaneous and mediastinal emphysema develops from the leakage of air into the cervical area. Hemoptysis is ordinarily mild and probably results from disruption of a bronchial artery. Dyspnea occurs from loss of functioning lung tissue. Tension pneumothorax is uncommon as the intrapleural air decompresses itself through the mediastinum. On auscultation, Hamman's sign is evident—a crunching sound synchronized with the heart beat; it is due to mediastinal emphysema. In the second pattern of injury, there is little or no communication between the torn bronchus and the pleural cavity, even though the transection may be complete. If pneumothorax does occur, it is relatively small. When an intercostal tube is inserted, the lung readily expands, and the pneumothorax does not recur after the tube is removed. The small rent in the pleura is quickly sealed off with fibrin and blood clot. The air generally escapes into the mediastinum and may produce surgical emphysema of varying severity.

If transection of the bronchus is complete and surgical repair is not performed promptly, the proximal and distal ends of the torn viscus are sealed by granulation tissue. As the granulation tissue obstructs the bronchus, the lung becomes atelectatic. If healing takes place without leaving any lumen in the bronchus, the collapsed lung does not become infected. However, if transection is incomplete and the granulation tissue forms a stricture, partial bronchial obstruction occurs and often results in pulmonary infection and eventually irreversible destruction of lung tissue.

A chest x-ray film does not demonstrate bronchial rupture. However, findings that indicate a need for other diagnostic procedures include deep cervical emphysema, pneumomediastinum, subcutaneous emphysema, pneumothorax, fractures of the upper five ribs, and air surrounding the bronchus. Air in the bronchus, visualized on a bronchogram, indicates a possible obstruction. Deep cervical emphysema is one of the earliest and most reliable of the indirect findings on the x-ray film. Fractures of the first three ribs heighten suspicion of associated major airway damage.

Bronchoscopy should be carried out promptly when tracheobronchial rupture is suspected, since it is the most reliable means of establishing the diagnosis. If bronchoscopy indicates that the bronchial tear involves less than one-third of the lumen, and if the thoracostomy tube underwater-seal drainage results in complete expansion of the lung, treatment may be conservative. However, in all other types of tracheobronchial injury, thoracotomy should be performed as soon as the patient's condition permits. (See Plates 10, 11 and 12 for surgical management.)



THOMPSON 017987

Subcutaneous Emphysema and Traumatic Asphyxia

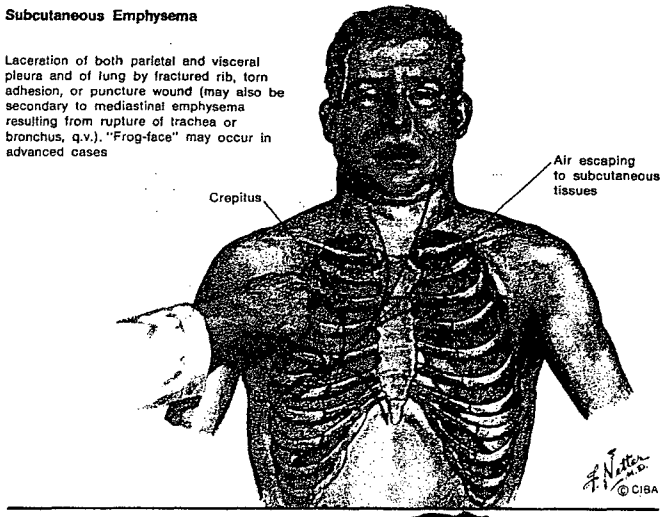
Subcutaneous emphysema is a condition in which air is present in the tissues under the skin, particularly in the region of the head, neck and chest. It has several causes: (1) A fractured rib may damage the lung as well as the parietal pleura. (2) Tearing of pleural adhesions from a previous pleuritis may permit escaping air to enter the subcutaneous tissues. (3) It may result from positive pressure anesthesia or mechanical ventilation and is then known as "surgical emphysema." (4) It may occur before or after tracheostomy—airway obstruction prior to tracheostomy causes high alveolar pressures and may lead to alveolar rupture, with air traveling to the mediastinum by the interstitial route; following tracheostomy and neck surgery, air passes through the cervical incision along the outside of the trachea and into the mediastinum during inspiration; airway obstruction facilitates the passage of air by creating excessive negative intrathoracic pressure during inspiratory effort.

The diagnosis of subcutaneous emphysema is readily evident by the palpation of crepitus in the subcutaneous tissues and by the grotesque appearance of the face and head ("frog-faced man") which may develop. A chest x-ray film is mandatory to determine the presence or absence of a pneumothorax, which, if present, must be promptly treated.

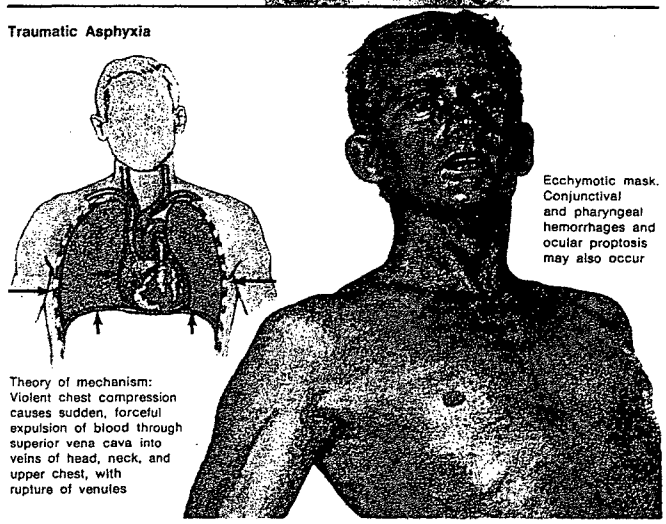
If subcutaneous emphysema is well tolerated, there is minimal risk to the patient, and heroic methods of therapy are not needed. An additional chest tube is sometimes required for more efficient removal of air from a coexisting pneumothorax. If the condition is severe, a tracheostomy may be performed; this permits the escape of air by incision through the layers of cervical fascia and also allows adequate ventilation of the patient.

Traumatic asphyxia is a condition in which there is violaceous discoloration of the skin of the head, neck, shoulders and upper chest, together with bilateral subconjunctival hemorrhages and scattered petechiae over the upper part of the body. It results from a severe compressive force upon the thorax and upper abdomen. This clinical picture was first described by Ollivier in 1837, when he saw it in patients crushed to death by crowds in Paris. He coined the term *masque ecchymotique*. This form of crush injury may also occur from a heavy falling object, as in the case of an individual working under an automobile, which then slips and crushes the chest or upper abdomen. Deep-sea divers sustain similar injuries from underwater explosions. Depending on the cause, traumatic asphyxia may be critical, with death following immediately.

Subcutaneous Emphysema



Traumatic Asphyxia



Of patients who survive the first few hours after injury, 90% will recover from traumatic asphyxia when it occurs as a single entity. Survival is directly related to the extent of associated injury.

Associated injuries are common and include injury to the chest wall, rib fractures, pulmonary contusion, pneumothorax and hemothorax. Damage to the heart and great vessels is rare. Sudden permanent loss of vision is attributed to retinal hemorrhage, and immediate transient loss of vision to retinal edema. The latter may be accompanied by papilledema, which is seen on funduscopic examination. There may be unilateral or bilateral subconjunctival hemorrhage, with or without conjunctival edema, and this is a fairly constant finding. Neurologic manifestations are frequent, as one-third of the patients become unconscious at the time of the injury. Intracranial or intracortical hemorrhages are rare even when injuries are fatal. Skeletal fractures are common.

No specific treatment is required for traumatic asphyxia, and all efforts are directed to management of associated injuries. However, the patient should be placed in an environment which will ensure a 40% oxygen concentration in the trachea. This concentration of oxygen not only provides safe oxygenation but also hastens absorption of any air within the mediastinum.

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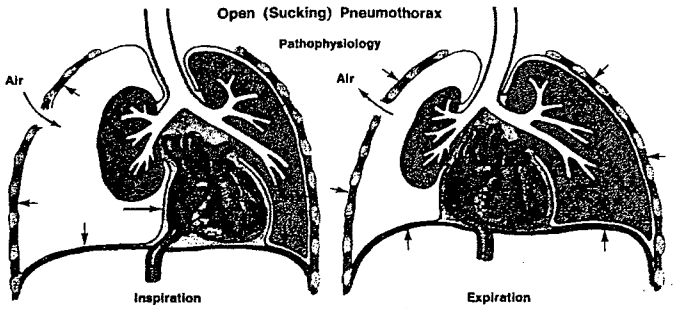
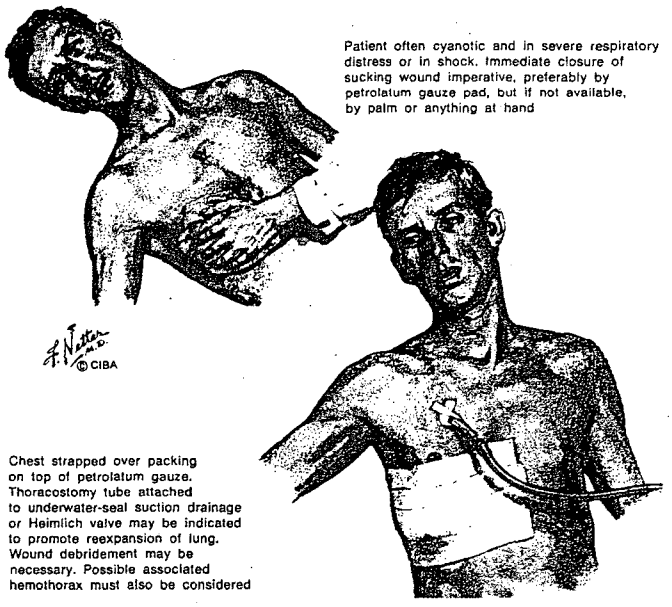
Open Pneumothorax



Air enters pleural cavity through open, sucking chest wound. Negative pleural pressure is lost, permitting collapse of ipsilateral lung and reducing venous return to heart. Mediastinum shifts, compressing opposite lung

As chest wall contracts and diaphragm rises, air is expelled from pleural cavity via wound. Mediastinum shifts to affected side and mediastinal flutter further impairs venous return by distortion of venae cavae



Patient often cyanotic and in severe respiratory distress or in shock. Immediate closure of sucking wound imperative, preferably by petrolatum gauze pad, but if not available, by palm or anything at hand

Chest strapped over packing on top of petrolatum gauze. Thoracostomy tube attached to underwater-seal suction drainage or Heimlich valve may be indicated to promote reexpansion of lung. Wound debridement may be necessary. Possible associated hemothorax must also be considered

Open pneumothorax usually results from a penetrating wound of the chest and is always a serious condition. Ancient warriors knew that if they could open an opponent's chest with a sword or lance the wound would always be fatal. In an open or "sucking" wound of the chest wall, the lung on the affected side is exposed to atmospheric pressure, which results in the lung's collapse and a shift of the mediastinum to the uninvolved side. Air passes into the chest more easily on inspiration than it can leave during expiration and this permits a progressive collapse of the lung. As the lung on the affected side is collapsed, the increased pleural pressure there pushes the mediastinum to the uninvolved side, thereby diminishing the contralateral lung volume. Because of the severe degree of venoarterial shunting that occurs in both lungs, resulting in profound ventilation-perfusion inequality, the patient becomes cyanotic and has serious respiratory distress.

The ability to tolerate the effects of a sucking wound of the chest depends on the patient's general condition and on whether previous fixation of the mediastinum has occurred. As the wound is sustained away from the hospital, the best first aid measure is the immediate restoration of the integrity of the chest wall by closure of the sucking wound with any material at hand such as a towel or other cloth, whether sterile or not; an occlusive dressing over the open wound is critically important to prevent death from anoxia.

Once the patient reaches the hospital emergency room, the sucking wound can be temporarily occluded with a massive dressing of petrolatum gauze, covered by dry gauze held in place by adhesive strips. A useful maneuver is to evacuate the pleural cavity by holding the wound open while the patient coughs or exhales forcefully and then manually to reapproximate the wound when the patient inhales. A large amount of blood or air may be removed by this procedure. Once the open penetrating wound is converted to a closed wound, a thoracostomy tube must be placed in the chest for drainage of any associated hemothorax or pneumothorax. The tube is connected to an underwater seal for evacuation of air and measurement of the amount of blood loss. Examination of such a wound, which is usually the result of gunshot or stabbing, must be very thorough. A chest x-ray film is taken to disclose possible foreign bodies, fractured ribs or other intrathoracic damage.

The patient is next taken to the operating room, where sterile technique must be used to carry out careful cleansing, debridement, meticulous examination and repair. Clean wounds seen in the first 8 to 12 hours after injury may be sutured initially, but older or contaminated battlefield or disaster wounds are better handled by simple suture of the muscles of the chest wall. Closure of the skin is completed several days later if reexamination under sterile conditions shows that the wound is clean. Antitetanus therapy is carried out with toxoid and human tetanus immune globulin. All patients should also receive antibiotics, as these wounds must be considered contaminated.

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Tension Pneumothorax

Tension pneumothorax may result from a variety of causes. In civilian life the most common cause is either a stab wound of the chest or a rib fracture, with the sharp end of the fractured rib lacerating the visceral pleura of the lung and permitting air to escape into the pleural space. In this cavity the rise above normal subatmospheric pressure, together with the lung elastic recoil, causes the lung to collapse partially or completely. Other traumatic causes of pneumothorax may be iatrogenic, such as the use of positive airway pressure during mechanical ventilation or anesthesia; cannulation of the subclavian or the internal jugular vein for hemodynamic monitoring; and performance of a tracheostomy, particularly in children. When respiratory distress or cyanosis is not relieved following establishment of a patent airway, pneumothorax should be suspected.

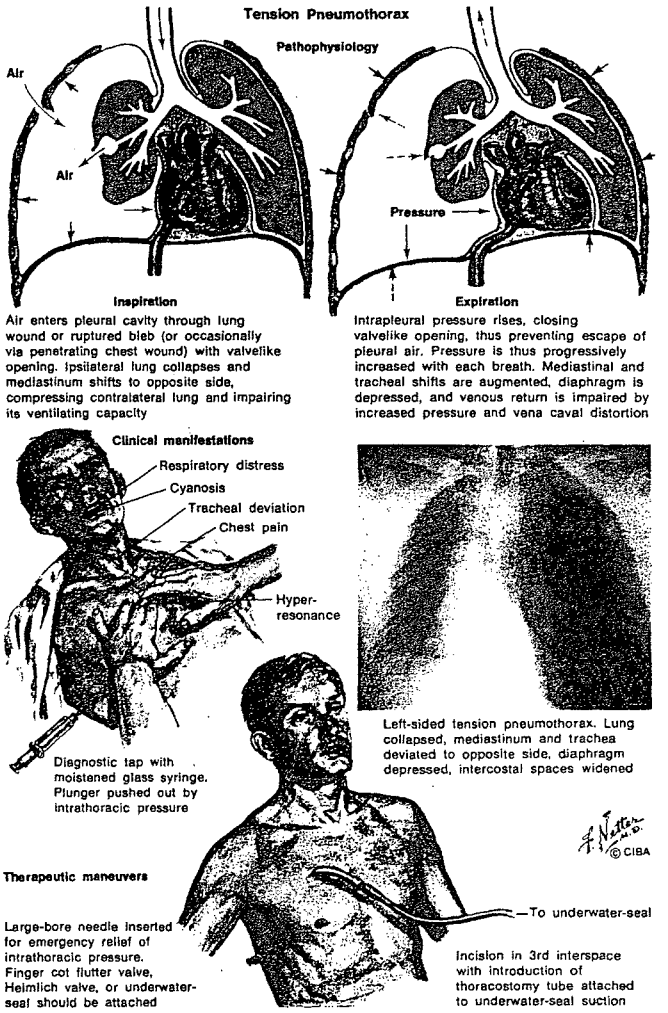
Thoracentesis is another relatively common cause of pneumothorax, usually by permitting air to enter through the needle. Laceration of the visceral pleura by the needle's point may also occur.

With any of these causes of pleural air leak the emergency situation of tension pneumothorax may arise. At each inspiration, intrapleural pressure increases because of a ball-valve mechanism that permits air to enter but not leave the pleural space. As the pressure constricts and distorts the venae cavae, the venous return to the heart is impaired, resulting in a decrease in stroke volume and cardiac output. Clinically, the patient experiences dyspnea, complains of chest pains, and becomes cyanotic because of shunting in the collapsed lung. The presence of hyperresonance and the absence of breath sounds, together with x-ray examination, should be useful in confirming the cause of the emergency.

On the electrocardiogram, four relatively consistent changes are observed: (1) a rightward shift in the mean frontal QRS axis, (2) a diminution in precordial voltage, (3) a diminution in QRS amplitude, and (4) an inversion of precordial T waves. A chest x-ray film indicates that the trachea and mediastinum are deviated to the side opposite the tension pneumothorax, while on the ipsilateral side the intercostal spaces are widened and the diaphragm is pushed downward. Since this critical emergency seldom permits time for x-ray confirmation, diagnostic needle insertion must be done. This distinct emergency requires immediate thoracostomy with underwater-seal drainage. Using local anesthesia a stab wound is made in the second anterior intercostal space on the affected side, two fingerbreadths lateral to the sternum to avoid the internal thoracic (internal mammary) vessels. A hemostat or scissors is used to separate the muscles, and the pleural space is entered just above the third rib to avoid bleeding from the intercostal vessels. A chest tube is then inserted into the pleural space and the incision closed with one or two sutures, which are additionally employed to secure the chest tube. Trocars, once commonly used for this purpose, are less frequently used today as they may lacerate organs and vessels.

If the tube is to be placed in the lower lateral chest wall—a useful site if blood or fluid is also present—care must be taken to avoid placing it subdiaphragmatically or through the diaphragm, which could lead to penetration of the liver or spleen.

Any patient with trapped air in the pleural space who is to be given positive pressure anesthesia or supported by mechanical ventilation should have a thoracostomy tube inserted to prevent development of a tension pneumothorax. Positive pressure breathing can cause alveolar rupture due to pulmonary overinflation. This may produce surgical emphysema, with diffusion of air via the mediastinal pleura or pretracheal fascia into the subcutaneous tissues of the neck. Subsequent rupture of the mediastinal emphysema through the pleura will result in a pneumothorax. Bubbles in the pulmonary interstitium cause increased airway resistance and splinting of the lungs in the inspiratory position. As airway resistance increases, the patient exerts greater ventilatory effort, thus forcing more air into the pulmonary interstitium. However, high concentrations of inspired oxygen will reduce a pneumothorax by displacing nitrogen.



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Martini's Atlas of the Human Body

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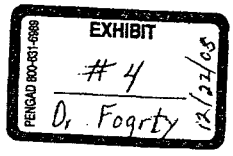

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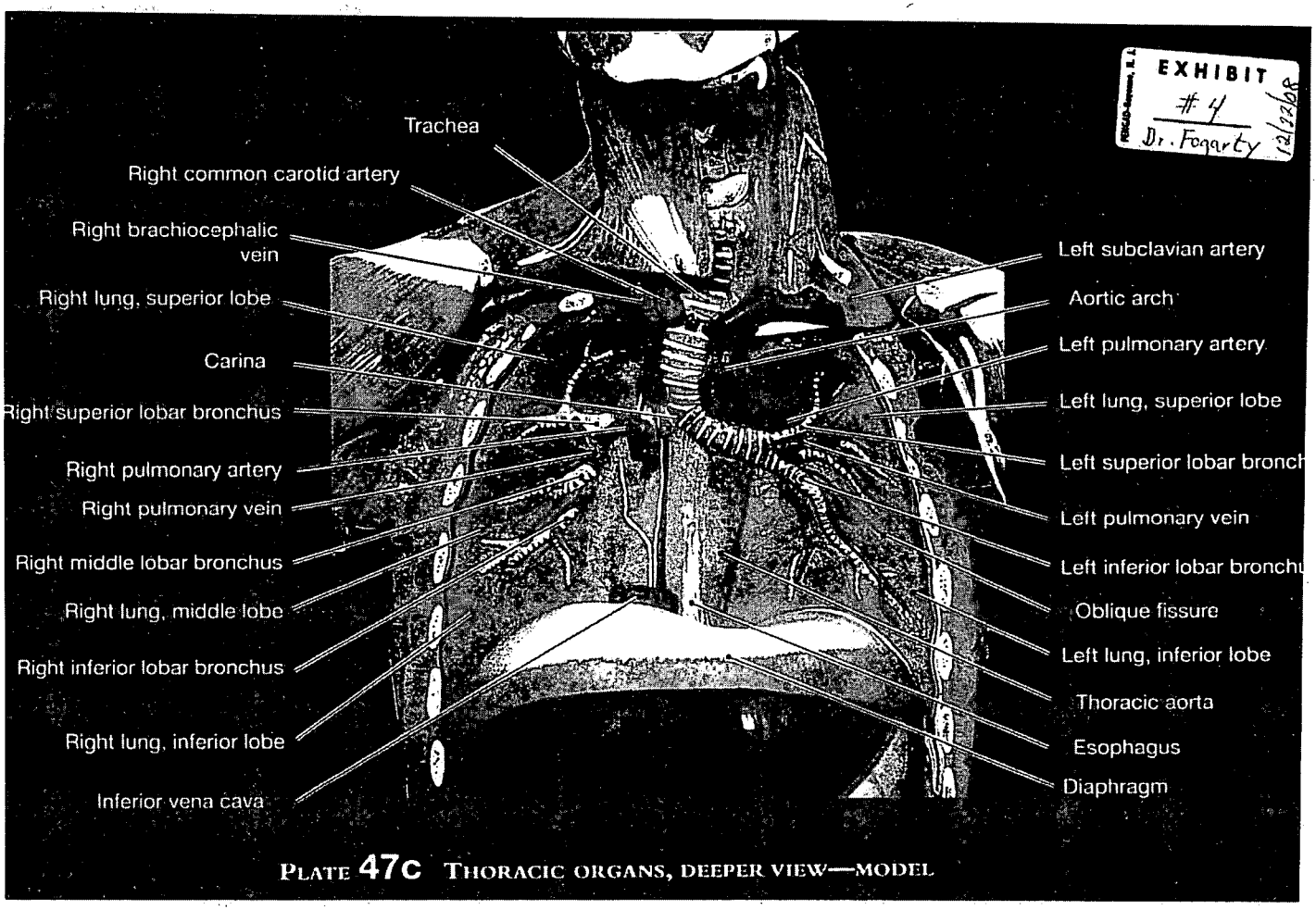

PLATE 47c THORACIC ORGANS, DEEPER VIEW—MODEL

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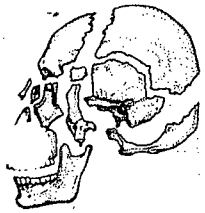
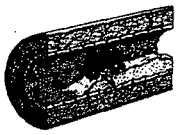
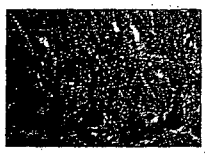
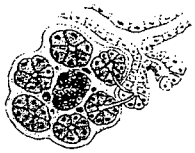
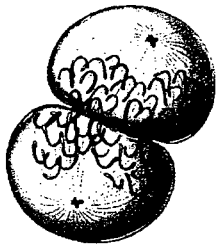
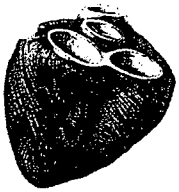





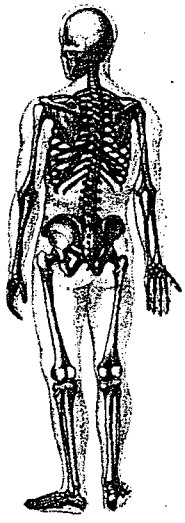


THE HUMAN BODY

AN ILLUSTRATED GUIDE TO ITS STRUCTURE, FUNCTION, AND DISORDERS

Editor-in-Chief
CHARLES CLAYMAN MD





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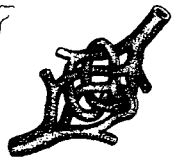

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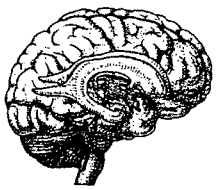

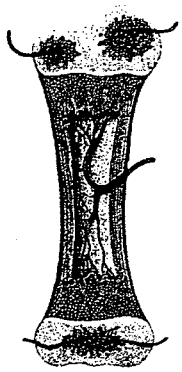

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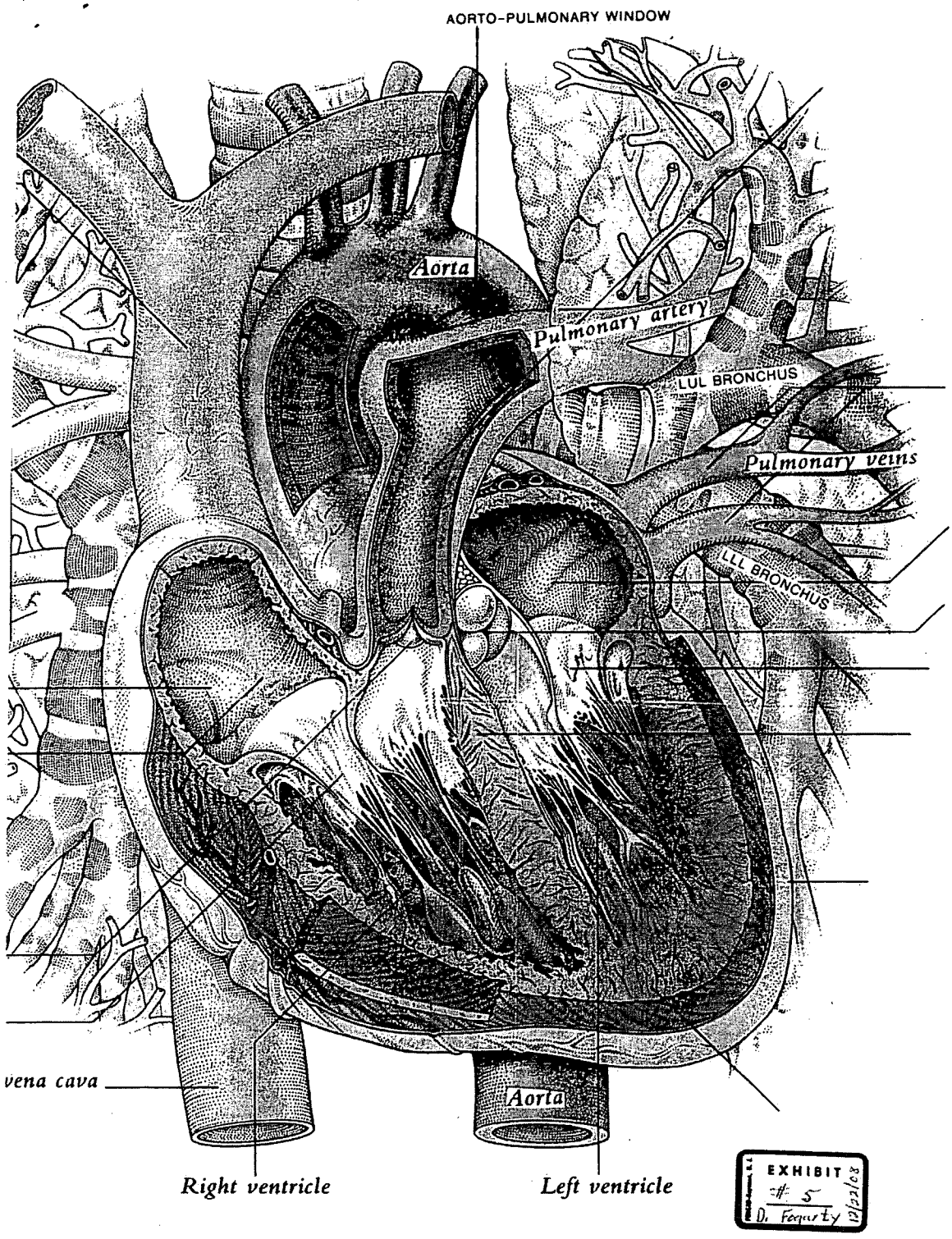

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Flexible Bronchoscopy, 2nd Edition

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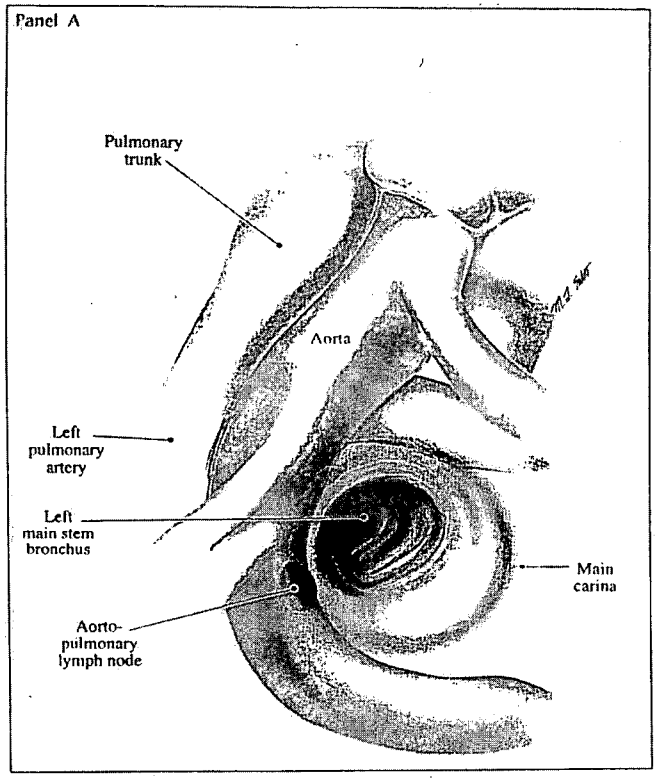

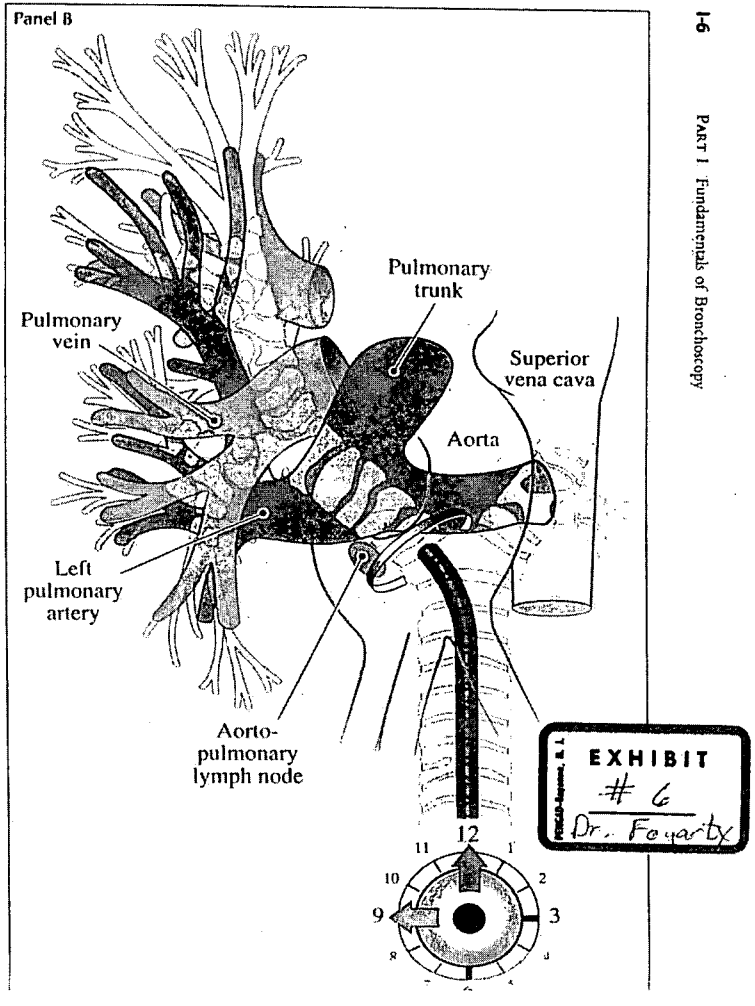

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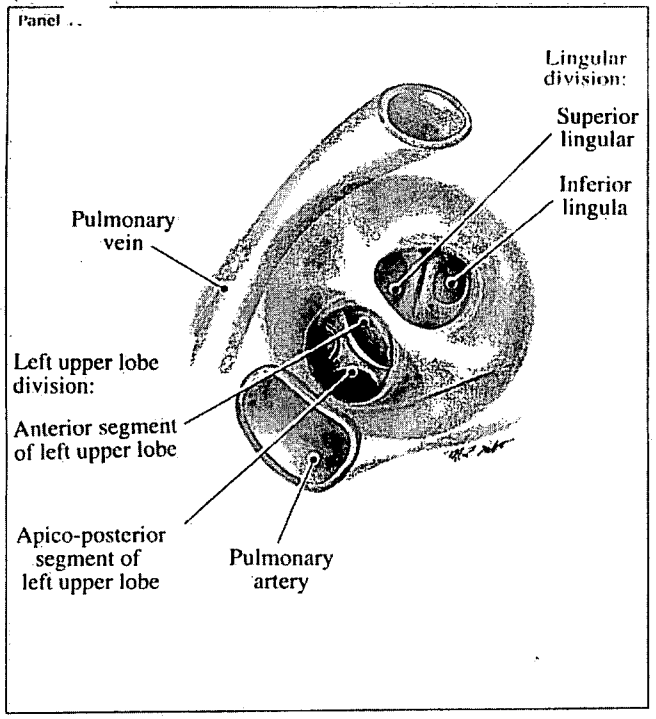
FIGURE 5-6. *Representation of normal anatomic relationships at the level of the left main stem bronchus orifice.*
Panel A illustrates the endoscopic view of the left main stem bronchus, with vessels and the aortopulmonary lymph node superimposed at the nine o'clock position.
Panel B shows an endoscopic clock-face view. The arrow at nine o'clock indicates the proper site for TBNA of aortopulmonary lymph node below the aortic knob. The arrow at twelve o'clock indicates the unsafe location (left pulmonary artery).



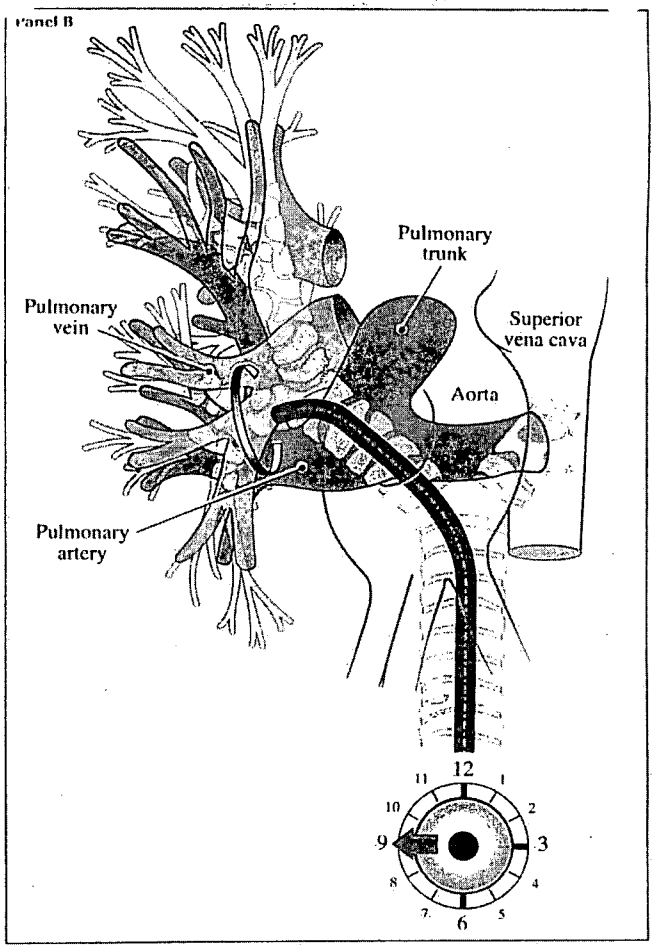


FIGURE 5-7. ***Representation of normal anatomic relationships at the level of the left upper lobe orifice.***
Panel A illustrates the endoscopic view of the left upper lobe bronchus, with vessels superimposed.
Panel B shows an endoscopic clock-face view. The arrow at nine o'clock indicates the location of the left pulmonary artery.

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Chapter

19

Bronchoscopy in Foreign Body Removal

ALBERT L. RAFANAN ATUL C. MEHTA

INTRODUCTION

gle most important instrument available to the clinician for the diagnosis and treatment of tracheobronchial foreign bodies is the flexible bronchoscope. The flexible bronchoscope is the "gold standard" for the diagnosis of airway foreign bodies and is the preferred instrument for its removal in adults (1).

Tracheobronchial aspiration of a foreign body occurs commonly in extremes of age—the young and the elderly. Aspiration of a foreign body presents with a myriad of symptoms. Clinical history and exam, as well as radiological techniques are helpful, but most often the diagnosis can only be made by direct visualization with a flexible bronchoscope. In adults, foreign body removal can often be accomplished during the initial procedure.

Bronchoscopic removal of an airway foreign body is both a highly challenging and rewarding procedure. The bronchoscopic approach is never the same, because permutations of foreign body type, location, and tissue reaction are numerous. Various objects pose different challenges to the bronchoscopist attempting the removal; but in expert hands, removal of the foreign body is rewarding as the success rate is high and the complication rate quite low.

This chapter reviews the clinical and radiographic presentation of foreign body aspiration, associated complications, and the available techniques for removal. Specific attention will be paid to removal techniques and current available accessories for the flexible bronchoscope.

INCIDENCE

In . . ., suffocation by a foreign body accounted for 3515 (1.3 per 100,000) deaths (2). In the past 10 years, death rates have been almost constant (2). Deaths from foreign body aspiration present in a bimodal pattern, with peaks at ages less than 1 (1.9 per 100,000) and greater than 75 years (10.7 per 100,000) (2). The death rate declines after age 5 but increases again beginning at the fourth decade of life. Most of these asphyxiating events occur at home (41%), in restaurants (29%), or in nursing homes or mental institutions (14%) (3).

Non-asphyxiating aspiration of foreign bodies, however, is more commonly seen in childhood. The incidence of airway foreign body aspiration has not decreased over time, but the *associated* morbidity and mortality has significantly decreased with greater awareness of clinicians and the development of better bronchoscopic and radiological technology. As outlined in Table 19-1, the majority of patients are under age 3. About 75% to 85% of all foreign body aspiration occurs in children less than age 15 (4–6). Small children are predisposed to aspiration because they tend to put objects into their mouths and have poor masticating and deglutition skills. Moreover, they often laugh, talk, cry, or play with food in their mouths. In adults, foreign body aspiration is more commonly seen in the elderly, mostly due to the failure of airway protective mechanisms (4–6). Factors that predispose adults to foreign body aspiration are listed in Table 19-2.

CLINICAL PRESENTATION

The clinical presentation of airway foreign bodies is largely dependent upon the type of foreign body, site of object impaction, and the age and mental state of the individual. Large objects can easily occlude the larynx and will present as severe coughing, choking, hoarseness, and gagging in the alert individual. Respiratory arrest and cyanosis can sometimes occur. In these instances, the Heimlich maneuver is recommended to expel the foreign body (7). In individuals with a depressed mental state or in young children, large foreign body aspiration can present solely as cyanosis and cardiac arrest. Basic life-support training dictates that during cardiac arrest, the airway always be examined before cardiac compression is performed.

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Table 19-1. Foreign Body Aspiration

Abdulmajid (12)	250	42% < 2 y	NA	85
Dantilidis (34)	90	65% < 2	59% < 24 h	78
Kashtalia (14)	41	50% < 16 mo	50% < 48 h	71
Black (60)	262	61% < 3 y	61% < 48 d	74
Wiseman (9)	157	80% < 3 y	48% < 24 h	65
Weissberg (41)	66	40% < 2 y	55% < 24 h	67
Banerjee (8)	223	63% < 3 y	52% < 24 h	66
Ebrahami (35)	1822	"Majority" 1–2 y	34% < 24 h	81
McGuirt (11)	88	61% < 3 y	NA	66
Puhakka (13)	83	59% < 2 y	68% < 24 h	59
Steen (23)	94	77% 1–3 y	70% < 72 h	89
Baharloo (6)	112	75% ≤ 8 y	40.3 ± 87 days (adult) 9.5 ± 16.4 days (child)	84
Hsu (100)	459	80.2% < 10 y	NA	80

Table 19-2. Risk Factors for Foreign Body Aspiration in Adults

1. Alcohol intoxication
2. Sedative or hypnotic drug use
3. Poor dentition
4. Senility
5. Mental retardation
6. Parkinson's disease
7. Primary neurologic disorders with impairment of swallowing or mental status
8. Trauma with loss of consciousness
9. Seizure
10. General anesthesia

If the foreign body is small enough to pass below the vocal cords into the subglottic or tracheal region, inspiratory stridor with bouts of coughing may be noted. If it passes into the bronchi, then there may be minimal symptoms other than a unilateral or localized wheeze. The classic triad of cough, wheezing, and choking is present only in a small percentage of patients (8,9). Common symptoms with a nonasphyxiating foreign body aspiration reported in the literature are listed in Table 19-3.

A high index of suspicion is most often necessary so as to avoid missing the diagnosis of a foreign body. Figure 19-1 is a bronchoscopic image obtained from a middle-aged female who had been complaining of a chronic cough and wheezing. She had been misdiagnosed with asthma and treated with multiple courses of antibiotics and steroids before she was referred to us. Chest radiograph was normal, but on examination, wheezing was localized to the right lower lobe. Bronchoscopy was performed and this revealed a vegetable material lodged at the right lower lobe lateral subsegment. Removal was performed successfully during the same bronchoscopic session with the techniques described below.

Table 19-3. Symptoms Associated with Foreign Body Aspiration in Children and Adults

Cough	83	61
Dyspnea	25	16
Cyanosis	25	Not reported
Fever	16	21
Wheezing	12	19
Choking	10	3
Hemoptysis	Not reported	21
Chest pain	Not reported	4
No symptoms	4	1

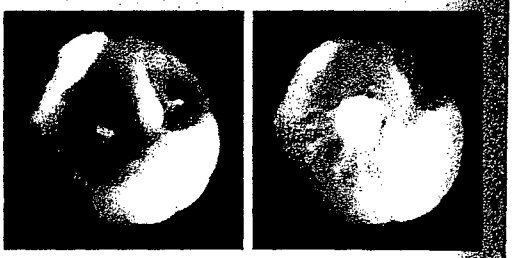

FIGURE 19-1. *Vegetable material lodged in the lateral basal segment of the right lower lobe, giving rise to chronic cough and wheezing.*

LOCATION OF THE FOREIGN BODY

In adults, the most common site of impaction is the right lower lobe bronchus because it is larger and more vertically continuous with the trachea (4,6,10). Foreign body aspiration ranges from 40% to 70% on the right, 30% to 40% on the left, and 10% to 20% in the laryngotracheal area (8,11,14). The foreign body, however, can be impacted at any subsegment (4). In children, the left and right mainstem bronchus diameter and the angle of takeoff are similar (15). Some authors report an almost equal incidence of aspiration to both main bronchi (16–18); however, others report an increased incidence of aspiration to the right mainstem similar to adults (20–22).

TYPES OF FOREIGN BODY

Foreign bodies in the airway are classified in two ways: inorganic and organic substances. In children, the most common foreign bodies are organic, such as peanuts, grains, nuts, and seeds (11,23). In adults, the foreign body type can be unpredictable, but the majority of aspirated foreign body is organic, usually plant material (4,5,10). In general, aspirated organic material can cause a more vigorous host response. Severe bronchial mucosal inflammation with the development of granulation tissue can occur in a few hours. Moreover, rehydration of organic foreign bodies such as beans, seeds, and corn can acutely cause them to swell and may lead to total obstruction. Aspirated grass inflorescences

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o migrate distally, creating a chronic inflammatory reaction requiring lung resection if not removed early (24–26).

Inorganic foreign bodies, such as metallic and plastic objects, can sometimes be tolerated for years with paucity of symptoms, because they may not cause any host reaction. In adults, dental equipment or prosthesis, tracheostomy tube segments, and endotracheal tube (ETT) appliances have been commonly reported (4). Aspiration of medications have been reported and this can cause a vigorous tissue reaction leading to excessive granulation tissue (27–29). Pill rehydration can also lead to rapid reexpansion and acute obstruction (30).

Lifestyle may also predispose to unusual types of aspiration. For instance, hypodermic needle aspiration was reported in nine drug addicts who held the needle between their lips while drawing heroin into a syringe (31). Similarly, activities such as the use of a blowgun may result in aspiration of the dart (32,33).

Cultural and regional differences also lead to variations in foreign body aspiration. Peanuts universally head the list in the United States and northern Europe with an incidence of 30% to 50% (8,9,11,13,23). Pumpkin seeds accounted for 22 (24%) of 90 cases reported from Greece with peanuts the second most commonly aspirated substance at 12 (13%) of 90 (34). Melon seeds are commonly aspirated in Middle Eastern countries (12,35). Watermelon seeds accounted for 1208 (66%) of 1822 cases of foreign body aspiration in Iraq, where watermelon is equently and young children are often given fruit without seeds removed (35). Prayer beads and worry beads are common in Islamic countries and explain their prominence in 42 (22%) of 188 cases among the nonorganic types (35).

DIAGNOSTIC AND RADIOGRAPHIC EVALUATION

A high index of suspicion for a possible airway foreign body obstruction is needed to avoid the potential complications that could arise from a delayed diagnosis. A careful history will elicit the diagnosis in 40% to 50% of patients (9,12,23). Although the classic triad of coughing, choking, and wheezing is present in only a small percentage of patients, 80% or more will have at least one feature of the triad (9). Physical exam can show stridor and decreased breath sounds, rales, and wheezing over the affected site.

The chest radiograph is often the initial diagnostic test ordered when foreign body aspiration is suspected. Unfortunately, this is of limited help. In one study, the chest radiograph was found to only have a diagnostic accuracy of 67%, sensitivity of 68%, and specificity of 67% (36). A definitive diagnosis can be made in the small percentage of patients with an opaque foreign body. Subtle signs such as air trapping may be present in 40% to 50%, with atelectasis, mediastinal shift, and p ary infiltrates present in a small percentage (8,37). F ory chest radiograph and fluoroscopy may identify a mediastinal shift during active respiration, confirming air trapping with a normal film (9,11,38).

Unusual radiographic presentations such as pneumomediastinum in a child under age 2 should suggest foreign body aspiration (39). Lateral neck films revealing a subglottic density or swelling may be suggestive in the patient with a laryngotracheal foreign body (40). However, initial localization of the foreign body by chest radiograph does not negate the need to perform a complete endobronchial examination, because the object can change position between the time of the initial radiographic examination and its removal (41). Further, other foreign bodies in addition to the one suggested by the chest radiograph, might be present in the airway (11).

FIGURE 19-2. *Aspirated tooth cap.*

Other radiologic diagnostic tests such as CT scan and V/Q scan (ventillation and perfusion lung scan) seldom help in making a definitive diagnosis (42,43). Radiographic evaluation is helpful, but flexible bronchoscopy is the gold standard in the identification and localization of an airway obstruction. It is recommended that patients with a definitive history of foreign body aspiration—even with a normal physical examination and radiographic findings—must undergo bronchoscopic investigation, because a delayed diagnosis can lead to irreversible complications (44).

Aspirated foreign bodies in adult airways may also be misdiagnosed as an endobronchial tumor (45) or even a peripheral lung cancer (46). Figure 19-2 reveals an aspirated tooth cap removed from the right bronchus in a patient referred with a diagnosis of cancer. The off-white color of the dental cap along with the surrounding granulation tissue contributed to the misdiagnosis. In children, the presence of granulation tissue in the airway should lead to an active search for a foreign body, because primary airway bronchopulmonary tumor are rare in children (47).

COMPLICATIONS OF FOREIGN BODY ASPIRATION

Acute complications from nonasphyxiating foreign body aspiration include the development of a pneumothorax, pneumomediastinum, and obstructive emphysema. More frequently, irreversible complications occur due to a delay in diagnosis, because the object can cause an excessive host reaction and lead

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Table 19-4. Complications of Delayed Removal of Airway Foreign Bodies (24,49)

1. Recurrent pneumonia
2. Bronchial stenosis
3. Bronchiectasis
4. Irreversible damage to the obstructed lobe
5. Recurrent hemoptysis
6. Chronic lung disease
7. Bronchopleural and bronchocutaneous fistulae
8. Pleural effusion
9. Empyema cavity
10. Osteomyelitis of the rib

to infection (Table 19-4). Complication rate is significantly higher in those patients with a delay in diagnosis of greater than 24 hours (40).

Frequently, the diagnosis of the presence of a foreign body can be missed because there may be no history of choking, aspiration, or precipitating event (48). In adults, the foreign body may frequently be lodged in the distal subsegmental airways and can present as subtle and nonspecific symptoms. This will most often lead to a delay of diagnosis (5). Delayed diagnosis as late as 13–25 years after the aspiration has been reported (6,10,49).

Because the airway caliber is much smaller in children, foreign bodies most often will be in the central tracheobronchial tree, thus most airway foreign bodies in children are symptomatic and diagnosed earlier compared to adults (6). In children, especially infants less than a year old, the average delay of diagnosis is significantly lower (6). Notwithstanding, a delayed diagnosis does occur in 12% to 26% of children (50). Some centers have reported a delay average of 35 days where children were treated for prolonged periods for asthma and pneumonia prior to the correct diagnosis (51).

MANAGEMENT OF FOREIGN BODY ASPIRATION

The patient with suspected foreign body aspiration should remain under medical observation until the diagnosis can be confirmed or excluded and an appropriate management plan for its removal is devised. Sudden, proximal migration of the object to the trachea may lead to asphyxiation and cardiopulmonary arrest, particularly in small children (14,52). Once a foreign body is identified, it should be removed promptly. The likelihood and extent of tissue reaction increases the longer a foreign body remains in the airway (9,23,53). Wiseman (9) notes absent or mild endobronchial inflammation in 69 (96%) of 72 patients presenting less than 24 hours after aspiration. Severe bronchial inflammation defined by the presence of erythema, edema, granulation tissue, and purulent secretions was noted in 31 (36%) of 85 patients presenting more than 24 hours after the event. However, in the absence of acute respiratory distress, a delay of several hours to ensure an organized coordinated approach to removal is appropriate.

Rigid bronchoscopy, fiberoptic bronchsocopy, and physical therapy have been proposed as possible management strategies. Thoracotomy has been required in a small number of cases when the above strategies failed or resection of bronchiectatic segment was required (1,9). Nonremoval of nonobstructing inert foreign body may be appropriate in selected cases, avoiding the morbidity associated with thoracotomy. The relative advantages and disadvantages of each therapeutic option will be discussed.

Postural Drainage

In 1973, Cotton and associates (54) reported their experience with bronchodilator inhalation and postural drainage in foreign body removal in 24 children age 10 months to 16 years. Ninety-two percent (n = 22) successfully coughed out the object; however, the other 8% (n = 2) had cardiopulmonary arrest as a result of proximal migration of the foreign body. In a report of 57 patients from the same institution, Campbell and colleagues (55) proposed a dual approach to foreign body removal. Centrally located foreign bodies (n = 29) were removed directly by rigid bronchoscopy. Children with peripherally located objects (n = 28) received 48 hours of postural drainage. Of 28 patients, the object was successfully coughed out in 64% (n = 18) with 8 of 10 remaining foreign bodies removed successfully via rigid bronchoscopy. No complications were encountered. Hospital stay was slightly longer (4.2 versus 3.4 days) in the chest physical therapy group.

Law and Kosloske (53) also compared postural drainage and bronchoscopy. The foreign body was cleared successfully in 12 (25%) of 49 children treated with postural drainage, whereas in 56 (89%) of 63 the object was removed successfully with rigid bronchoscopy. Complications were more frequent and hospital stay longer in those patients requiring bronchoscopy after a failed course of chest physical therapy. Cardiopulmonary arrest was not reported in that series, but the same authors subsequently reported a cardiopulmonary arrest with postural drainage using the same protocol at their institution.

In summary, bronchodilator inhalation and postural drainage are not recommended in the initial management of foreign body aspiration; proximal migration of the object may result in cardiopulmonary arrest in a small percentage of patients (14). A delay in proceeding to bronchoscopy increases the risk of complications such as pneumonia and atelectasis, while decreasing the likelihood of successful bronchoscopic removal. Recent advances in bronchoscopic technology make bronchoscopy a safe, reliable, and superior method of foreign body removal. Further, bronchoscopy permits direct visualization of the bronchial tree to ensure complete removal of the foreign body.

Rigid Bronchoscopy

The invention of the bronchoscope allows the removal of aspirated objects without resorting to thoracotomy. This has significantly led to a decrease of morbidity and mortality

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FIGURE 19-3. *A. Forceps. B. Four-prong flexible grasping hooks. C. Dormia basket. D. Fogarty balloon.*

In 1897, Killan removed the first airway obstruction using a rigid endoscope (57). In 1936, Jackson reported a decrease in mortality from 24% to 2% with successful removal of foreign bodies in 98% with his new bronchoscopic system (58). With increasing experience and better optical and grasping instruments, successful removal of foreign bodies by the rigid bronchoscope has improved (18,22). The success rate using rigid bronchoscopy exceeds 95% to 99% in several large reported series (4,12,14,23,34,35,59). Rigid bronchoscopy in the pediatric population is performed under general anesthesia. Ventilation may be achieved via the bronchoscope and complete control of the airway is ensured. A variety of bronchoscope sizes are available, increasing from a 4-mm outer diameter sheath for use in infants.

In addition to improved airway visualization, the development of more sophisticated extraction instruments has contributed to the improved success rate for bronchoscopic foreign body removal. Available instruments include the optical forceps that permit complete visualization of both the object and the grasping jaws during use of the instrument (60). Alligator forceps, four-prong flexible grasping hooks, the Dormier basket, and the Fogarty balloon are also available (Figure 19-3) (52).

The type of foreign body should dictate the choice of extraction instrument. Depending on the location of the object, more than one instrument is frequently used. Forceps are used in the removal of a flat nonorganic foreign body. However, forceps may fracture a round organic object during attempted removal (14). The basket or Fogarty balloon technique described by Kosloske (61) are more appropriate in this instance. Figure 19-4 reveals a pea embedded in the bronchus and its subsequent intact removal with a Dormier basket. The pea readily fractured as it was removed from the basket. The Fogarty balloon technique consists of passing the balloon to the foreign body. The inner sheath and telescope are withdrawn 8–10 mm within the outer sheath, creating a hollow space in the tip of the bronchoscope. The balloon is inflated and the object is retracted into the tip of the bronchoscope. Once secured, the entire assembly is removed. Complications with this technique are rare, although

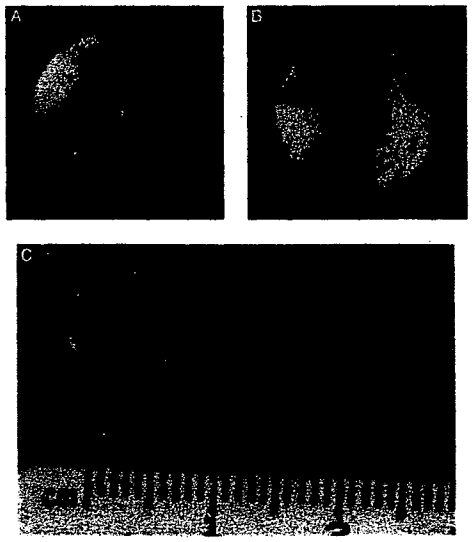

FIGURE 19-4. *Clockwise from upper left: A. Pea embedded in mainstem bronchus. B. Pea encircled by Dormier basket. C. Pea removed in one piece, but fragments with removal from the basket.*

separation of a catheter tip in the bronchial tree has been reported related to excessive traction on the Fogarty balloon catheter (62).

More unusual presentations have mandated an equally creative approach to foreign body removal. Robinson (63) describes a toothpick device used to manipulate an object in the airway, thereby permitting its removal with the forceps and a specially designed corkscrew to remove a plastic bullet with a central hole.

The sharp foreign body poses its own unique set of challenges. For example, the sharp end of an aspirated needle may embed in the airway mucosa. Bending the needle in the middle

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may disengage the needle tip and allow its safe removal. If possible, sharp objects should be removed along with the bronchoscope with the pointed end shielded within the bronchoscope to minimize trauma to the airway mucosa and lessen the likelihood of the object becoming lost when passing through the glottis (31). Rigid bronchoscopy is preferable in this setting because it affords better control of the sharp object.

Inflammation and the development of surrounding granulation tissue may impede or prevent removal of some objects. Neodymium: yttrium-aluminum-garnet (Nd:YAG) laser has been used to vaporize the granulation tissue freeing the foreign body (64,65). Nd:YAG laser poses additional risks and should only be used by those endoscopists skilled in its use. Occasionally, Nd:YAG may avoid the need for a thoracotomy when more traditional extraction methods have failed.

Flexible Bronchoscope

In 1968, Ikeda developed the flexible fiberoptic bronchoscope. The flexible fiberoptic system allowed bronchoscopy to be performed under local anesthesia and better visualized the distal airways. Initially, concerns about its safety and use were understandably raised (66). However, with development of expertise and experience, the flexible bronchoscope has almost completely supplanted the rigid bronchoscope; 99% of all bronchoscopies in the United States are performed with the flexible bronchoscope (67).

In the evaluation of a foreign body in adults, the flexible bronchoscope is the initial diagnostic tool. With the procedure in hand, removal of the visualized object can be attempted. This will spare the patient added cost, risk, and inconvenience of having to undergo a second procedure—rigid bronchoscopy with general anesthesia.

The flexible bronchoscope was initially used in the 1970s to remove airway foreign body obstructions. Successful removal was achieved in five of the seven cases using a flexible forceps (68–72). Zavala and Rhodes subsequently developed new grasping forceps and wire baskets for the flexible bronchoscope and demonstrated in animals that various endobronchial foreign bodies (e.g., screw, safety pin, paper clip, coins, chicken vertebra, peanut, etc.) can be successfully removed (73,74). Since then, several case reports have described successful removal of various foreign bodies by flexible bronchoscopy: teeth, windscreen glass, ear plugs, pins, nails, fish bone, peanuts, and coins (75–80).

In Table 19-5, we list the major series of foreign object removal with a flexible bronchoscope. The success rate of the flexible bronchoscope in removing a total of 426 airway obstructions is 86%. In our own experience, we have removed 31 foreign bodies with a flexible bronchoscope with a success rate of 100% (unpublished data). In the management of airway foreign bodies *in adults*, the flexible bronchoscope has gained acceptance as the preferred initial instrument for both the diagnosis and removal of airway obstructions (5,81,82).

Table 19-5. Case Series of Airway Foreign Body Removal by Flexible Bronchsocopy

[illegible]	[illegible]	[illegible]	[illegible]
Hiller (89)	7	6	[illegible]
Cumanan (101)	300	267	[illegible]
Clark (102)	3	3	[illegible]
Nunez (103)	17	12	[illegible]
Lan (10)	33	32	[illegible]
Limper (4)	23	14	[illegible]
Chen (5)	43	32	[illegible]
Total	426	366	[illegible]

Table 19-6. Objections to the Use of the Flexible Bronchoscope

1. Lack of airway control
2. Narrow working channel
3. Flimsy extraction instruments
4. Loss of object in the subglottic area

In our discussion on removal techniques below, we show why a skilled operator can easily overcome most objections. However, objections regarding the use of the flexible bronchoscope have not ceased (Table 19-6) (83). Only with increased experience and use of the flexible bronchoscope in the removal of foreign bodies can all doubts be erased. It was just 26 years ago when a state-of-the-art article on flexible bronchoscopy stated "because of inability to control the airway, we cannot support the technique of transnasal insertion without an ETT" (66).

REMOVING AN AIRWAY FOREIGN BODY WITH A FLEXIBLE BRONCHOSCOPE

General Guidelines

To be successful in the removal of airway obstructions, the following basic bronchoscopic techniques are recommended. These general principles also apply to all bronchoscopic procedures (Table 19-7).

Rule One

Complications occur when a bronchoscopy is performed for unclear reasons or for the wrong indications. Prior to any bronchoscopic intervention, the objectives and end point of the procedure should be carefully reviewed. Bronchoscopy performed for the wrong reasons will often lead to complications and mistakes. Mistakes beget mistakes. A grave mistake would be to attempt foreign body removal in children via flexible bronchoscope under local anesthesia (84,85). Childrens' narrow airways make asphyxiation by the foreign body more likely. In addition, adequate conscious sedation and cooperation from children is often difficult to obtain, making flexible bronchoscope removal even more difficult. The flexible bronchoscope is useful as a diagnostic tool when the evidence of foreign body aspiration is not convincing. If a foreign body is found, then rigid bronchoscopy

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19-7. The Seven General Rules of Bronchoscopy

- Complications occur when a bronchoscopy is performed for unclear reasons or with wrong indications.
- Preparation ensures 50% success rate.
- Bronchoscopy is a three-handed procedure.
- The good bronchoscopist has excellent skills, but an excellent bronchoscopist is created by excellent support and backup.
- Time and commitment are essential.
- Know your limitations.
- Each

is to be performed for extraction (43,84). The flexible bronchoscope has been used to remove foreign objects successfully in children, but this is always with general anesthesia (86). Additionally, in these instances, the rigid bronchoscope is always available for possible conversion in a moment's notice. The flexible bronchoscope is only an adjunct and supplement to rigid bronchoscopy in the removal of foreign bodies in the pediatric age group (88).

Rule Two

Preparation ensures a 50% success rate. Adequate preparation is essential for a successful bronchoscopy. Problems and complications generally arise when one takes "short-cuts." All bronchoscopic accessories for foreign body removal should be ready and tested prior to the procedure. Multiple accessories may be needed to remove the object. One should always be ready to manage difficult and unexpected situations as impromptu and innovative adaptation of techniques may be needed in challenging airway obstructions (88,89).

If radiologic studies reveal the exact type and location of a foreign body, then practice sessions with the bronchoscopic team should be done prior to the actual removal. A duplicate object can be placed in a lung model at the same site of impaction and the most appropriate instrument to use can be determined.

Rule Three

Bronchoscopy is a three-handed procedure. A common mistake is to attempt bronchoscopy alone. An extra pair of hands (i.e., trained assistant) is always needed to insert and manage the accessories of the bronchoscope (e.g., grasping forceps, basket, etc.) so as to allow the bronchoscopist to concentrate on maneuvering and manipulating the bronchoscope and its accessories to the desired position.

Rule Four

... trained personnel are necessary for a smooth and uneventful ...

A skilled and experienced operator knows that a successful bronchoscopy is a team effort. Baharloo and associates report less time and stress for the participants when the usual team of experienced physicians and nurses performed the foreign body removal (6). The bronchoscopic team must have well-defined roles. A nurse may be assigned to administer sedation and monitor vital signs. A bronchoscope assistant, trained in the use of all bronchoscopic accessories, helps the physician with the procedure. In addition, thoracic surgery and anesthesiology need to be within reach to help with unplanned complications.

Rule Five

Time and commitment are essential. Most unsuccessful bronchoscopies occur because the clinician has other commitments and is in a hurry to finish the case. Patience should be practiced and the physician should be committed to take whatever time is necessary to remove the foreign body. A failed bronchoscopic procedure increases the risk of the patient having to undergo another procedure. Further, if the object is not removed within the first 24 hours, the likelihood and extent of normal tissue reaction increases the longer a foreign body remains in the airway (9,23,53). However, in the absence of acute respiratory distress, a delay of several hours to ensure an organized coordinated approach to removal is appropriate.

Rule Six

Know your limitations. Adult airway obstruction is relatively uncommon and opportunities for acquiring the necessary skill may be infrequent. Removal of a foreign object is probably the most challenging flexible bronchoscopic procedure, and this task may need to be delegated to a member of a group or to another institution with the more experience and skill. Complications with foreign body removal have been shown higher in the hands of less-experienced physicians (6). In the same way, the success rate of foreign body removal using either the rigid or the flexible bronchoscope will largely depend on the experience and skill of the operator rather than the instrument per se.

Rule Seven

Each case should be viewed as a teaching or training opportunity. More experienced and skilled operators need to pass on their skills. Pulmonary fellows and associate clinicians should be encouraged to actively participate in the removal of all airway obstructions. By doing so, the clinician is not only engaged in the care of patients but is also ensuring the survival and refinement of the art of bronchoscopy.

Anesthesia and Analgesia

The flexible bronchoscope allows removal of the foreign body with local anesthesia under conscious sedation, unlike the rigid bronchoscope, which is performed under general anesthesia. An advantage of performing foreign body removal with conscious sedation is that it preserves the cough reflex, which can further facilitate the removal. An object brought forward to the trachea by bronchoscopic techniques described below can often be coughed out spontaneously by the patient.

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The fact that foreign body removal by flexible bronchoscopy is done with conscious sedation and without a secure airway has led to much criticism. There has been much concern about the possibility of losing the object in the narrow subglottic area leading to potential asphyxiation. To our knowledge, though, no incident of this kind has been reported in the medical literature. Notwithstanding, in the rare event of this occurring, immediate intubation—either with bronchoscopic guidance or with a direct laryngoscope—can always be performed to secure the airway. Varying sizes of ETT as well as a laryngoscope are always available in most bronchoscopy suites for the rare happenstance of complications occurring with bronchoscopy. Extraction can then proceed via ETT. Another approach (aside from emergent intubation) would be to reintroduce the flexible bronchoscope to push the foreign body into the distal airways thus clearing up the upper-airway obstruction.

In difficult cases, when conscious sedation cannot be achieved adequately, proceeding with rigid bronchoscopy under general anesthesia is the best option. In those instances when the object is too distal and inaccessible to rigid bronchoscopy removal, the foreign body can be removed with a flexible bronchoscope via ETT. When the object is larger than the diameter of the tube, then the ETT may need to be withdrawn in conjunction with the bronchoscope and the secured foreign body (90,91). Prompt reintubation can then be performed. An alternative to the use of ETT with general anesthesia is the laryngeal mask airway. Flexible bronchoscopy can be performed with reasonable airway control even with deeper sedation (92).

Accessories for the Flexible Bronchoscope

Currently, various instruments for the flexible bronchoscope are available for the use of removing airway obstructions. Of the various instruments listed below, the instrument of choice is often dependent upon the type and location of the foreign body and the accompanying host tissue reaction.

Grasping Forceps

The forceps is probably the most commonly used instrument for airway obstruction removal. Several forceps designs are available and vary in relation to cup size and shape, mechanisms to rotate the cups (rotating forceps), presence or absence of teeth, centrally placed needle assembly or fenestration. Among the grasping forceps are the w-shaped, alligator jaws, rat-tooth, shark-tooth, and covered tips forceps.

The selected forceps should have a jaw size large enough to enclose the full diameter of the foreign body. In cases when a firm grip is needed to prevent a hard object from slipping, the alligator jaws, rat-tooth, or shark-tooth forceps is recommended. For more delicate manipulations, a w-shaped or a covered-tips forceps may be used. In general, grasping forceps are only used for the removal of flat or thin inorganic (e.g., coins, pins, screw, clips, etc.) or hard organic object (e.g., bone), as attempted removal of friable organic foreign body will cause it to fracture and disperse.

Balloon Catheters

Inflatable balloon catheters are probably the most underused clearly underutilized tool available for removal of [illegible] objects. A Fogarty catheter (size 4–7) can be passed through the working channel of the bronchoscope and inflation of the balloon is achieved with injection of 1–3 ccs of air. Also specially designed inflatable balloon catheters to use in conjunction with the bronchoscope are also available. The use of the balloon catheter is discussed in the section on retrieval technique.

Dormia Basket

A modified version of the Dormia basket used by gastroenterologists and urologists to retrieve calculi from the common bile duct and bladder, is also available for the bronchoscope. The wings of the basket are normally retracted within a 1.6-mm diameter Teflon catheter. The basket is opened in the airway and maneuvered to allow its "wings" to surround and ensnare the foreign body. The basket is most useful in the removal of large and bulky objects.

Fishnet Basket

The fishnet is a modified version of a polypectomy snare. A mesh of thin thread is attached to a wire snare for easy opening and unfolding. The net is normally retracted within a catheter for easy passage through the channel of the flexible bronchoscope. Advancing the snare forward allows the fishnet to be slowly released to surround the object. The catheter is then slowly retracted to enclose the airway obstruction within the fishnet. Once this is accomplished, the basket, the captured foreign body, and the bronchoscope are then removed as a single unit. This fishnet basket is also most useful in the removal of bulky objects.

Three- or Four-Prong Snares

These snares are useful in the removal of large airway obstructions. The snare is released surrounding the foreign body. The handle of the snare is then squeezed causing the prongs at the distal end to come together capturing the object. Once secured, the foreign body, snare, and flexible bronchoscope are withdrawn carefully as a single unit. Because the prongs are very flimsy, it is not advisable to use this accessory for the removal of solid and fixed airway obstructions.

Magnet Extractor

A magnetic extractor consists of a flexible probe with a magnetic cylinder at its tip. This accessory is specially designed for passage through the working channel of the flexible bronchoscope. Small and mobile metallic foreign bodies, such

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…n forceps or cytology brushes, can be removed easily with … instrument (93,94).

Cryotherapy

…otherapy is often used for the cryodestruction of tracheo-…nchial lesions. The system consists of a liquid cryogen or …lant (usually nitrous oxide or nitrogen) that is delivered …er pressure to a specially designed cryoprobe for the flex-… bronchoscope. Extremely low temperatures (below −15° C …40° C) are created at the cryoprobe and this causes coagu-…n necrosis of tissues.

…Cryotherapy can be useful for foreign body removal. The …yoprobe is placed in direct contact with the object. Coolant …en applied until the point of contact is frozen, bonding the …eign body to the probe. This technique is particularly useful … the removal of blood clots, mucus balls, friable organic …terial, and small inorganic objects (95).

Modified from Monden Y, Morimot T, Taniki T, et al. Flexible bronchoscopy for foreign body in airway. Tokusyhima J Exp Med 1989;36:35–39, with permission.

FIGURE 19-5. *Use of a Fogarty catheter in removal of the endobronchial foreign body.*

…moval with the Flexible Bronchoscope

…nchoscopy is performed using the oral approach when-… foreign body removal is anticipated, to avoid losing the …ject in the narrow nasal passage (96). Airway exam con-…d to the suspected lobe of the airway obstruction is ini-… erformed. The suspected location of the airway …struction is examined last. A thorough and careful exam is …ne because more than one airway foreign body may be pre-…. When the object is visualized, the shape and structure …the foreign body in relation to the surrounding areas are …efully examined before an extraction attempt is made. The …ure foreign body may not be visible bronchoscopically and …view of radiologic films may be necessary during the pro-…ure to determine the position of the unseen portion. The …propriate bronchoscopic accessory is then determined based … the size, shape, position, and density of the object (see …ove).

… for foreign body removal with a flexible bronchoscope, …ery care should be taken to not push the object farther …wn the airway. In general, our procedure has been to use … Fogarty balloon to dislodge the foreign body and to bring …roximally to the trachea, before attempting removal …,82). The Fogarty balloon catheter is positioned just dis-…l to the object. The balloon is then inflated and the for-…n body is pulled out from the subsegments to the trachea …ure 19-5). Once in the trachea, the object is then easily …nable to removal. We have often also asked the patient …t up and cough up the foreign body once it has been dis-…ged to the upper trachea. We usually employ this tech-…ue for small, soft, and friable objects. This has worked in …% of our cases.

…A large misconception is that the foreign body is removed …ugh the working channel of the bronchoscope. This is never …e case. The key to removing foreign bodies lies in being able …adequately secure the object by either grasping or enclosing it with the bronchoscopic accessory. Once the object is snared, all three (bronchoscope, grasping instrument, and object) are removed simultaneously from the patient as a unit. During removal, the bronchoscopist must make every attempt to continuously visualize the object, always keeping it in the center of the airway.

Tissue reaction to the foreign body is also an important factor in object removal. In the event that a foreign body is enclosed within a vigorous and hemorrhagic granulation tissue, extraction may be difficult. Sometimes the surrounding granulation tissue has to be cleared prior to removal of the object. In these instances, bronchoscopic removal under general anesthesia may be warranted. Laser photoresection may be used in removing a large object by breaking it into manageable small pieces (97,98) or by vaporizing surrounding granulation tissue (64). Other modalities, such as bronchoscopic electrocautery, can also be used to similarly vaporize surrounding granulation tissue. Some authors suggest the use of a short course of steroids prior to removal procedures (8,43).

Hemoptysis is a rare complication of foreign body removal. This is probably better controlled with a rigid bronchoscope but, in careful hands, hemoptysis is extremely rare. Rees describes a single case of hemoptysis with foreign body removal from his review of 2500 similar cases (99). There is no reason to favor rigid over flexible bronchoscopy in object retrieval for fear of massive hemoptysis (10,82). Whenever hemoptysis does occur, our practice is to instill an epinephrine solution (1:20,000) through the bronchoscope to achieve topical vasoconstriction with decrease in blood flow and eventual thrombosis of the bleeding vessels. We also find cold saline (4° C) instillation to be effective in bleeding cessation. Cold saline causes hypothermic vasoconstriction and eventual thrombosis of the bleeding vessel.

Removal of a sharp object is an unmistakable challenge. The key to removing this type of the foreign body is to locate

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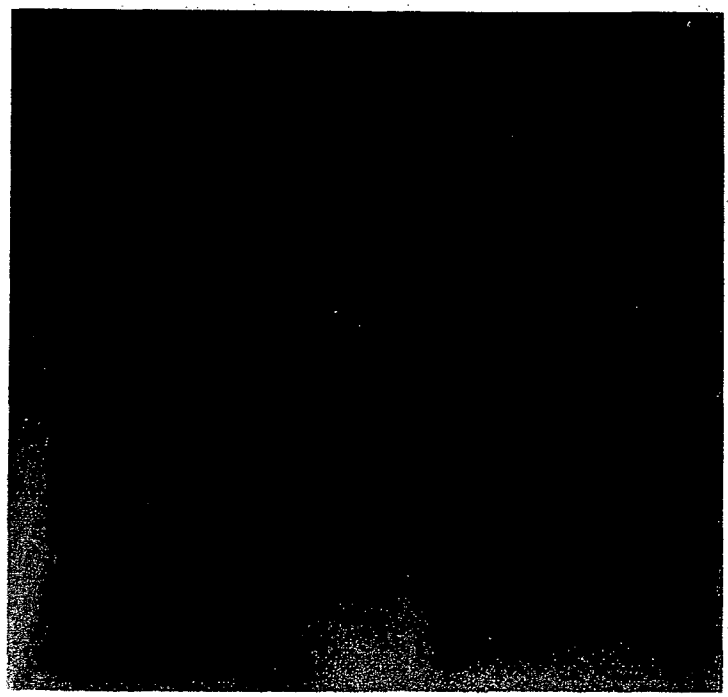

FIGURE 19-6. *A 34-year-old male who aspirated a pushpin into his left lower lobe.*

the sharp end and to attempt its dislodgment. Once the sharp end is freed, the object can be grabbed and removed. Grasping the shaft or the other end of a pointed instrument increases the difficulty of removal because this will most likely be caught in the mucosa. We recently had a case of a 34-year-old male who aspirated a pushpin. Removal of the pushpin was initially and unsuccessfully attempted with rigid bronchoscopy at another institution. The presenting chest radiograph showed an area of atelectasis associated with a metallic pin (Figure 19-6). On initial bronchoscopy at our center, it was noted that the pushpin was lodged in the basal segments of the left lower lobe, and granulation tissue has surrounded the point (Figure 19-7). Initial attempts at removal of the pointed end were unsuccessful using a Fogarty balloon or by a rat-tooth forceps. Laser photocoagulation had to be performed to vaporize the granulation tissue surrounding the pointed end. Once the granulation tissue had been cleared, the sharp end was grasped with a forceps and removed successfully with a forceps through a flexible bronchoscope using the techniques described above. Removal of a foreign body often requires the use of multiple bronchoscopic accessories, and improvisations. Inventive adaptations of basic techniques may be required.

FIGURE 19-7. *Bronchoscopic image of the pushpin with tip lodged in the bronchial mucosa.*

SUMMARY

The incidence of foreign body aspiration has not changed in the past 5 years, although the morbidity and mortality have significantly improved with the development of bronchoscopic equipment. Nonasphyxiating foreign body aspiration is

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children but can occur in any age group. Organic material most commonly aspirated. Signs and symptoms of adult foreign body aspiration are most often nonspecific. Misdiagnosis and delay in diagnosis frequently occur. A delay in diagnosis most often leads to late complications and higher morbidity. A high index of suspicion is warranted to prevent a delayed diagnosis. Radiographic evaluation is often initially done, but may often be nondiagnostic. In adults, examination with the flexible bronchoscope remains the diagnostic procedure of choice and is the gold standard in the identification and localization of an airway obstructions. In children, rigid bronchoscopy under general anesthesia is recommended because airways are smaller and the risk of asphyxiation is higher. The flexible bronchoscope can be useful as the initial diagnostic procedure in cases with no definitive history.

In adults, removal of a foreign body with a flexible bronchoscope under local anesthesia can be safely and successfully performed during the initial examination. Review of large series of object removals indicates a success rate of 86% in over 600 procedures with flexible bronchoscopy. Increased experience, improved instrumentation, and the ability to remove distally located foreign bodies have made it a viable therapeutic alternative in adults. Several accessories, specially designed for removal of airway obstructions via the flexible bronchoscope are currently available. Anesthetic and airway considerations and general and specific guidelines on removal of airway obstructions by fiberoptic bronchoscopy have been discussed.

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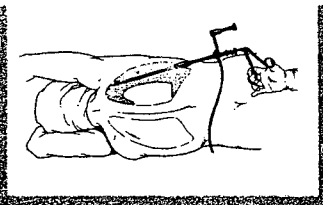

INTERVENTIONAL PULMONOLOGY

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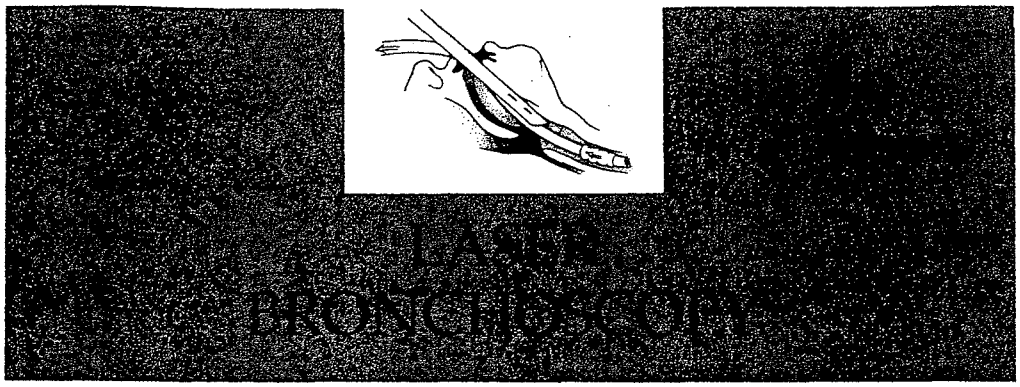
CHAPTER 5



LASER BRONCHOSCOPY

James J. Fenton and John F. Beamis, Jr.

The epidemic of cancer of the lung, which developed in the 1960s, resulted in many patients having malignant obstruction of the central airways. Conventional therapy, such as external radiation therapy, chemotherapy, or dilation techniques with rigid bronchoscopy, often proved to be inadequate to relieve the symptomatic obstruction. The application of sophisticated laser technology for the treatment of various tracheobronchial obstructions, using standard rigid and flexible bronchoscopes, has proved to be a major advance in the treatment of these patients and was the original stimulus for the specialty of interventional pulmonology. The successes of laser bronchoscopy have stimulated interest in other endobronchial therapies, such as cryotherapy, electrocautery, and brachytherapy.

Laser bronchoscopists represent a significant proportion of interventional pulmonologists but a relatively small minority of bronchoscopists in general. Laser bronchoscopists must be experts in diagnostic bronchoscopy techniques, become knowledgeable in laser physics and laser tissue interaction, and be comfortable dealing with patients with respiratory insufficiency, acute hypoxemia, and airway bleeding. This chapter reviews laser physics, tissue interaction, and laser safety as it relates to bronchoscopic applications. It also addresses indications, contraindications, and techniques of laser bronchoscopy. Familiarity with this chapter will not make one a laser bronchoscopist, but we hope it will serve as a basis for beginning clinical application.

Laser Light

A *light amplification* by *stimulated emission* of *radiation* (LASER) beam is an intense form of electromagnetic energy channeled into parallel, synchronized rays of light of the same wavelength that are used for many industrial and medical applications. Light represents a portion of the electromagnetic spectrum designated with wavelengths between 100 and 20,000 nm. Included in this range is ultraviolet light, visible light, and infrared light (Fig. 5-1). Visible light is perceived by the human eye as different colors, with the shorter wavelengths of 400 nm seen as violet blue and the longer wavelengths of 700 nm seen as red light. All light is produced by the spontaneous or stimulated emission of energy by atoms, the smallest components of a molecule. The nucleus of the atom contains positively charged particles called protons and neutral particles called neutrons. Orbiting the nucleus are negatively charged electrons, which balance the positively charged protons. Each electron orbit corresponds to a certain energy level, and the greater the distance from the nucleus, the higher the energy level of the electron. Light is generated when electrons surrounding an atom spontaneously drop from an orbit with a higher energy level to one with a lower energy level (Fig. 5-2). For this release to occur, the atom must first be "excited" to the higher level by an external photon of energy. Photons are discrete particles of radiant energy that travel in waves and provide the energy necessary to form light. The energy of a photon is related to the frequency (Hz) of the wave multiplied by a constant (Planck's constant = 6.623×10^{-34} joule seconds) and is inversely proportional to the wavelength. This influx of energy propels the electron to a more distant orbit corresponding to a higher energy level. If an atom in an excited state is again stimulated by a photon of the same energy as the one absorbed, two photons of equal energy and frequency will be released when the electron's orbit decays to a lower level.[1] This release is termed stimulated emission of radiation and is the basis for laser light energy. When the process is ampli-

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Figure 5-1

Electromagnetic spectrum.

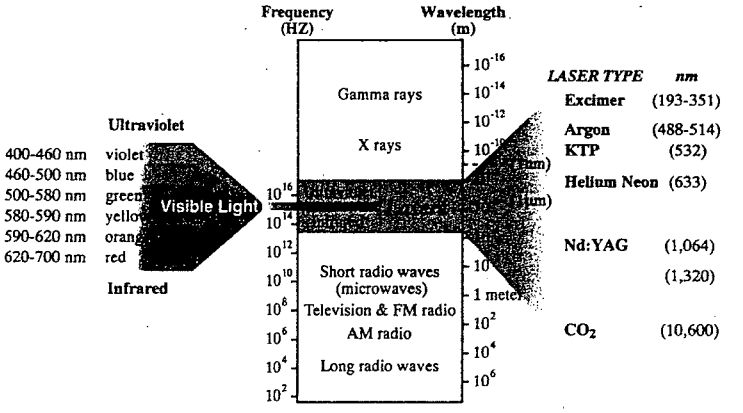

Figure 5-2

Generation of light.

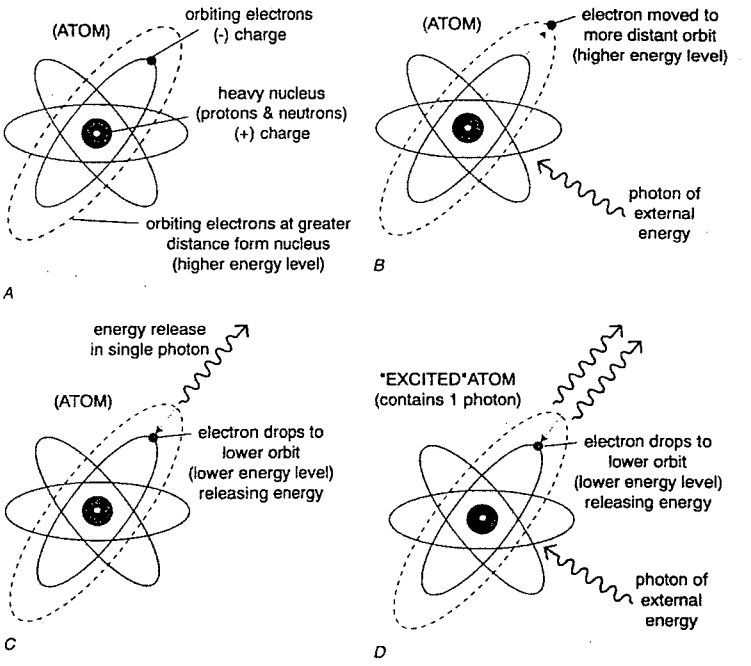

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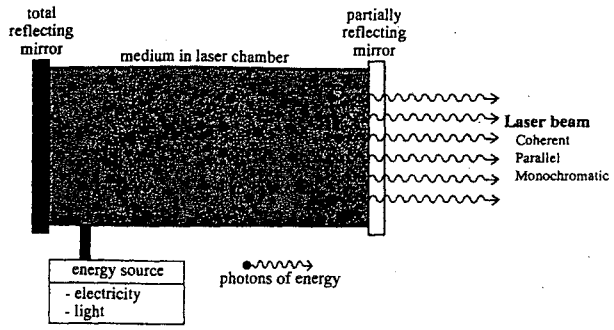
Figure 5-3



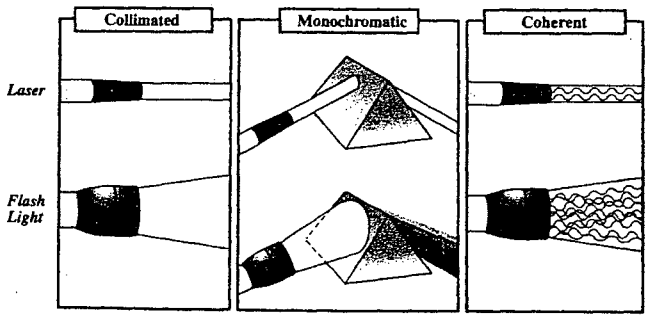
Components of a laser.

fied to an intense level by an external energy source, a specialized form of light energy is created, which we term laser light.

Lasers create their special form of light energy by using an optical cylinder containing a medium consisting of solids, gases, or dyes (Fig. 5-3). The cylinder contains a fully reflective mirror at one end and a partially reflective mirror at the other end. Atoms of the active laser medium become stimulated when an external source adds thermal, electrical, or optical energy to the system. Spontaneous emission of energy occurs as electrons change orbit around the atoms within the medium, giving off energy in various directions. As the photons of energy bounce off the walls, mirrors, and other atoms within the cylinder, intensification of the electromagnetic energy occurs. The light energy leaves through the partially transmissive mirror at a rate that is dictated by the incoming external energy source. The energy is emitted as laser light and follows the special properties of stimulated light emission.[2,3]

Three unique properties of laser light make lasers particularly useful[1,3] (Fig. 5-4). First, all waves of laser light are in phase with each other and have identical frequencies, wavelengths, and velocities as they travel through space. This property is known as coherence, and it results in a concentration of laser power at the target point. Waves of laser light are also considered monochromatic because they have nearly the same color, wavelength, and energy. This characteristic permits all of the radiant power to be centered in a narrow electromagnetic spectral band. Finally, all waves of laser light are essentially parallel and thus are considered collimated. This property permits lasers to travel great distances with minimal loss of intensity of light energy. Ordinary light energy (i.e., incandescent bulbs) will scatter in multiple directions at varied wavelengths, making it good for illumination but inadequate for more precise medical applications. Laser light, on the other hand, is emitted in a narrow, parallel bundle with minimal scatter into space,[3,4] making

Figure 5-4



Properties of laser light

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it particularly useful as a surgical tool. Compared with most other forms of light, lasers also have a high luminosity (brightness), which makes them useful for light therapy.

Two other important characteristics of laser light determine a laser's impact on a target. The transverse electromagnetic mode (TEM) is one measure of a laser's distribution of intensity in a cross-sectional dimension. Although lasers are collimated and coherent, the impact configuration on a target is not perfectly uniform, as illustrated in the ideal mode (Fig. 5-5). Instead, the actual cross-sectional impact configuration of most lasers is symmetric in a bell-shaped or gaussian distribution, with more beam intensity being concentrated in the center of the target. This impact configuration is termed basic mode.

In addition to the TEM, a laser beam's intensity is also determined by its power density, which is the concentration of power per unit of cross-sectional area of the beam. Optical lenses focus the laser beam into a small focal spot, creating a high power density in that area. For each laser, the beam focus is fixed to prevent divergence and loss of power density. The power density is a function of the size of the focal spot. The smaller the focal spot, the higher the power density (Fig. 5-6). The power density can also be intensified by increasing the incoming power of the beam, which is usually in the range of 20 to 100 watts (W) for most medical lasers.[1] Therefore, power density is proportional to incoming power and inversely proportional to the area of the focal spot. Although the power consumed by a laser is less than that of an ordinary light bulb, the intensity of a concentrated beam makes it useful for cutting, coagulating, and vaporizing tissue.

A laser's TEM and power density are important determinants of the laser beam's effect on the target tissue. Because the TEM determines the profile of the beam's effective cross-sectional area, it also determines the pattern of tissue interaction (Fig. 5-7). The tissue cavity created by laser destruction has the same configuration as the intensity profile (basic mode) of the laser beam. The extent of tissue destruction is a function of the amount of absorption, the length of exposure, and the power density of the laser beam. When laser light is applied to tissue, some of the energy penetrates into the tissue and is absorbed producing heat, whereas the rest of the energy is reflected back (Fig. 5-8). Power density at the surface of the tissue will be higher than the power density farther inside because of the partial reflection of energy. Absorption attenuates the original power density incrementally as it passes deeper into the tissues. The distance below the surface of the tissue at which the power density has decreased to a percentage of the original level (usually 1 percent) is termed the attenuation depth.[3] It is differentiated from penetration depth, which is the distance at which the laser energy no longer has significant effects on the tissue. Laser beams can still have a considerable effect on tissues even after 99 percent attenuation if the exposure is prolonged or if the power density of the original beam is very high. For instance, if the laser beam has an original power density at the surface of 100 W/cm^2, only 1 W/cm^2 will be present at the 99 percent attenuation depth. However, if the original power density at the surface is 10,000 W/cm^2, 100 W/cm^2 will be present at the 99 percent attenuation depth. The attenuation depth is a function of the tissue type and the wavelength of the laser light,

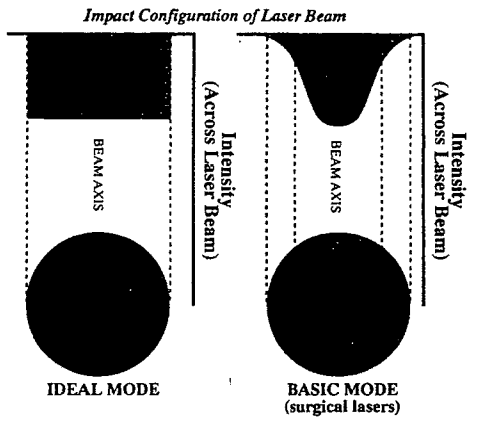

Figure 5-5

Cross-sectional profile of laser beam intensity.

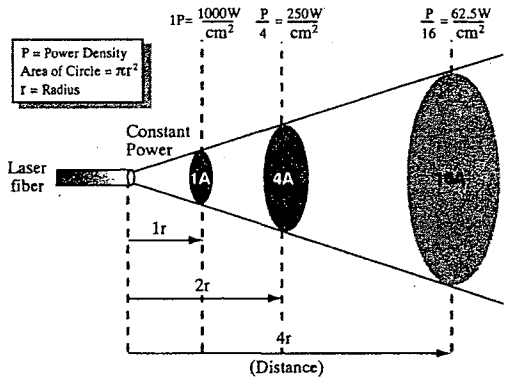

Figure 5-6

Relationship of power density to distance.

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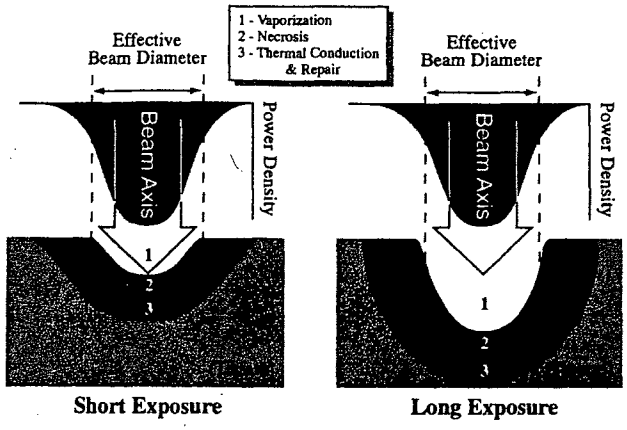
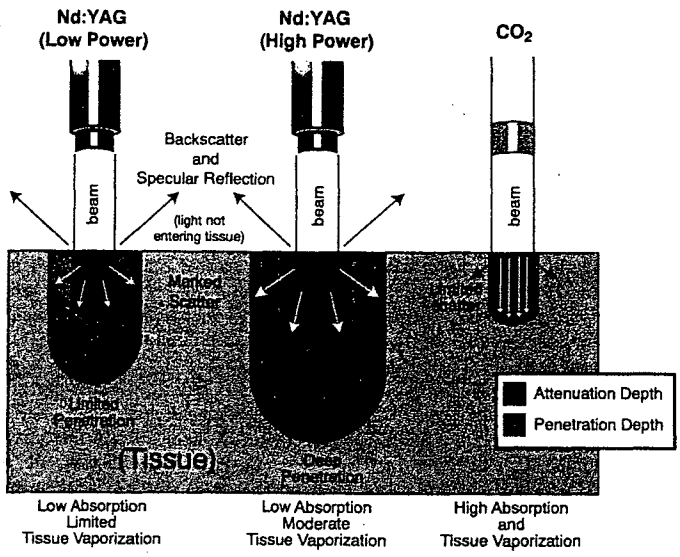
Figure 5-7



Zones of tissue injury from laser exposure.

Figure 5-8



Tissue laser absorption characteristics.

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whereas the penetration depth is dependent on the tissue type, wavelength, and the power density.

The amount of attenuation that occurs secondary to absorption is termed the attenuation coefficient.[3] This value is the sum of the absorption coefficient (α) and the scattering coefficient (σ) [$A = \alpha + \sigma$]. Each laser has a different scattering characteristic when the beam penetrates living tissues, but the amount of scattering within tissues is generally dependent on the tissue type and wavelength of the laser beam. Lasers that have high scatter coefficients function well as coagulators, whereas lasers that have high absorption coefficients are more useful for precision cutting. For instance, a carbon dioxide (CO_2) laser has a high absorption coefficient that produces rapid tissue vaporization and makes it an ideal cutting instrument. Its low scattering coefficient, however, limits its ability to photocoagulate bleeding tissues. In contrast, a neodymium, yttrium, aluminum, garnet (Nd:YAG) laser functions well as a coagulator because of its high scattering coefficient, but it is a relatively poor cutting instrument. Nevertheless, the Nd:YAG laser is capable of serving both functions because at higher power settings or within dark tissues, more absorption and vaporization occur. The main determinant of a laser's effect on a particular tissue is the proportion of the scattering and absorption coefficients at the wavelength of the individual laser.

Lasers can interact with living tissues in different ways.[2] Light energy is converted into heat energy, enabling the thermal effects of laser radiation to be used for cutting, vaporization, and coagulation of tissues. Because of the high water content, laser energy is readily absorbed by living tissues. This laser energy is rapidly converted into heat, which results in cell destruction. Lasers can also mechanically disrupt tissues either by pressure waves or by inducing vaporization of intracellular or extracellular water, resulting in separation of tissue layers. This interaction is useful in the removal of cataracts or intravascular atheromatous plaques. Laser light energy can also stimulate various biochemical reactions by interacting with photosensitizing chemicals absorbed by abnormal tissues. This use of laser light is termed photodynamic therapy, which is used in the diagnosis and treatment of patients with tracheobronchial malignancies.[5–8]

The performance characteristics of individual lasers are determined by the substance used as the laser medium. Each substance produces varying wavelengths of emitted light. The first laser used a synthetic ruby crystal as a laser medium; now, commonly used materials include argon, krypton, fluorescent organic dyes, gold vapor gas, helium-neon, potassium titanyl phosphate (KTP), CO_2, and a combination of erbium (Er) or Nd:YAG.

The argon gas laser has a wavelength of 514 nm in the visible blue-green spectrum of light and can be transmitted through optical fibers. Because of its blue color, however, much of its energy is absorbed in hemoglobin, which greatly limits its use in photoresection of endobronchial malignancies.[9] The gold vapor and liquid dye lasers are used to excite the photosensitizer dihematoporphyrin ether, which is selectively retained by tumor cells.[7,8] By exposing the tissue to appropriate laser light, clusters of tumor cells can easily be identified and treated. The helium-neon gas laser has no therapeutic role in laser bronchoscopy, but it produces light in the visible spectrum, making it useful as an aiming guide for other lasers, such as the CO_2 and Nd:YAG laser. The KTP laser uses a solid medium similar to the Nd:YAG laser and has been used in photocoagulation and resection of tracheobronchial stenosis.[10]

The CO_2 laser has commonly been used for lesions of the aerodigestive tract.[11] The CO_2 laser has a long wavelength of 10,600 nm, resulting in prompt absorption by most living tissues. This invisible infrared electromagnetic energy is rapidly converted to thermal energy, resulting in vaporization of the water in the tissue. If the tissue has a high water content, absorption is further enhanced and tissue destruction is more precise. The CO_2 laser's high absorption and low scatter coefficients give it a predictable depth of penetration and make it ideal for precise surgical applications.[3,12] Tonsillectomy, adenoidectomy, and uvulopalatopharyngoplasty (UPPP) have been performed with the use of the CO_2 laser.[13] Although well accepted for the treatment of benign and malignant lesions of the head and neck,[14] its use in tracheobronchial malignancies has been limited. The CO_2 laser can seal small vessels and lymphatics up to 0.5 mm in diameter,[15,16] but it is an ineffective photocoagulator and cannot reliably control bleeding from larger vessels. Another important drawback of the CO_2 laser is its cumbersome articulated mirror delivery system, which requires a micromanipulator and surgical microscope for operation. Use of this system for lower airway tumors requires precise alignment of the laser beam down the entire length of a rigid bronchoscope. This complex set-up makes resection difficult and often precludes the use of certain suction devices. At present, there is no commercially available flexible optical fiber for the CO_2 laser that allows its use with a fiberoptic bronchoscope.

The Nd:YAG laser has been used extensively for the treatment of patients with tracheobronchial malignancies because the laser beam is delivered through a quartz optical fiber, which is easily adaptable for use with either the flexible or rigid bronchoscope.[17] The Nd:YAG laser operates in the invisible near infrared range of the electromagnetic spectrum at a wavelength of 1064 nm. At this wavelength, scattering exceeds absorption for most lighter colored tissues, which makes the Nd:YAG laser effective at coagulating large amounts of tissue. If the tissue is darker pigmented or

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if a higher power setting is used, absorption and vaporization can be increased. The wide power range (5 to 100 W) of the Nd:YAG laser contributes to its versatility by permitting photocoagulation at low settings and vaporization at higher settings. The Nd:YAG laser penetrates to about 6 mm and will coagulate vessels of up to 2 mm in diameter. A new type of Nd:YAG laser has been developed with a wavelength of 1320 nm, which may have advantages over the current system because of slightly less tissue scatter.[9] The Nd:YAG laser fiber can be fitted with a sapphire tip to permit a contact operational mode, but because these tips limit viewing, contact probes are usually not used in tracheobronchial endoscopy.[4] Because the noncontact Nd:YAG laser is the most common laser used for tracheobronchial disease, the rest of this chapter will concentrate on the use of this laser for bronchoscopic applications.

Indications

The Nd:YAG laser has been used for more than 15 years to reestablish airway patency in patients with primary bronchogenic and metastatic malignancies, benign tumors, tracheal stenosis, and tumors of uncertain prognosis.[18] Malignant tracheobronchial obstruction from primary bronchogenic carcinoma is the most common indication for Nd:YAG laser bronchoscopy and accounts for 49 to 75 percent of the cases (Table 5-1).[18–20,22–24] The most common primary tumor cell type treated by the Nd:YAG laser is squamous cell carcinoma followed by adenocarcinoma.[19,20] Tracheobronchial obstruction as a result of endobronchial metastasis from renal, thyroid, colon, breast, and esophageal carcinomas account for between 6 and 18 percent of laser bronchoscopies and is the next most common indication for the procedure. Although they are responsible for less than 10 percent of the cases of tracheobronchial obstruction, benign tumors, such as hamartomas, fibromas, papillomas, lipomas, and amyloidomas, are an excellent indication for use of the Nd:YAG laser.[21] Benign tumors often originate from a pedicle base in the tracheobronchial mucosa and are usually not vascular, making them particularly attractive for flexible endoscopic laser resection.[22] Laser treatment of the base of lesions may help prevent recurrences, and in some cases, treatment of lesions, such as hamartomas and papillomas, can be curative. Endobronchial amyloid and tracheopathia osteoplastica are usually not curable by laser resection, but these lesions are relatively slow growing and often do not require multiple treatments.[23]

At many institutions, tracheal stenosis represents a relatively common indication for laser bronchoscopy, accounting for 10 to 27 percent of the cases. Tracheal stenosis usually occurs after translaryngeal intubation or tracheostomy, but it can occur without a known cause or in response to granulomatous or diphtherial infections. Personne and coworkers[22] have identified three main types of iatrogenic stenoses (Fig. 5-9). The diaphragm type of stenosis (type I) consists of a concentric fibrotic intraluminal stricture without involvement of the tracheal wall and is ideal for laser resection. The second type of stenosis (type II) involves extrinsic, "bottle-neck narrowing" of the trachea sec-

Table 5-1
INDICATIONS FOR LASER BRONCHOSCOPY

Author	*Year*	*Patients*	*Bronchogenic Carcinoma*	*Metastatic Carcinoma*	*Tracheal Stenosis*	*Benign Tumor*	*Uncertain Prognosis*	*Miscellaneous*
Cavaliere et al.[19]	1994	1884	1419 (75%)	105 (5.6%)	Not included	156 (8%)	143 (8%)	61 (3.2%)
Cavaliere et al.[23]	1988	1000	612 (61%)	37 (3.7%)	139 (13.9%)	59 (5.9%)	64 (6.4%)	89 (8.9%)
Brutinel et al.[24]	1987	116	71 (61%)	17 (14.7%)	Not included	9 (8%)	13 (11%)	6(5%)
Beamis et al.[20]	1991	269	200 (74%)	36 (18%)	27 (10%)	6 (2%)	Not included	Not included
Personne et al.[22]	1986	1310	643 (49%)		389 (27%)	75 (5.7%)	57 (4%)	146 (11%)
Dumon[18]	1985	544	278 (51%)		132 (24%)	31 (6%)	20 (4%)	83 (15%)[a]

[a]Suture removal, 29; hemorrhage, 20; foreign body, 4.

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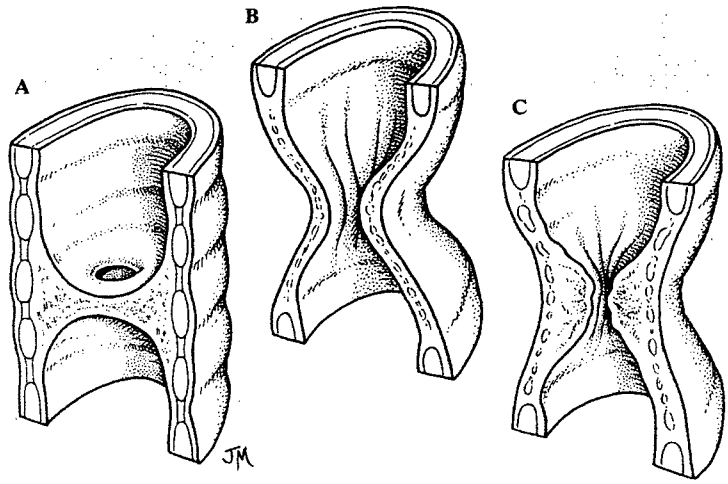
Figure 5-9

Types of tracheal stenosis. *A*, Type I; *B*, type II; *C*, type III.



ondary to collapse of the tracheal wall. Because no intraluminal component is present, use of the Nd:YAG laser for this type of narrowing is contraindicated. The last type of stenosis (type III) is a combination of the first two types and may be acceptable for laser therapy of the intraluminal fibrotic ring in certain situations. If stenosis is suitable for endoscopic therapy, the laser is used to make radial incisions in the tracheal scar before gentle rigid bronchoscopic dilation of the tracheal or subglottic stenosis.[25,26] Some patients with severe obstruction of the lower airway may require a permanent tracheostomy or implantation of a silicone stent or a Montgomery tracheal T tube to maintain patency of the airway.[27,28] If implantation of the stent fails to achieve long-term patency, tracheal sleeve resection may be necessary, but symptomatic clinical improvement after relief of tracheal obstruction using laser bronchoscopy has been well documented.[25,26,29]

A less common indication for endobronchial laser therapy is treatment of tumors of uncertain prognosis, which include carcinoid, adenoid cystic, spindle cell, mucoepidermoid, and other mixed cell types. These lesions should be resected surgically if possible, but in many instances, surgery is impossible because the lesions are widespread or the patient is a poor operative candidate. The Nd:YAG laser can be used to treat these low-grade malignant tumors effectively, which accounts for approximately 5 percent of laser bronchoscopies. Other infrequent uses for the Nd:YAG laser include treatment of tracheobronchial granulomas,[23] removal of suture threads, control of hemorrhage from biopsy sites or necrotic mucosa,[18] and even vaporization of granulation tissue surrounding an aspirated foreign body.[30]

Nd:YAG laser bronchoscopy is indicated for almost any centrally obstructing lesion within the airway lumen of the tracheobronchial tree, but some lesions are more favorable for treatment than others (Table 5.2). Tracheal and bronchial main stem lesions are more easily treated than lesions in the distal bronchi, and they represent the primary indication for laser bronchoscopy. Although location of the lesion is a primary concern, the appearance of a lesion is also important. For instance, mechanical resection of short, polypoid lesions is technically easier than resection of lesions that involve a longer portion of the airway. Because

Table 5-2
CHARACTERISTICS OF LESIONS FOR LASER BRONCHOSCOPY

Favorable lesions for laser resection	Unfavorable lesions for laser resection
Tracheal and main stem lesions	Extrinsic lesions
Polypoid lesions	Diffuse lesions with extensive submucosal involvement
Short lesion length	Upper lobe and segmental lesions
Large endobronchial involvement	Long tapering lesions
Visible distal bronchial lumen	Total bronchial obstruction
Functional lung distal to the obstruction	

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much of laser bronchoscopy involves the use of the rigid bronchoscope to physically resect the tumor, long tapering lesions with extensive submucosal infiltration make the procedure technically more difficult and often reduce the chances for a successful outcome. Complete obstruction of the airway lumen also complicates the procedure because it makes it difficult to know the course of the bronchus beyond the area of obstruction. This information is crucial to avoid inadvertent perforation of the airway wall during laser resection. Most patients do not have complete airway obstruction, and a passage beyond the lesion can often be found by gently probing the area with a suction catheter or a flexible bronchoscope. If the course of the bronchus can be determined, mechanical and laser resection can proceed. Otherwise, complete obstruction of the airway lumen is a contraindication to laser bronchoscopy, and it represents the most common reason for not performing laser resection.[31]

Contraindications

Because the procedure is often used as palliative therapy for individuals with severe malignant tracheobronchial stenosis, there are actually few contraindications to laser bronchoscopy. Dumon[18] stated that "since it [laser bronchoscopy] is almost always used in a high-risk patient population, the normal limitations used for conventional bronchoscopic application must be expanded." He added that the only absolute contraindication to laser bronchoscopy is lack of an intraluminal lesion. Because lesions extrinsic to the airway are not amenable for treatment, it is important to confirm that the airway narrowing is not the result of compression from mediastinal tumors, lymphadenopathy, lobar collapse, or from type II tracheal stenosis. Failure to recognize extrinsic airway compression as a cause of airway narrowing can result in inadvertent perforation of the tracheobronchial wall. Except for extraluminal disease, there are few other reasons not to consider laser resection even in patients who are at a higher surgical risk. Personne and colleagues[22] performed laser resection on 267 patients "in extremis" with severe hypoxia or coma and recorded only a 2.7 percent mortality rate. A low rate of fatal complications of 0.3 to 3 percent has been confirmed by three other large series.[18,20,23] This low perioperative mortality rate indicates that the procedure can be an acceptable palliative treatment even for very ill patients.[22]

Although there are few absolute contraindications to laser bronchoscopy, a number of relative contraindications need to be considered (Table 5-3). A preoperative evaluation is often used to identify cardiovascular and respiratory problems that might place the patient at an unacceptably high risk for complications.

Table 5-3
CONTRAINDICATIONS TO LASER BRONCHOSCOPY

Absolute contraindications
Extraluminal disease
Relative contraindications
Cardiovascular
Recent myocardial infarction
Ventricular arrhythmias
Conduction abnormalities
Hypotension
Decompensated congestive heart failure
Respiratory
Severe obstructive lung disease
Extensive tumor involvement
Involvement of pulmonary artery
Unsalvageable lung distal to obstruction
Chronic collapse
Small cell carcinoma cell type
Posterior tracheal wall location or tracheoesophageal fistula
Extensive preprocedure radiation therapy
Electrolyte abnormalities
Bleeding diathesis
Sepsis
Tracheobronchial malacia

Postoperative myocardial infarction and cardiac arrest account for 30 to 60 percent of perioperative deaths, and respiratory insufficiency from persistent obstruction accounts for another 40 percent of fatal outcomes.[18,20,23] Although knowledge of underlying cardiopulmonary problems is important and may preclude surgery in some individuals, the palliative benefits of laser bronchoscopy frequently outweigh the small risk of postprocedural complications. In many instances, respiratory insufficiency is both the primary indication for the procedure and the reason why the patient is a higher surgical risk. For some patients, bronchoscopic laser resection represents the only chance for rapid relief of dyspnea. Failure to wean patients from mechanical ventilation after bronchoscopy is infrequent and usually occurs as a result of being unable to establish an effective airway and not from underlying obstructive lung disease.

It is important to know whether there is functional lung distal to the obstruction. Lung parenchyma that is severely damaged by radiation treatments or recurrent postobstructive pneumonia is unable to participate in gas exchange even when the obstruction is re-

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moved.[32] In addition, significant tumor involvement of the pulmonary artery can result in irreversible ventilation-perfusion inequalities, negating any effects of laser resection. Bronchography,[32] angiography,[33] and computed tomography of the chest can be helpful in evaluating lung parenchyma in the region of the obstruction. Nonfunctional lung found distal to the region of obstruction represents a strong relative contraindication to laser resection.

The type and location of the lesion may be additional relative contraindications to laser bronchoscopy because they influence the likelihood of procedural complications. Tumors involving the posterior tracheal wall can extend into the esophagus, increasing the risk of perforation or fistula formation during laser applications. Some authors[32] even suggest esophageal endoscopy before laser resection to identify patients at risk for tracheoesophageal fistula. The risk of airway erosion and perforation is also increased by extensive preprocedure radiation therapy, which can distort and soften the tracheal wall.[18] Particular caution should be taken with upper lobe lesions because laser treatment can result in excessive bleeding owing to the proximity of major vessels. The cell type of the tumor can influence the success of the procedure and may be an indication to use other methods of treatment. For example, small cell carcinoma of the lung is often diffuse and usually contains a large extrabronchial component, making the lesion unfavorable for laser resection. Bleeding related to small cell carcinoma, however, may be treated effectively with the Nd:YAG laser. Coagulopathies, electrolyte abnormalities, hypotension, and sepsis represent other obvious contraindications to laser endoscopy and should be corrected before the procedure.

Anesthesia

The method of anesthesia delivery for Nd:YAG laser bronchoscopy depends on the type of bronchoscopic technique. For flexible bronchoscopies, light intravenous conscious sedation is usually employed in a fashion similar to standard diagnostic bronchoscopy. If the patient is intubated, however, intravenous general anesthesia can be given. Apesthesia for the rigid bronchoscopic procedure is usually accomplished by a combination of intravenous agents, including midazolam, propofol, fentanyl, and occasionally a depolarizing neuromuscular blocker. If a closed rigid bronchoscopic method is preferred, ventilation is achieved through the side arm of the bronchoscope. Inhalational anesthetic agents can be used with a closed system, but there may be more potential for cardiopulmonary complications.[34] Some bronchoscopists prefer to operate through the open end of the rigid bronchoscope, and thus a different type of ventilation is required. Perrin and colleagues[35] prefer spontaneous assisted ventilation, but other authors[20,36–38] use a manual Venturi jet ventilation technique. Our system consists of an air-oxygen blender (Bird/3M, Palm Springs, CA) combined with a high pressure (50 psi) manual injector attached to the side port of the rigid bronchoscope.[39] This method of ventilation enables the surgeon to operate through the open end of the rigid bronchoscope while ventilation is maintained by manually injecting an air-oxygen mixture at 20 to 60 breaths per minute.[37,38,40] A high frequency jet ventilation technique has also been described wherein a machine delivers approximately 300 breaths per minute.[41] The effectiveness of manual Venturi jet ventilation has been well validated,[42,43] and the use of continuous CO_2 monitoring is not required. Standard O_2 pulse oximetry is recommended to avoid inadvertent desaturation events during the procedure. After rigid bronchoscopy, most patients are easily extubated in the operating room after clearance of the intravenous anesthesia. Patients usually stay a few hours in the postanesthesia care unit after which they are either transferred back to their hospital room or discharged. General anesthesia for rigid laser bronchoscopy can be performed safely through various techniques, and most elderly or debilitated patients can tolerate the intervention without difficulty. Anesthesia during rigid bronchoscopy will be described in Chap. 21.

Techniques for Laser Bronchoscopy

RIGID VERSUS FLEXIBLE BRONCHOSCOPY

The Nd:YAG laser can be used with either a flexible or rigid bronchoscope, and which instrument is better has been discussed widely.[44,45] Ironically, the original papers in the early 1980s by Toty[46] and Dumon[47] described the use of the Nd:YAG laser with both the flexible and rigid bronchoscopes. For the next few years, the flexible bronchoscope was used alone or in conjunction with an endotracheal tube or rigid scope in the majority of laser resections.[24,31,48,49] Subsequently, reports of major complications, including deaths resulting from massive hemorrhage[24,34,50] and airway fire[51] began to surface, and by the late 1980s, many authors[24,52] advocated using the rigid bronchoscope for most Nd:YAG laser resections. Despite this claim, Chan and coworkers[44] compared results of 61 Nd:YAG laser procedures performed with a flexible bronchoscope with results of 51 procedures performed through a rigid bronchoscope on 79 patients and found no difference in the complication or survival rates between the two groups. The authors suggested that the rigid scope should be used for proximal lesions and the flexible scope for distal lesions and recommended

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that laser bronchoscopists should be proficient in both techniques. Each method is associated with certain advantages and disadvantages.

Flexible Bronchoscopy

The major advantage of the flexible bronchoscope is its versatility and familiarity to the pulmonologist. In the 1991 Bronchoscopy Survey by the American College of Chest Physicians,[53] the flexible scope was used by more than 80 percent of responding physicians at some point in their practice. The popularity of the flexible scope for laser procedures may partly be related to the limited number of physicians who are trained in rigid bronchoscopy. In this survey, only 8.4 percent of the responders used the rigid scope in their practice. This trend away from the use of rigid bronchoscopy limits the choice of methods to apply the Nd:YAG laser, but in some instances, flexible bronchoscopy may actually be the preferred technique. The flexible scope is small and maneuverable, which permits easier access to distal airway lesions and improves visualization of the bronchial tree. Aiming the laser beam is also easier with the flexible scope because the operator has more control over the tip of the laser fiber. Because of its size and controllability, it may also be passed through the rigid bronchoscope for dissection and coagulation purposes. Usually, the flexible bronchoscope is reserved for lesions that do not have a propensity for hemorrhage, such as granulomas, papillomas, and small distal malignant tumors. The flexible laser bronchoscope is ideal for recurrent tumors and pedunculated tumors with a narrow base. The versatility and familiarity of the flexible scope make it well adapted for the safe and effective laser resection of specific lesions within the tracheobronchial tree (Table 5-4).

Other proposed advantages of flexible bronchoscopy for laser applications include potential cost savings and the avoidance of general anesthesia. Unfortunately, these probably only represent theoretical advantages. Because flexible bronchoscopy is often performed outside of an operating room setting, it can be more convenient and less costly than rigid bronchoscopy. For large obstructing lesions, however, multiple procedures are often required, frequently negating any anticipated cost savings. In one study,[54] an average of 1.97 treatments were required to obtain a response compared with only one treatment session using a rigid bronchoscope. Additionally, each procedure may be more time consuming for the operator because removal of tumor debris is less efficient through the flexible bronchoscope. The frequent need for multiple procedures and the increased investment of time minimize the proposed advantages of flexible bronchoscopy for laser photoresection.

Another theoretical advantage of the flexible bronchoscope is the potential to avoid the inherent risks of general anesthesia, including myocardial infarction, arrhythmia, hemodynamic instability, CO_2 retention, barotrauma, and prolonged neuromuscular weakness.[34,36,55] Unger and others[45,56] advocate the use of flexible bronchoscopy for most tracheobronchial laser procedures and report no significant anesthesia-related hemodynamic or ventilatory complications in more than 290 procedures performed under topical anesthesia.[57] Cardiovascular complications, such as myocardial infarction, however, can still result from flexible bronchoscopy,[54] especially if severe hemorrhage or airway compromise occurs. In fact, the only deaths in some studies using flexible bronchoscopy for laser procedures have not been the result of anesthetic complications but rather due to uncontrollable hemorrhage.[24,34,54] Although complications related to general anesthesia for rigid bronchoscopy have been well documented,[20,22,23,55] the overall rate of occurrence is exceedingly low. Cavaliere and coworkers[19] reported respiratory failure in only 0.5 percent, cardiac arrest in

Table 5-4
INDICATIONS FOR THE FLEXIBLE FIBERSCOPE IN LASER BRONCHOSCOPY

In combination with a rigid bronchoscope
Benign tumors (granulomas, papillomas)
Small malignant tumors
Distal tumors
Less than 50% obstruction of airway lumen
Recurrent tumors
Narrow based pedunculated tumors
Hemoptysis photocoagulation

SOURCE: Adapted from Ramser ER, Beamis JF Jr: Laser bronchoscopy. *Clin Chest Med* 1995; 16:415–426.

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0.4 percent, and myocardial infarction in 0.2 percent of 2253 cases in which more than 90 percent were performed under general anesthesia using a rigid bronchoscope. In a separate prospective study[35] of 124 interventional rigid bronchoscopies, no cardiac complications occurred, and transient reversible hypoxemia was seen in only 15 percent of cases. Avoidance of complications from general anesthesia and potential cost savings represent only theoretical advantages of flexible bronchoscopy, but they may still be important considerations in some patients.

Rigid Bronchoscopy

Although there may be advantages to flexible bronchoscopy for certain situations, the rigid bronchoscope is now generally preferred for most large obstructing tracheobronchial lesions.[20,22,23,52] Rigid laser bronchoscopy has a number of important advantages over flexible bronchoscopy, including efficiency, effectiveness, and, most important, safety. It is usually more efficient because larger pieces of tumor material can be removed through the rigid scope, significantly reducing the time of the procedure and the total number of procedures required.[44,54] Often only one procedure is required because the barrel of the bronchoscope can be used to "core" out the obstructing endoluminal lesion and quickly reestablish airway patency. The barrel can also be used to dilate a narrowed trachea and possibly eliminate the need for surgical resection. Other advantages of rigid bronchoscopy include the ability to perform stent implantation or removal at the time of the laser intervention. Both silicone stents and self-expandable metal stents can be placed through a rigid bronchoscope.

Although improved efficiency is desirable, the most important advantage of rigid bronchoscopy is safety. Dumon and colleagues[52] commented that they could not overstress that flexible laser bronchoscopy in patients with major obstructive malignancy is dangerous, and this type of instrumentation does not have the potential for effective response in the event of a major crisis. Personne and coworkers[58] outlined three safety priorities for laser bronchoscopy—maintenance of ventilation, effective suction, and a clear visual field. They felt the rigid bronchoscope was the most effective instrument to accomplish these goals. With rigid bronchoscopy, the airway is secure, and light general anesthesia can be administered for patient comfort and surgeon convenience. Maintaining a clear field and patent airway is more easily achieved with the rigid bronchoscope because of better suctioning capabilities. With the flexible scope, suction is limited because the working channel is partially occluded by the laser fiber. Control of bleeding is also superior with the rigid bronchoscope because the barrel of the scope can be used to tamponade the hemorrhaging site. An epinephrine soaked gauze pad can even be passed through the rigid scope and placed directly on the bleeding area. Although some physicians[59] report that the bleeding rate may actually be higher with the rigid technique because of the tendency to use the scope as a shearing tool, most authors[52,53] believe the ability to maintain a patent airway and control any excessive bleeding is of paramount importance. Thus, the rigid bronchoscope is a safer instrument for laser application in patients at higher risk for procedural complications.

Both rigid and flexible bronchoscopy are associated with advantages and disadvantages that need to be considered when deciding on the best technique to employ the Nd:YAG laser. Each case should be handled individually, but the primary advantages of the rigid bronchoscope are its efficiency, effectiveness, and safety in the treatment of large malignant obstructing lesions of the tracheobronchial tree. For distal small airway lesions or nonvascular benign tumors, the flexible bronchoscope can be used safely and effectively for laser applications. Debate will likely continue as to which is the best technique for laser bronchoscopy, but the answer is more likely a factor of the type and location of the lesion rather than the actual bronchoscopic instrument used. Bronchoscopists performing laser photoresection of tracheobronchial lesions should be proficient in both techniques to assess the risks and benefits of each technique as it applies to a particular patient.

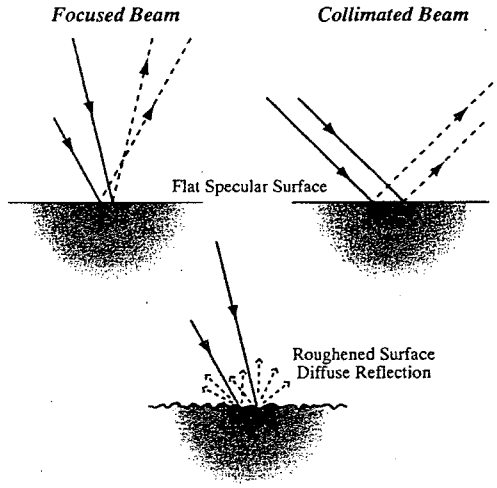

Figure 5-10

Reflection characteristics of surfaces.

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Safety

Laser safety requires the knowledge of the properties of individual lasers and the potential hazards that can arise with improper use. Each laser has a different capacity for producing injury, and the American National Standards Institute (ANSI) has classified lasers (I to IV) based on the degree of their potential hazard.[60] This classification system uses an accessible emission limit (AEL) and a maximum permissible exposure (MPE) limit for various organs.[1] The AEL is the amount of laser radiation that can be collected by a specific detector per unit of area. The MPE corresponds to the total energy absorbed by the tissue and is a function of the wavelength of the laser and the duration of exposure. A class I rating is given to lasers that do not emit hazardous levels of radiation and represent the lowest risk for injury. Class II lasers are also very safe if exposure duration is limited to less than 0.25 s in the visible band of light because the natural aversion reflex of the eye is rapid enough to avoid injury by this type of laser. Their low power gives an AEL of below 1 mW, which is the arbitrary power level that separates class II lasers from the next laser class. Class III lasers have a wide power range between 1 and 500 mW and can be potentially dangerous even if viewed momentarily. Most surgical lasers are classified as class IV because they have a power output above 500 mW. The main safety risks for surgical lasers are thermal and ocular injuries related to accidental reflection of laser light.

Inadvertent injury to the patient and operating room personnel is an important safety concern with the use of class IV surgical lasers. Misdirected laser light energy can reflect off instruments and specular (shiny) surfaces located near the operating field causing corneal, retinal, and thermal injury to exposed areas (Fig. 5-10). Surgical instruments can be roughened or blackened to help diffuse and absorb these poten-

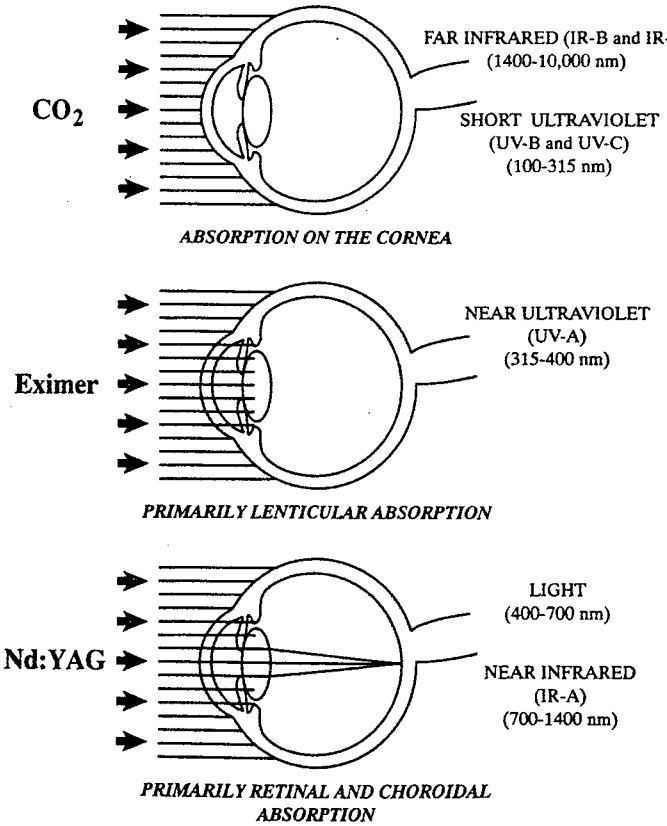

Figure 5-11

Primarily retinal and choroidal absorption.

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tially dangerous reflections of laser light.[61] Even if a laser beam is reflected, it retains much of its focus and intensity because of the collimation and coherence properties of laser light.[62] The dangers of reflected laser light are often not readily apparent because Nd:YAG and CO_2 lasers have wavelengths in the invisible range of the electromagnetic spectrum. The bronchoscopist may actually be at the highest risk for injury because Nd:YAG laser light can scatter and reflect back along the endoscope. This is usually not a concern with the CO_2 laser as the optics of the system protect the operator from injury. To avoid inadvertent injury from reflected laser light, safety glasses or eye shields are mandatory for all operating room personnel as well as for the patient. In addition, the windows in the procedure room should be covered to protect anyone outside the room from becoming accidentally exposed. Signs indicating the use of laser light should also be placed on the doors entering the room. Certain built-in precautions, such as foot pedals for laser activation and a standby mode, help to avoid accidental deployment of laser energy.

One of the most well-recognized hazards of class IV surgical lasers is retinal or corneal injury. Although the eye has a natural lid aversion reflex that limits exposure to bright light, the power density of certain lasers is great enough to produce significant damage. Because of their various wavelengths, lasers affect the eye in different ways (Fig. 5-11). Laser beams with short wavelengths in the ultraviolet region (100 to 400 nm) or long wavelengths in the far infrared region (1400 to 10,000 nm) of the electromagnetic spectrum are absorbed by the cornea and lens of the eye. Lasers with wavelengths in the visible and near infrared region (400 to 1400 nm), such as the Nd:YAG laser, are more dangerous to the retina. This area of the electromagnetic spectrum has been termed the retinal hazard region because laser light of this wavelength can be focused by the lens onto the retina with a magnitude of up to 100,000 times.[62] If the beam becomes focused onto a small point on the retina, significant damage can occur from thermal effects. If the damage is in an area, such as the fovea of the macula, irreversible loss of fine vision can occur. Unfortunately, the loss of vision is usually permanent because neural tissue has limited ability to regenerate itself. For this reason, all lasers in classes II to IV should be considered potentially dangerous to the eye if adequate precautions are not taken. The type of eye protection is important because safety glasses are designed for use with lasers of a specific wavelength. Eye protection manufactured for use with one type of laser may not be protective against lasers with a different wavelength. For instance, clear plastic safety glasses are adequate for brief exposures to CO_2 laser energy because of the limited penetration of CO_2 laser light, but a Nd:YAG laser can easily penetrate plastic or glass. For protection against the Nd:YAG laser, special eye wear with an optical density of 7.0 at 1064 nm is required.

Although ocular damage is the most feared safety risk, the skin and airway mucosa are also susceptible to injury from the laser. The likelihood of injury to the skin may actually be greater than to the eye because of the larger area of exposure. Lasers in the visible and near infrared region (400 to 1400 nm), such as the Nd:YAG laser, can produce thermal injury severe enough to create third-degree burns.[62] The CO_2 laser, however, has a longer wavelength (10,600 nm) that limits skin penetration and reduces the risk of a severe burn. Nevertheless, thermal injury can still occur if exposure is prolonged or if plastic, paper, or cloth items near the surgical field are accidentally ignited by the laser. The airway mucosa is also vulnerable to thermal injury because airway fires can occur if the flexible bronchoscope, endotracheal tube, or plastic suction catheter is accidentally ignited by the laser.[51] A polyvinyl chloride (PVC) endotracheal tube should not be used with a CO_2 laser because it is flammable, and toxic gases can be released from the burned plastic. The use of a red rubber tube with aluminum wrapping can reduce the risk of airway fires caused by the CO_2 laser.[63] This special tube should not be used with a Nd:YAG laser because the darker rubber tube may actually absorb more laser energy. The risk of airway fires can also be reduced by limiting the power of the Nd:YAG laser exposure time and the F_{IO_2}.[64] The use of a metallic rigid bronchoscope will also substantially reduce the risk of airway fires, although with proper precautions, a flexible bronchoscope or endotracheal tube can be used safely during laser applications. Although airway fires and burns are rare events, they are important safety considerations when using most types of surgical lasers.

The composition of the smoke plume generated by the laser has also recently come under investigation.[65] In 1988, a questionnaire study by Lobraico and coworkers[66] demonstrated an association between CO_2 laser treatment of papillomas and the subsequent development of these lesions in the treating physicians. Furthermore, Garden and colleagues[67] demonstrated the presence of intact human papillomavirus (HPV) DNA in the vapors of laser-treated verrucae and cautioned practitioners about the potential transmissibility of infection. Abrahamson and coworkers,[68] however, were unable to demonstrate HPV DNA present in the smoke plume from vaporization of laryngeal papillomas unless direct suction contact was made with the tissue during surgery. The presence of human immunodeficiency virus (HIV) DNA in laser smoke has also been documented, but sustained growth of the cultured cells did not occur, possibly because of damage produced by the laser energy.[69] The risk of clinical disease in surgical personnel from viral transmission has not yet been established, but special safety

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Table 5-5
DUMON'S 10 COMMANDMENTS OF SAFE YAG LASER RESECTION[18]

1. Know the anatomic danger zones: Aortic arch, pulmonary artery, and esophagus being the main hazard areas.
2. Have a well-trained laser team, including an anesthetist specialized in light general anesthesia and two assistants drilled in emergency response procedures.
3. Screen patients carefully: Any endoluminal growth is amenable to laser resection, but purely external compression is beyond the reach of the technique.
4. Use the rigid bronchoscopic technique (custom-made open tube, light general anesthesia, straight telescope, and two suction catheters) for any high-grade obstruction, especially if malignancy is involved.
5. Monitor blood gases and cardiac performance. At the least sign of hypoxemia, interrupt treatment long enough to oxygenate the patient, if necessary under closed-circuit conditions.
6. Fire the laser parallel to the wall of the airway; never aim directly into it.
7. Coagulate at will but avoid using the laser at high power settings; mechanical resection after laser coagulation is preferable to laser resection alone whenever possible.
8. Do not neglect hemorrhage, for even slow bleeding will lead to hypoxemia if left unattended.
9. Terminate each procedure with a thorough laser irradiation of the resected area and a tracheobronchial toilet to remove all secretions and/or debris.
10. Keep the patient under observation in a specially outfitted recovery room for a reasonable period of time.

precautions, such as smoke evacuation systems, are recommended until further studies can be performed.

Certain guidelines need to be followed for the safe operation of the Nd:YAG laser during bronchoscopy (Table 5-5). For flexible bronchoscopy, these recommendations concentrate on the prevention of hemorrhage and airway fires (See Table 2-1). To help avoid these complications and achieve successful results, the location of the tip of the laser fiber should be known at all times. When firing the laser, the tip of the fiber should be at least 4 cm from the distal end of an endotracheal tube and at least 4 mm from the end of the bronchoscope to prevent ignition of the plastic. The concentration of inspired oxygen should also be 40 percent or less to decrease the risk of airway fires. The tip of the laser fiber is best positioned 0.4 cm to 1 cm from the lesion and should be kept clean at all times. When appropriately positioned, the laser should also be fired parallel to the airway wall in pulses of 0.4 to 1 s in duration with a setting of 20 to 40 W. The goal of Nd:YAG laser application should not be to vaporize the tumor completely but rather to photocoagulate the lesion to produce hemostasis and necrosis. Residual tumor can be removed mechanically with biopsy forceps, a balloon catheter, or vigorous suctioning, eliminating the need for vaporization. Aggressive use of laser energy should also be avoided because penetration of the Nd:YAG laser is often deeper than is apparent on the surface, and the full extent of tissue necrosis is not complete until 24 to 48 h after the procedure.[45] Instead, repeat bronchoscopy is recommended in a few days to assess the extent of the remaining tumor and need for further treatment. For smaller lesions, subsequent bronchoscopy may not be necessary, but for large obstructing lesions, a multiple stage procedure is often the safest approach. If these guidelines are followed, Nd:YAG laser bronchoscopy can safely and effectively be performed through the flexible bronchoscope with successful palliation in more than 80 percent of patients.[56]

For rigid bronchoscopy, the same Nd:YAG laser fiber is passed down the barrel of the scope along with a suction catheter and telescope. The laser fiber is aimed at the lesion by manipulating the rigid scope itself. The laser power settings remain at 20 to 40 W, with a pulse duration of 0.4 to 1 s. The metal rigid bronchoscope is nonflammable, and thus the laser fiber does not have to extend beyond the end of the scope. It is important, however, to keep the flexible suction catheter out of the laser field to avoid any chance of fire. The laser fiber should be in close proximity (<1 cm) to the lesion because laser energy disperses as it exits the tip of the fiber, and the distance to the lesion determines the effective power density. As with flexible laser bronchoscopy, the initial goal should be photocoagulation of the tumor and not vaporization. Debridement of the remaining tissue can be accomplished by alligator forceps or a suction catheter. If needed, the beveled end of the rigid bronchoscope can be also used to shear off parts of the tumor once photocoagulation

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has devitalized the tissue. Care must be taken not to perforate the airway wall with the rigid scope. It is always important to know the path of the distal airway before aggressively advancing the scope beyond the tumor. The flexible scope can be helpful for blunt dissection of the tumor and in evaluating the airways distal to the main obstruction. After most of the tumor has been removed by these means, hemostasis can be achieved through further laser photocoagulation.

Outcome

Although laser bronchoscopy has become more commonly used for benign and malignant tracheobronchial obstruction,[18–20,22] no randomized controlled trials exist proving a survival benefit in treated patients. Numerous studies, however, have shown a significant palliative benefit with regard to relief of dyspnea, control of hemoptysis, and facilitation of weaning from mechanical ventilation. In 1419 patients with bronchogenic carcinoma, Cavaliere and coworkers[19] achieved satisfactory immediate results corresponding to a normal airway lumen gauge or significant improvement in ventilation in 93 percent of patients. Brutinel and colleagues[24] found that airway caliber was improved in 79.7 percent of 182 sites and that even completely obstructed airways could be opened 57.7 percent of the time. In a previous study at the Lahey Clinic,[20] subjective symptomatic relief was demonstrated after 313 of 400 procedures (78.3 percent) in patients with benign and malignant disease.

Although many of the larger studies relied on subjective measurements of improvement, other studies have documented objective benefits in pulmonary function tests, performance scores, and even ventilation-perfusion scans after laser bronchoscopy. Spirometry and flow volume loops have shown immediate functional improvement, with increases in peak expiratory flow rates ranging from 26 to 512 percent.[70,71] Waller and coworkers[72] showed a mean overall improvement in FEV_1 of 27 percent and symptomatic relief in 103 of 116 patients whose main complaint was dyspnea. Gelb and Epstein[49] reported significant improvement in Karnofsky performance scores, dyspnea index, and FEF_{25-75} in 23 of 27 patients with incomplete malignant obstruction of the tracheobronchial tree. Jain and colleagues[73] also used Karnofsky scores in patients treated by Nd:YAG laser photoresection and reported an improved performance status in 13 of 15 patients lasting between 2 and 13 months. Other performance scores, such as the simple 0 to 4 symptom score used by Clarke and coworkers,[74] confirmed good symptomatic relief in 73 percent of their first 200 patients consecutively treated with laser bronchoscopy.

Ventilation-perfusion relationships have also been studied in patients undergoing laser bronchoscopy. George and colleagues[75] found that both ventilation and perfusion improved after laser treatments in 23 of 28 patients (82 percent) and that spirometric values, 6-min walking distance, Karnofsky performance index, and breathlessness scores also improved significantly. In addition, it appears that improvements are not simply transient. Although some patients with benign and malignant tracheobronchial lesions may require multiple procedures, Emslander and coworkers[76] reported complete or partial removal of tumor in 74 percent of 224 laser applications and showed that in 72 percent of the successful results, the stenoses were still open after 4 to 6 months.

Nd:YAG laser photocoagulation is also effective at controlling hemoptysis[9,73,74] from malignant endobronchial lesions, with a response rate estimated to be 60 percent.[9] Although photocoagulation for hemoptysis has shown initial success, long-term benefits were not as easily maintained as with treatment for relief of dyspnea. Clarke and coworkers[74] reported that patients who were treated principally for hemoptysis tended to have a recurrence of their symptoms within 30 days of treatment, whereas those who were treated for dyspnea or cough tended to experience recurrence much later.

Laser bronchoscopy has also been shown to be beneficial for patients with impending respiratory failure as well as for those who require mechanical ventilation. Radiation therapy can relieve cough, chest pain, and dyspnea in 60 to 80 percent of patients, but it only relieves atelectasis in 25 percent of patients, and improvement is usually delayed.[77] External beam radiation therapy is a common palliative intervention for patients with bronchogenic carcinoma, but only laser bronchoscopy provides the means for rapid resolution of symptoms. In one series,[70] laser bronchoscopy was successful at relieving breathlessness and avoiding mechanical ventilation in 11 of 14 patients who had respiratory distress on presentation. The authors[70] concluded that laser treatment provided an excellent method of resuscitating patients with life-threatening tracheal obstruction, enabling subsequent management, such as radiation therapy, chemotherapy, or tracheobronchial stenting. Laser bronchoscopy may also facilitate weaning from mechanical ventilation in patients with respiratory failure caused by endoluminal obstruction. Stanopoulos and colleagues[78] reported that laser bronchoscopy improved the clinical status of 9 of 17 mechanically ventilated patients by permitting successful extubation. This subgroup of patients had appreciably shorter requirements for mechanical ventilation and a longer survival. The initial use of Nd:YAG laser bronchoscopy for treatment of an endobronchial lesion can be debated, but the palliative use of laser therapy in an inoperable, symptomatic pa-

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Table 5-6
SURVIVAL DATA OF PATIENTS WHO UNDERWENT LASER BRONCHOSCOPY

Author	*Number Patients*	*Number Primary*	*Number Metastatic*	*Percent Improved*	*Survival 3 Months*	*Survival 6 Months*	*Survival 1 Year*	*Mean*	*Median*
Cavaliere et al.[23]		333		92%	75%	50%	26%		
Beamis et al.[20]	236	200	36		60%	34%	10%		
Brutinel et al.[24]		71	17	79%	65%[a]	55%[a]	28%		
Kvale et al.[31]				92%					
Dumon[18]	278			85%					
Eichenhorn et al.[80]		19		84%	75%[a]	70%[a]	35%[a]		340 days
Clarke et al.[74]		105	12		72%	45%	25%		5.9 months
Desai et al.[79]		47			55%	42%	21%	208 days	143 days

[a]Estimate by Kaplan-Meier curve.

tient has been shown to be beneficial for relief of dyspnea, control of hemoptysis, and weaning from mechanical ventilation.

Laser bronchoscopy is clearly a valuable tool in providing immediate symptomatic relief, but its survival benefit is more difficult to demonstrate (Table 5-6). Randomized studies[79] evaluating this palliative treatment in terminal patients has been considered unethical. Although the issue of survival is a difficult one, it appears that there may be a survival advantage for patients undergoing laser resection of malignant tracheobronchial obstruction. In a preliminary study of 19 patients treated with laser photoresection, Eichenhorn and coworkers[80] found a median survival of 340 days, which was greater than 198 to 266 days found in historical control subjects using irradiation alone.[81,82] In another study using historical controls, Brutinel and colleagues[24] compared 71 patients with bronchogenic carcinoma treated with Nd:YAG laser photoresection with 25 patients who would have received laser treatment had it been available. They found that 76 percent of the control subjects were dead within 4 months, and all were dead within 7 months. By contrast, 60 percent of patients in the laser-treated group were alive at 7 months and 28 percent were alive at 1 year. Desai and colleagues[79] also found a significant increase in survival in a subgroup of patients treated with emergent laser resection compared with historical control subjects who had emergent radiation therapy alone. In mechanically ventilated patients, Stanopoulos and coworkers[78] showed an increased survival (98 days versus 8.5 days) in patients who were weaned after emergent laser resection of an obstructing lesion. The addition of brachytherapy to laser resection may also contribute to increased survival. Shea and colleagues[83] found an improved mean survival time (41 weeks versus 16 weeks) in patients treated with both endobronchial brachytherapy and Nd:YAG laser photoresection.

Although a survival advantage was suggested by these data, the retrospective design of the studies makes statistical validation difficult. Furthermore, other authors[84] failed to show any overall survival benefit for patients undergoing laser treatment. Although Desai and coworkers[79] found improved survival in a subgroup of patients treated emergently, they did not find an overall increase in survival in patients who underwent elective laser photoresection. Clarke and colleagues[74] also gave no evidence that laser treatment prolongs life and suggested that patients die of progression of their primary disease rather than obstruction of the bronchi. Nevertheless, patients on mechanical ventilation or with impending respiratory failure likely represent a subgroup of patients who may have a survival benefit from laser photoresection. A survival advantage may also be seen if endobronchial brachytherapy is combined with laser resection.

Absolute survival, however, may not be the best way to judge the importance of a palliative intervention in symptomatic patients. The rapid relief of dyspnea and improved performance provide justification for laser bronchoscopy in most patients. Laser bronchoscopy has been shown to be an effective method for immediate relief of respiratory symptoms related to both benign and malignant tracheobronchial obstruction. It is complementary to other modes of therapy, such as radiation, chemotherapy, stenting, or surgery, and often provides the time necessary to initiate these treatments. Relief of endoluminal obstruction also facilitates the treatment of postobstructive

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pneumonia. After 11 years and more than 1500 patients, Cavaliere and coworkers[19] concluded that laser therapy is no longer considered a treatment of last resort but instead has its own role in the therapy of cancer of the lung. Laser bronchoscopy should be an initial consideration for patients with severe tracheobronchial obstruction irrespective of survival analysis.

TECHNIQUE OF RIGID BRONCHOSCOPY

More than 80 percent of the laser bronchoscopy procedures performed at our institution are performed using a rigid bronchoscope. This is our preferred method of laser application for patients with high-grade obstruction of the trachea, main bronchi, bronchus intermedius, and occasionally lesions at the origin of the lower lobe bronchi. Patients undergo rigid bronchoscopy as described in Chap. 3. The procedure takes place in a standard operating room. Laser safety precautions are followed strictly. Personnel in attendance include the bronchoscopist, the anesthesia team (M.D. or certified registered nurse anesthetist), a scrub nurse, a circulating nurse, and a nurse whose sole responsibility is to operate the laser. For most routine laser applications, the Storz ventilating bronchoscope (Karl Storz Endoscopy-America, Culver City, CA) is used. If use of a stent is likely, the Dumon-Harrell rigid bronchoscope (Bryan Corp, Woburn, MA) may be used. The Storz bronchoscope is preferred because it has its own inner light source and thus can be used without a telescope. This permits the use of rigid suction instruments and large biopsy and alligator forceps to remove bulky tumor fragments. The Storz bronchoscope does not have specific channels for the laser fiber and flexible suction catheter as does the Dumon-Harrell bronchoscope. We do not consider this a disadvantage because we prefer to place the laser fiber, suction catheter, and telescope through the open end of the bronchoscope. These three instruments within the barrel of the bronchoscope "stent" each other, enabling easy maneuverability. Since we prefer to use Venturi Jet ventilation, we are not concerned about air leaking from the open end of the bronchoscope. Although we initially used a beam splitter to permit direct vision down the telescope and video display, we currently perform the procedure guided solely by the image on a video monitor. A three-chip CCD video camera (Smith and Nephew, Andover, MA) produces an excellent video image, permitting the operator, the anesthesiologist, and support personnel to follow the procedure. A sketch of our standard setup for laser bronchoscopy is shown in Fig. 5-12.

As described in Chap. 3, the patient is brought to the operating room suite and administered general anesthesia and muscle relaxation. One of the three methods to intubate the trachea with a rigid bronchoscope is employed. When the bronchoscope is below the vocal cords and near the level of the lesion, the laser fiber and a plastic suction catheter are passed through the open end of the bronchoscope along with the optical telescope (Fig. 5-13). When the lesion to be treated is tracheal stenosis, the laser is used at short pulse durations and at relatively high power. A setting of 0.7-s pulse duration and 40 W of power might be used. Because the Nd:YAG laser is not a good cutting tool, it will not cut fibrotic stenosis as well as a CO_2 laser might. However, at short pulse durations and relatively high power (but never more than 50 W of power), the Nd:YAG laser becomes a fairly good cutting tool. Several cuts are made in the region of stenosis, usually at the four quadrants. Care is taken to deliver the laser energy parallel to the airway. After a laser cut has been made in the stenotic web, the tissues tend to fall apart. It may take several laser shots to heat the tissue sufficiently to produce vaporization, but when vaporization begins, the tissue usually cuts easily with minimal or no bleeding. When sufficient radial incisions have been accomplished, the rigid bronchoscope is used to dilate the area of stenosis. Often bronchoscopes of several diameters, beginning with the smallest available, must be used to dilate the airway. On occasion, we use Jackson dilators (Karl Storz Endoscopy-America, Culver City, CA) to stretch

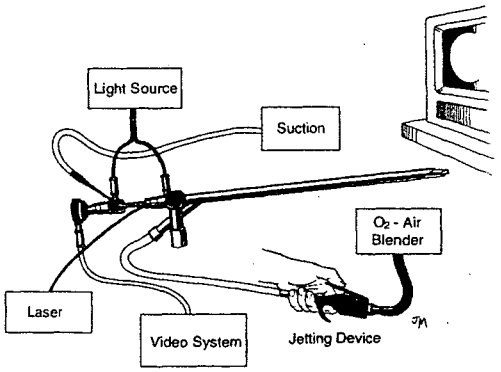

Figure 5-12

Laser bronchoscopy setup currently used at Lahey Clinic Medical Center.

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Figure 5-13

Positioning of patient, bronchoscopist, and rigid bronchoscope during laser bronchoscopy.

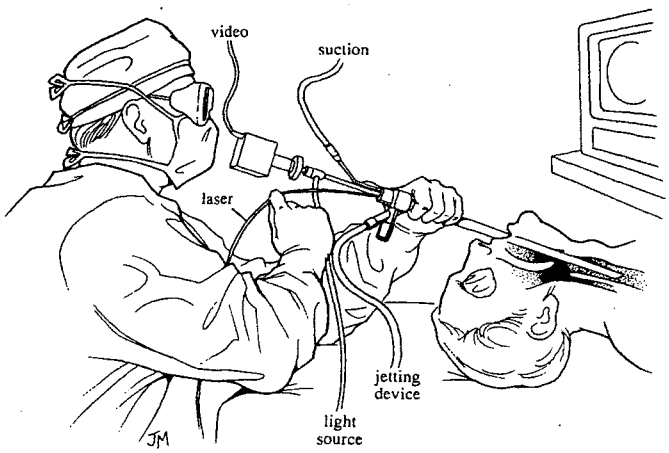

Figure 5-14

Rigid bronchoscopy technique of Nd:YAG laser bronchoscopy. *A.* Photocoagulation of lesion; suction catheter close to lesion. *B.* Lesion resected with tip of bronchoscope and delivered into barrel of scope. *C.* Distal airway is suctioned of secretions. *D.* Laser fiber passed through flexible bronchoscope within the rigid bronchoscope to treat base of tumor.

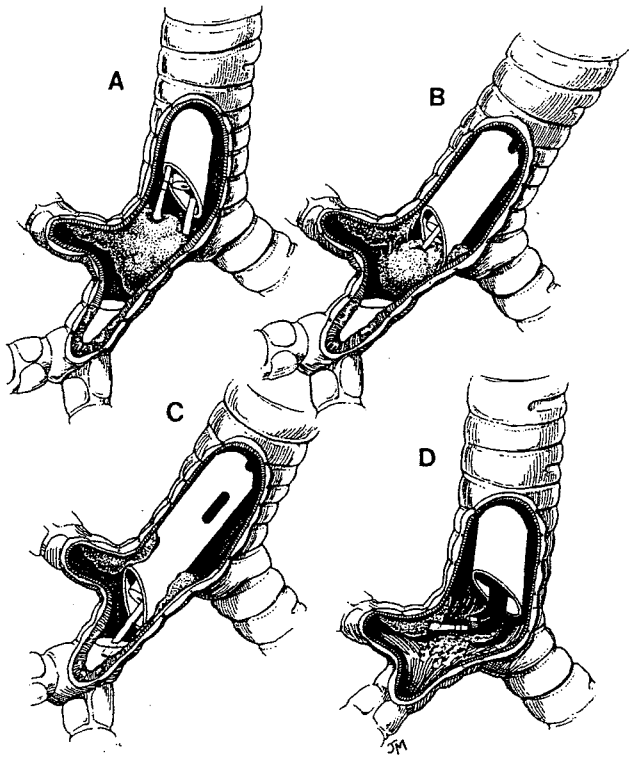

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Figure 5-15

Chest roentgenogram of patient before (*A*) and after (*B*) laser bronchoscopy for metastatic endobronchial obstruction.

the airway. The goal in the treatment of tracheal stenosis is to use as little laser energy as possible to prevent further airway inflammatory changes that might lead to restenosis.

In treating malignant endobronchial obstruction, the rigid bronchoscope is brought as close to the superior margin of the tumor as possible without irritating the tissues and producing bleeding. The laser is used at energies to promote photocoagulation rather than vaporization. Usually Nd:YAG laser power settings of 30 W at 1-s pulse duration are used. Because the blood often spatters, the tip of the telescope is kept within the barrel of the bronchoscope. The laser fiber is advanced approximately 1 cm distal to the tip of the bronchoscope. The suction catheter is held by the fingers of the right hand and is used to probe the tumor and remove any bleeding and necrotic debris from the surface of the tumor. Initially, multiple brief laser shots are used to photocoagulate the surface of the tumor. The aiming light from the laser helps direct each laser shot. An attempt is made to "paint" the entire surface of the tumor without producing vaporization. As the tumor becomes photocoagulated, it often shrinks to some degree. Again, it is important to fire the laser parallel to the direction of the airway. In near total or total obstruction, one must be careful not to fire the laser into the wall of the airway, possibly leading to perforation. When the tumor is sufficiently photocoagulated, the bronchoscope is gently advanced using the tip of the bronchoscope to shear the tumor from the bronchial wall. Knowing when the tumor has been photocoagulated sufficiently to permit safe resection takes considerable experience. The bronchoscope is advanced in a corkscrew type of motion, with any pressure being applied along the normal airway wall rather than toward the tumor bed. Permitting the tip of the bronchoscope to dig into the tumor bed could lead to airway perforation. As tumor fragments are resected, they are delivered through the barrel of the bronchoscope using the suction catheter or an alligator forceps. When the airway caliber has been established by tumor resection and dilation with the bronchoscope, the bed of the tumor is photocoagulated using brief laser shots. This technique prevents delayed bleeding. The tumor resection procedure using the rigid bronchoscope is shown in Fig. 5-14. After the airway lumen has been reestablished, secretions distal to the area of obstruction are suctioned clear. The bronchoscopist must always remember that the treatment of most endobronchial tumors is palliative treatment and that viable tumor will usually remain in the airway wall. The goal is to achieve sufficient airway caliber to permit

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Figure 5-16

Laser bronchoscopy with flexible bronchoscope.

reestablishment of function in the distal airways and drainage of secretions without damaging the airway wall by aggressive laser or bronchoscopic manipulation (Fig. 5-15). When laser resection has been completed and the muscle relaxants are reversed, the patient is permitted to awaken from anesthesia. All attempts are made to extubate the patient in the operating suite. Because most patients are in the last stages of malignancy, it is desirable not to reintubate the patient and to have the patient leave the operating suite breathing spontaneously without need for endotracheal tube or ventilator. Patients are discharged several hours after the procedure or occasionally after one night's hospitalization. Endobronchial brachytherapy may be performed within 24 h after laser resection.

TECHNIQUE OF FLEXIBLE BRONCHOSCOPY

The 15 to 20 percent of laser procedures performed with a flexible bronchoscope (Fig. 5-16) in our institution are for lesions with less than 50 percent airway obstruction, to photocoagulate or vaporize benign lesions, or to coagulate bleeding tumors that cannot be resected. The procedure is performed in our bronchoscopy suite. A standard fiberoptic bronchoscopy technique is used, with topical anesthesia to nares and

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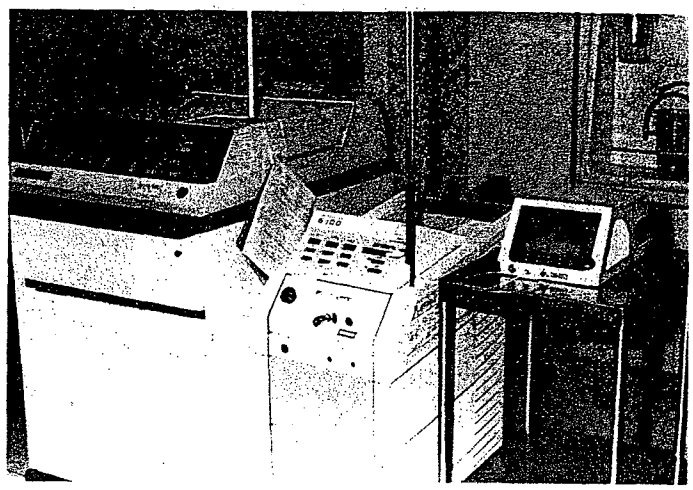
Figure 5-17

Nd:YAG lasers. *Left*, Heraeus 8900: 100-W, water-cooled laser circa 1985. *Middle*, Laser Sonics 5500: 60-W, air-cooled laser circa 1995. *Right*, Cerlas D980 NM diode laser with tissue interaction; properties similar to those of Nd:YAG laser (Ceram Opec, East Long Meadow, MA).

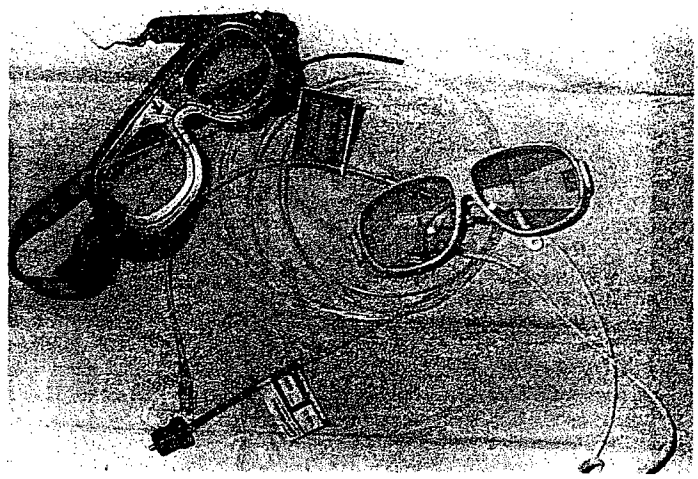


posterior pharynx and conscious sedation with midazolam and meperidine. The bronchoscope is passed transnasally to the level of the lesion. The laser fiber is passed down the working channel of the bronchoscope. It is important that the laser fiber tip be placed at least 1.5 to 2 cm from the tip of the bronchoscope. The laser settings are usually 1-s pulse duration with 30 W of power. Since the laser fiber occludes the bronchoscope working channel to the point that suctioning is inefficient, the procedure must be halted frequently to clean the region of any debris and char that develops from the laser heat. Firing the laser into char may set off a spark, which could lead to a disastrous airway fire. Fragments of tumor or tissue can be removed with biopsy forceps or with suction. After the procedure, the patient is observed for a brief period of time and then discharged. When the goal of the procedure is to photocoagulate the surface of a bleeding tumor, the initial laser shots are made at the base of the tumor in a circumferential manner. As the tumor shrinks and becomes devascularized, the laser shots are aimed closer to the center of the bleeding site. This method often results in effective palliation of hemoptysis for days to several weeks.

Occasionally, patients with high-grade airway obstruction are treated with fiberoptic bronchoscopic

Figure 5-18

The 1.8-mm coaxial quartz fiber for Nd:YAG laser application. Protective goggles and glasses for Nd:YAG laser usage.



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laser application under general anesthesia. In this instance, the patient is intubated with a large endotracheal tube (8 to 9 mm if possible), and the scope is passed into the airway through a standard swivel adapter that permits mechanical ventilation with the scope through the endotracheal tube. In this situation, Mehta's rule of 4s (see Table 2-1) must be followed. Again, the surface of the tumor is photocoagulated with the laser. Because resection is not performed as easily as with the rigid bronchoscope, the tumor must be at least partially vaporized. Tumor fragments can be removed with suction or biopsy forceps. Balloon catheters can be used to dilate and probe the airway further. Occasionally, endoscopy snares are used to remove fragments of tumor. Because it is difficult to remove large pieces of tumor, this procedure may take a considerable amount of time. Some physicians prefer to photocoagulate the lesion extensively at one setting and then to return in 24 to 48 h for removal of devitalized tumor. As with other general anesthetic techniques, all attempts are made to extubate the patient at the end of the procedure.

EQUIPMENT

Lasers used for bronchoscopy are shown in Fig. 5-17. Protective eye wear is shown in Fig. 5-18.

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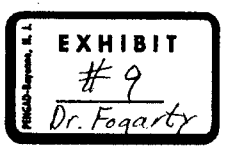

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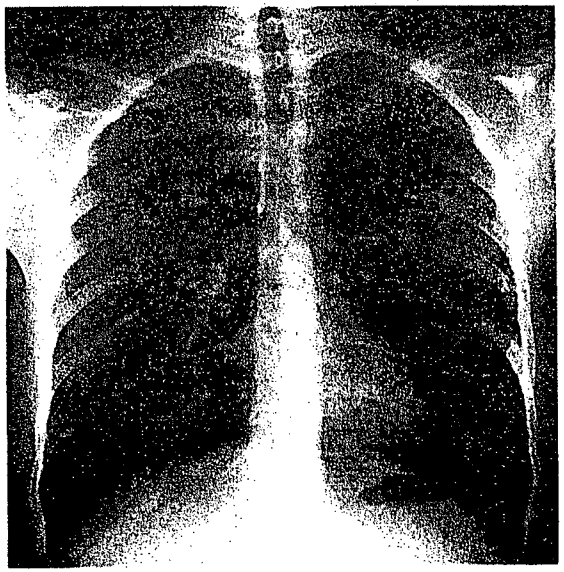

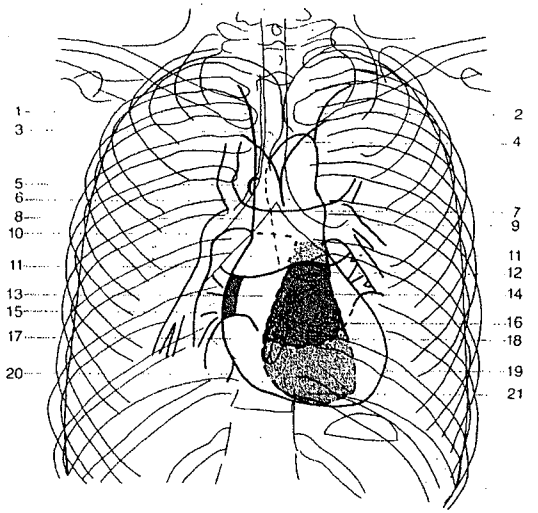

1 Contour of the right brachiocephalic vein
2 Contour of the subclavian artery
3 Anterior junction line
4 Aortic arch
5 Azygos vein
6 Superior vena cava
7 Main pulmonary artery segment
8 Right pulmonary artery
9 Left pulmonary artery
10 Interlobar pulmonary artery
11 Right lower lobe pulmonary artery
12 Pulmonic valve
13 Left atrium
14 Aortic valve
15 Confluence of pulmonary veins
16 Mitral valve
17 Right atrium
18 Tricuspid valve
19 Left ventricle
20 Inferior vena cava
21 Right ventricle

EXHIBIT #9 Dr. Fogarty

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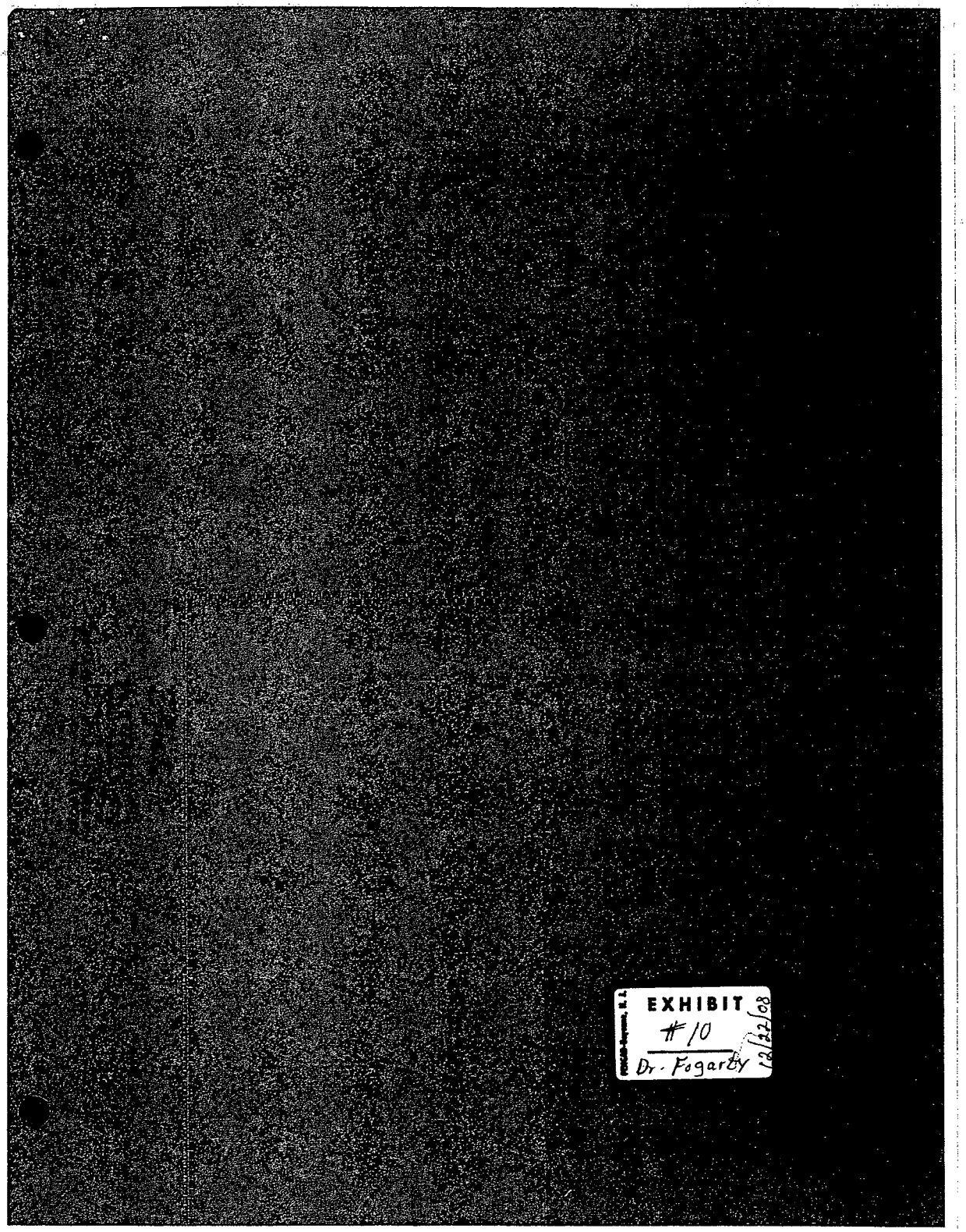

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Tracheobronchial foreign bodies in adults.

Limper AH, **Prakash UB**.

Mayo Clinic, Rochester, Minnesota.

STUDY OBJECTIVE: To define the clinical spectrum of tracheobronchial foreign body aspiration in adults, assess predisposing conditions, evaluate the efficacy of bronchoscopy, and determine outcome and complications. DESIGN: Retrospective analysis of a consecutive clinical series. SETTING: A tertiary care, referral-based medical center. PATIENTS: Sixty consecutive adult patients (over 16 years of age) evaluated for tracheobronchial foreign body aspiration. INTERVENTIONS: All 60 patients had bronchoscopic evaluation; 59 of them had foreign bodies identified and removal was attempted using either rigid or flexible fiberoptic bronchoscopy. MAIN RESULTS: Of 60 consecutive patients, 25 had underlying impairment of protective airway mechanisms (primary neurologic disorders, trauma with loss of consciousness, or sedative or alcohol use). Fifty-seven were successfully managed with bronchoscopy. Fiberoptic bronchoscopy was successful in 14 of 23 patients, and rigid bronchoscopy was successful in 43 of 44 patients, including 6 of 7 patients in whom previous fiberoptic bronchoscopy had failed. Thoracotomy was required in 3 patients. Complications of bronchoscopy were rare and not serious. Chronic complications of prolonged foreign body impaction included bronchiectasis in 3 patients. CONCLUSIONS: Although rare, tracheobronchial foreign body aspiration in adults can occur in various clinical settings. High clinical suspicion is necessary for diagnosis. Removal of foreign bodies can usually be accomplished with bronchoscopy.

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Tracheobronchial straight metallic pin aspiration in young Jordanian females.

El-Khushman HM, Sharara AM, Sa Ada MA, Hijazi MA.

King Hussein Medical Center, PO Box 2399, Tela'a Al-Ali, Amman 11953, Jordan. helkhushman@hotmail.com

OBJECTIVE: To define the clinical spectrum of tracheobronchial straight metallic pin aspiration in adults, assess predisposing conditions, evaluate the efficacy of bronchoscopy, and determine the outcome and complications at the largest 2 hospitals in Jordan. METHODS: Retrospective analysis of 60 consecutive clinical cases from 2 referral-based medical centers (32 patients at King Hussein Medical Center [KHMC] and 28 patients at Al-Basheer Hospital). Medical records of adult patients (>13 years of age) who presented with history of straight metallic pin aspiration over 6-year period (July 2000 and July 2006) were analyzed. Clinico-radiological features and location of the pins were studied. The flexible fiberoptic bronchoscopy (FFB) was used for foreign body (FB) identification and removal in all KHMC patients; video assisted rigid bronchoscope under general anesthesia was used at Al-Basheer Hospital. RESULTS: All patients were females <28 years of age. Fifty-six patients (93%) presented within the first 24 hours after aspiration. Medical history was suggestive of FB aspiration in all patients. Chest x-rays demonstrated the radio opaque pins in all patients. At bronchoscopy, the intermediate bronchus was the most common site of FB lodgment (62%). Ninety-two percent of patients were discharged on the same day of the procedure. CONCLUSION: Tracheobronchial straight metallic pins are relatively frequent FB in Jordanian young females and can occur in a very specific clinical setting. Removal of these FBs can usually be accomplished successfully by FFB.

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Extraction of pins from the airway with flexible bronchoscopy.

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BACKGROUND: Tracheobronchial foreign body aspiration is a worldwide health problem which often results in life threatening complications. Standard flexible bronchoscopy (FB) is used increasingly in the treatment of tracheobronchial foreign body aspiration in adults and older children, especially in the removal of aspirated foreign bodies which have entered into the peripheral bronchi. OBJECTIVES: In the present study, we discuss how to minimize complications and increase the success rate of FB in the aspiration of pins, and recommend techniques to facilitate the application. METHODS: The study was performed at a community hospital in Van, the Harran University Hospital in Sanliurfa and the Sutcuimam University Hospital in Kahramanmaras, Turkey. Between 2000 and 2005, 23 female patients between the ages of 12 and 23, who were admitted to the clinics and diagnosed as having tracheobronchial headscarf pin aspirations were included in our study to evaluate the efficiency of FB. Diagnosis of the patients was established by history, FB and radiological methods. All patients received transoral FB under local anesthesia. RESULTS: FB was successfully applied in all cases. During removal, the pins in 2 patients dropped at the proximal trachea and subglottic zone, and were ingested into the gastrointestinal track. In both cases, the pins were spontaneously excreted from the body in the stool within one day. No other complication was detected in the other patients during or following bronchoscopy. CONCLUSIONS: Our study suggests that FB is a safe, easy and successful method used in the removal of foreign bodies, such as pins, from the tracheobronchial trees. By employing FB, indications of thoracotomy and other invasive methods can be reduced especially in the cases of pins localized in distal airways and in the evaluation of suspected foreign bodies. (c) 2007 S. Karger AG, Basel.

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Extraction of dental crowns from the airway: a multidisciplinary approach.

Weber SM, **Chesnutt MS**, **Barton R**, **Cohen JI**.

Department of Otolaryngology and Head and Neck Surgery, Oregon Health and Science University, Portland, Oregon 97239, USA.

We describe two cases of airway foreign bodies (FB) consisting of a dental crown. The shape and composition of dental crowns complicate their extraction from the tracheobronchial tree, sometimes necessitating thoracotomy. We describe the use of a multidisciplinary approach involving rigid and flexible bronchoscopy in concert with the use of wire snares under fluoroscopic guidance for extraction of these challenging FB. These cases illustrate that this multidisciplinary approach can allow successful extraction of the difficult FB from much of the tracheobronchial tree and the avoidance of thoracotomy.

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FULL-TEXT ARTICLE

Combined rigid and flexible endoscopic removal of a BB foreign body from a peripheral bronchus.

Ruegemer JL, **Perkins JA**.

Otolaryngology-H/N Surgery, Madigan Army Medical Center, Tacoma, WA 98431, USA.

Aspirated foreign bodies (FB) in the peripheral tracheobronchial tree may present challenging management problems for the bronchoscopist. Critical to successful removal is maintaining airway control while minimizing endoscopy time. An innovative approach utilizing rigid and flexible bronchoscopy in removal of a distal impacted airway is presented. Difficulties encountered as well as advantages of this combined approach are discussed.

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LASER BRONCHOSCOPY

Evan R. Ramser, DO, and John F. Beamis, Jr, MD

LUL unfavorable location for Laser

The use of Laser (*L*ight *A*mplification by *S*timulated *E*mission of *R*adiation) for treatment of endobronchial disorders has become increasingly accepted over the past 15 years. With proper patient selection, laser bronchoscopy can dramatically improve quality of life and occasionally the length of life itself.[4, 11, 21] It has also been well demonstrated that reopening a previously obstructed airway can dramatically improve ventilation/perfusion matching in addition to improving overall functional status.[22] In general, any tissue capable of absorbing and reacting to the thermal effects of laser light can be potentially treatable by laser bronchoscopy. In skilled hands, the use of laser through either a flexible or rigid bronchoscope is a safe technique. Recognizing that this is a procedure frequently performed on patients with limited pulmonary reserve and impaired functional status, the morbidity and mortality from laser bronchoscopy are impressively low. In the majority of patients, this is a purely palliative therapy. It is most important that the patient and operator keep this in mind and maintain realistic expectations. This review describes the principles of laser bronchoscopy and various methods of photoresection of endobronchial lesions. In addition, the results of the past 2 years of laser bronchoscopy at the Lahey Clinic are reviewed.

HISTORY

The first laser used to treat airway disorders was the carbon dioxide (CO_2) laser. In the early 1970s, Strong and Jako[40] described the first experimental and clinical applications of the CO_2 laser with the treatment of several laryngeal disorders. Because of the excellent results of laser therapy on the larynx, it was only natural that these investigators would extend laser application below the vocal cords.[41, 42] Using a special adaptor, a CO_2 laser was attached to a rigid bronchoscope and laser bronchoscopy was performed. In 1973, Strong and associates[41] reported on their first experiences with CO_2 laser bronchoscopy. They described a series of 15 patients, both adults and children, who received a total of 70 treatments. All but two of the patients underwent treatment for laryngotracheal papillomatosis. Two patients underwent procedures for tracheal stenosis. Although some recurrent papillomas developed, there were no complications as a direct result of the laser surgery. This initial experience proved that laser treatment could provide precise resection and tissue destruction in a confined area with excellent hemostasis.

The first treatment of endobronchial malignancy with laser is frequently credited to LaForet and co-workers[25] who used Strong's apparatus to resect the endobronchial portion of a muco-epidermoid carcinoma obstructing the distal trachea. The lesion was partially vaporized and carbonized and multiple tumor fragments were extracted re-establishing a tracheal lumen and resulting in marked improvement in the patient's dyspnea.

As more experience with CO_2 laser bron-

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choscopy was gained, it became apparent that this laser was an ideal tool to remove granulation tissue and papillomatosis and to resect tracheal stenosis.[1] It also became apparent, however, that there were significant limitations to CO_2 laser bronchoscopy.[43] The nature of the CO_2 laser wave-length prevents the use of a flexible conductor or fiber and requires that the laser be shot down the barrel of the rigid bronchoscope. This prevents the use of optical telescopes and limits visualization of the laser-tissue interaction. The hemostatic properties of the CO_2 laser are limited to capillary bleeding, as may occur with benign conditions, but has proved to be inadequate to control bleeding in the treatment of bulky vascular endobronchial cancers.[43]

Recognizing the mechanical limitations of CO_2 laser delivery systems, Toty and associates[44] performed laser bronchoscopy with a neodymium yttrium aluminum garnet (Nd:YAG) Laser which delivers laser energy with a flexible conductor. The conductor was a flexible quartz fiber which permitted application through a rigid bronchoscope and also could be passed through the channel of a flexible fiberoptic bronchoscope. Toty and associates'[44] first report described 164 patients undergoing 317 laser procedures for various indications including new and recurrent obstructing malignant tumors, benign tumors, latrogenic stenosis, and granulomas. There were two immediate postoperative deaths, but no significant intraoperative complications. Soon thereafter Dumon and colleagues[45] reported on a series of 111 patients treated by endobronchial Nd:YAG laser application. Similar results of rapid palliation of obstructing endobronchial malignancy and the ability to improve tracheal stenosis in a minimally invasive fashion were noted. These two initial studies of bronchoscopic Nd:YAG laser therapy laid the groundwork for much of the development in this field. From these studies it became apparent that the Nd:YAG laser would be a more technically acceptable tool and that it could be used via flexible or rigid bronchoscopes requiring minimal modification of available equipment.

LASER LIGHT

Lasers are sources of intense light or electromagnetic radiation. Except for photodynamic therapy (discussed by Edell and Cortese elsewhere in this issue), laser bronchoscopy relies on the thermal effect of laser radiation. Light energy is transformed into heat as the laser interacts with living tissue. Although some lasers emit visible light, the CO_2 and Nd:YAG lasers produce invisible light in the infrared and near-infrared range of the electromagnetic spectrum, respectively.[46] Medical laser machines usually incorporate a red light producing helium-neon laser to act as an aiming light. The CO_2 laser wavelength, 10.6 μm, is strongly absorbed by water and thus by all biologic tissues. This laser can precisely vaporize tissue with minimal and predictable depth of penetration.[46, 47] Blood vessels and lymphatics up to 0.5 mm in diameter can be sealed by the thermal effect of the CO_2 laser.[48] The CO_2 laser cannot reliably control bleeding when larger vessels are involved. The laser energy is not deeply conducted to surrounding tissues and produces controlled tissue destruction with minimal surrounding edema. The CO_2 laser must be delivered via a cumbersome articulated mirror system which is connected to a rigid bronchoscope using a specialized coupling device.[49] The laser beam must be precisely aligned to traverse the entire length of the bronchoscope before striking the airway pathology. The simultaneous use of optical telescopes and suction devices is usually not possible. A flexible fiber with which to transmit the CO_2 laser wavelength is still not available.

Nd:YAG laser energy, on the other hand, can be delivered through flexible quartz fibers. The laser beam is thus brought close to the area to be treated resulting in more accurate therapy. The Nd:YAG laser produces a unique laser-tissue interaction characterized by photocoagulation.[46, 47] There is considerable scattering of the laser energy throughout a volume of tissue that is determined by the amount of energy supplied and the duration of the impact. The tissue absorption of the laser energy is color-dependent: darker tissues absorb the laser energy more strongly than lighter tissues. The volume of tissue affected by laser application is thus greater and deeper but less precise than that of the CO_2 laser. Coagulation of protein and blood vessels deep to the surface results in excellent hemostasis.[46] The Nd:YAG laser can be used in a contact or noncontact mode and delivered through flexible or rigid endoscopes.[50] The laser beam is usually delivered via a coaxial delivery system that promotes cooling of the fiber tip. The beam then exits the fiber with a divergence of 10 degrees. Using the noncontact mode the amount of laser energy delivered to a specific tissue can be controlled by altering the distance between the fiber tip and the tissue. Various tissue interactions such as coagulation, cutting, or carbonization can be achieved.

INDICATIONS

Now with more than 20 years of worldwide experience with laser bronchoscopy, the primary indication for the procedure has become palliation of central airway obstruction by either primary or metastatic malignant tumors. These comprise approximately 65% to 80% of Nd:YAG laser cases reported in multiple series.[2, 7, 14] The next most common indication is tracheal stenosis, usually postintubation in origin. Less-common indications include benign endobronchial tumors, tumors of uncertain prognosis such as carcinoid tumors,[43, 45] foreign bodies,[24, 45] amyloid,[45] and broncholiths.[45]

Laser bronchoscopy is a therapy for central airway diseases. Best results have been achieved in treating lesions in the trachea, main bronchi, and bronchus intermedius.[1, 7] The more distal the area treated, the less rewarding the results. The endoscopic characteristics of favorable and unfavorable lesions for laser bronchoscopy are listed below:

Favorable Lesions
- Polypoid lesions
- Large endobronchial component
- Distal lumen visible
- Lesion confined to trachea and main bronchi
- Short length
- Functioning lung distal to obstruction

Unfavorable Lesions
- Obstruction by external compression
- Long tapering obstruction
- Extensive submucosal disease
- Total obstruction
- Upper lobe and segmental lesions
- Chronic collapse

Laser bronchoscopy is for the most part a treatment of palliation of symptoms of airway obstruction. Dyspnea is the most common symptom requiring palliation. Cough, relief of postobstructive infection, and hemoptysis are other common indications.[1] Laser bronchoscopy can be curative for benign conditions such as benign tumors and tracheal stenosis. Sutedja and co-workers[51] have documented that intraluminal typical bronchial carcinoids can be completely eradicated with bronchoscopic therapy including Nd:YAG laser therapy. Although there have been occasional anecdotal reports of cures of superficial bronchial cancers with laser bronchoscopy,[52] one cannot reliably expect photodestruction of even the most superficial lung cancer with the Nd:YAG or CO_2 laser.

Despite its somewhat cumbersome delivery system, the CO_2 laser remains an excellent tool for treatment of laryngeal and subglottic lesions. When focused to a small spot size, this laser is useful as a precise cutting tool for producing limited radial cuts in tracheal stenosis as described by Shapshay and associates.[53] In a defocused mode, the laser can ablate tissue such as papillomatosis and granulation tissue.[46] Because the Nd:YAG laser can perform all the functions of the CO_2 laser below the larynx plus offer superb hemostasis in the treatment of bulky vascular central airway neoplasms and be delivered close to the lesion with a flexible quartz delivery fiber, the Nd:YAG laser is the preferred laser for most tracheobronchial applications. The remainder of this article is confined to discussing Nd:YAG laser bronchoscopy.

RIGID VERSUS FLEXIBLE BRONCHOSCOPE

Bronchoscopists continue to be divided into two groups regarding the use of the rigid or flexible instruments for laser bronchoscopy. Personne and colleagues'[42] original technique used a rigid bronchoscope with special channels for suction and jet ventilation. Dumon and colleagues'[45] initially used a flexible bronchoscope through a rigid bronchoscope to direct the laser beam, a technique adopted by Hetzel and co-workers.[54, 55] Dumon soon abandoned the flexible scope for most procedures realizing that the laser fiber could be successfully aimed if passed through a rigid bronchoscope along with an optical telescope and suction catheter.[14, 47] Several "laser bronchoscopes" with special channels for the laser fiber and suction catheter have been designed and marketed.[52, 56] Our technique is modified after that of Dumon and uses a standard ventilating bronchoscope.[1, 56] An optical telescope, a suction catheter, and the laser fiber are passed through the open end of the rigid scope (Fig. 1).

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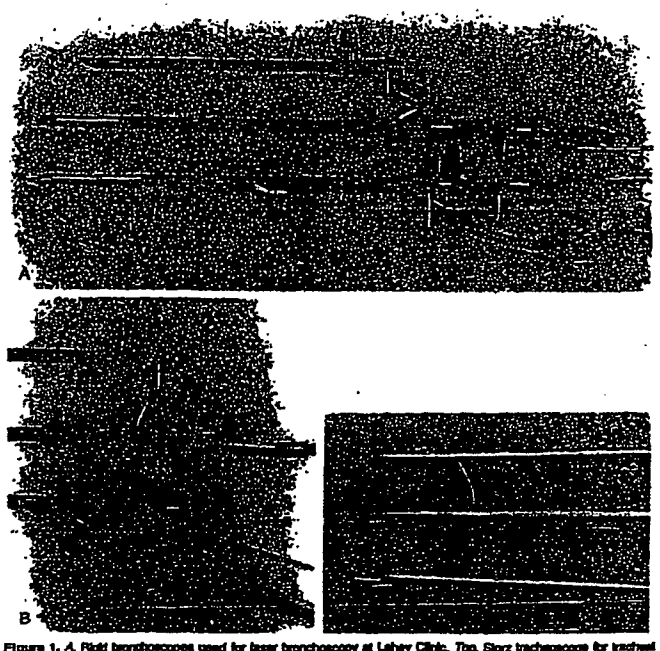

Figure 1. *A*, Rigid bronchoscopes used for laser bronchoscopy at Lahey Clinic. *Top*, Storz tracheoscope for tracheal lesions. *Middle*, Dumon-Harrell universal bronchoscope with suction catheter, telescope, and laser fiber. *Bottom*, Storz ventilating bronchoscope with suction catheter, telescope, laser fiber, and Venturi jet adaptor. *B*, Open end of bronchoscopes. *C*, Working end of bronchoscopes with usual orientation of telescopes, suction catheter, and laser fiber.

Some groups prefer to use the flexible fiberoptic bronchoscope alone.[5, 7, 14] The laser fiber is passed through the working channel of the bronchoscope. The bronchoscope is introduced either with or without an endotracheal tube. The patient can be treated under local or general anesthesia with this technique.[5, 14] Brutinel and co-workers[5] began using the flexible bronchoscope but switched to the rigid instrument and emphasized the shorter treatment times and more rapid removal of necrotic material with the forceps of the rigid bronchoscope. The optical telescopes available with rigid bronchoscopes offer visualization superior to that of the flexible instrument. The suctioning capabilities are enhanced and can be used simultaneously with the laser, unlike suctioning with flexible fiberoptic bronchoscopic laser application.

Chan and associates[6] compared their experience with 124 Nd:YAG laser procedures performed over a 5-year period. The fiberoptic bronchoscope was the sole instrument for the first 2 years and the rigid bronchoscope was used for the latter 3 years. There was no difference in survival rate or complication rate between procedures performed with the two instruments. It did appear that the rigid bronchoscope was superior in the treatment of proximal lesions, whereas the flexible instrument was recommended for distal lesions. Procedure times were significantly shorter with the rigid instrument. Although personal preference and experience will always result in two approaches to laser bronchoscopy, it is probably best for patient care that the laser bronchoscopist is skilled in both rigid and flexible bronchoscopy as these techniques are complimentary rather than competitive.

TECHNIQUE

Nd:YAG laser bronchoscopy using a flexible fiberoptic bronchoscope can be performed on awake, spontaneously breathing patients using sedative/analgesic agents and standard anesthetic techniques for diagnostic fiberoptic bronchoscopy. The bronchoscope is introduced transnasally or transorally and the laser fiber is passed through the working channel of the bronchoscope. Patients may also be treated using general endotracheal anesthesia and controlled ventilation. Whenever the Nd:YAG laser is used through a flexible bronchoscope, close attention must be paid to the location of the laser fiber tip in relation to the tip of the bronchoscope and the endotracheal tube. As a general rule, the bronchoscope should be advanced at least 4 cm past the distal end of the endotracheal tube and the tip of the laser fiber should be at least 1 cm from the tip of the bronchoscope.[14] The inspired oxygen concentration should be kept lower than 40%. With the tip of the laser fiber 4 to 10 mm from the lesion to be treated, the laser is fired in pulses of 0.5 to 1 second at energy settings between 20 and 40 watts. The goal of treatment with this technique is to either (1) vaporize a small lesion completely, or (2) provide enough photocoagulation that the lesion will necrose and slough off to be either coughed out or manually debrided.

Tumor fragments can be removed with endoscopic scissors, biopsy forceps, and balloon catheters. Some bronchoscopists prefer to use the contact method of Nd:YAG laser application when flexible bronchoscopy is used. This method allows a tumor to be cut off at its base with excellent coagulation. Our practice has been to limit Nd:YAG laser application with the fiberoptic bronchoscope to spontaneously breathing patients undergoing transnasal fiberoptic bronchoscopy. Our indications for laser bronchoscopy with a fiberoptic bronchoscope are outlined below:

- Benign condition, such as suture granuloma, papillomatosis
- Recurrent obstructions
- Narrow based, pedunculated tumors
- Airway obstruction < 50%
- Photocoagulation for hemoptysis
- In conjunction with rigid bronchoscopy

More extensive lesions are treated with a rigid bronchoscope.

The rigid bronchoscope offers many advantages for laser bronchoscopy including a large conduit for ventilation and suctioning, ability to tamponade areas of hemorrhage, and ability to rapidly remove large pieces of obstructing tumor allowing for rapid establishment of an airway.[14] In addition, the optical telescopes used with rigid bronchoscopy provide far better visibility than current fiberoptic bronchoscopes. Also the bevel tip of the rigid bronchoscope can be used for debridement and resection of obstructing endobronchial lesions. The main disadvantage in promoting laser bronchoscopy with a rigid bronchoscope is that most pulmonologists have not had training and experience with this instrument. However, if one has a solid background in fiberoptic bronchoscopy and the cooperation of anesthesia and surgical colleagues, developing proficiency in rigid bronchoscopy is not an insurmountable task.

For most distal tracheal and bronchial applications we have used a standard ventilating bronchoscope (Karl Storz America, Culver City, CA) (Figs. 1 and 2). If the lesion to be treated is confined to the mid or upper trachea, the Storz-Shapshay Tracheoscope is used (Karl Storz America) (Fig. 1). If the placement of a silicone endobronchial stent is required, we usually switch to a Dumon-Harrell Universal Bronchoscope (Bryan Corporation, Woburn, MA) (Fig. 1). The optical telescope, suction catheter, and laser fiber are placed through the open end of the rigid bronchoscope (Fig. 1). We have not believed it necessary to use bronchoscopes specifically designed for laser therapy. In fact, we have found the open-ended bronchoscope easier to use. With this technique, equipment can be removed rapidly and larger suction and biopsy forceps can be quickly inserted to suction blood or remove tumor fragments.

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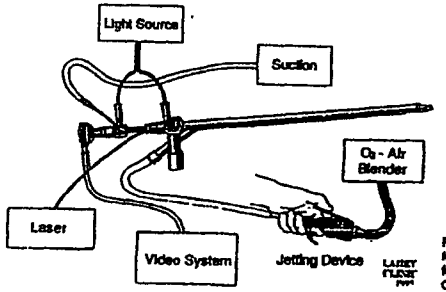

Figure 2. Rigid bronchoscope system for Nd:YAG laser bronchoscopy performed at Lahey Clinic. (From the Lahey Clinic, Burlington, MA; with permission.)

The Nd:YAG laser setting is similar to that used with flexible fiberoptic applications. Pulses of 30 W and 1 second duration are used most commonly. The tip of the telescope, laser fiber, and suction catheter are kept in close proximity near the distal end of the bronchoscope. The laser can easily be aimed by a twisting motion on the bronchoscope. Because the laser energy emerges from the tip of the laser fiber at a 10- to 15-degree angle, the power density of each laser shot is determined by the distance from the laser tip to the lesion. Initially, lower powers are used to photocoagulate the lesion. The lesion can then be partially removed by vaporization or by debulking. Once the tumor has been photocoagulated, the real advantage of rigid bronchoscopy can be used. The bronchoscope can be advanced through the obstruction, coring out the tumor, or the beveled edge of the scope can be used to shear off protruding tissue. It is imperative to identify a track into the distal airway to guide the debridement of tissue in order to avoid perforation of the airway. If the path of the distal lumen cannot be identified by probing with the suction catheter or the flexible bronchoscope, aggressive laser therapy or debridement with the rigid bronchoscope should not be attempted. Once the tumor has been debulked, the laser can be used again to photocoagulate the remaining tumor bed. Figure 3 depicts the removal of a right mainstem obstructing tumor using laser bronchoscopy.

ANESTHESIA

Anesthetic management of patients undergoing laser bronchoscopy is a challenge. Patients with smoking-related malignancies often have significant coronary and peripheral vascular disease along with moderate to severe chronic airflow obstruction. Cancer patients may have unpredictable prolonged or shortened effect of various anesthetic agents and muscle relaxants.[7] The presence of blood, clots, and laser-generated smoke in the airway may result in further airway obstruction and bronchospasm. In addition to addressing the above problems, the anesthesiologists must relinquish total control of the airway to the bronchoscopist. Rontal and associates[36] have made recommendations for anesthetic management of tracheobronchial laser surgery including the following: a team approach involving bronchoscopists, anesthesiologists, laser operator, and assisting nurses who are each aware of their own responsibilities; use of video monitoring equipment so that all team members can maintain awareness of each stage of the procedure; an emphasis on local anesthesia and spontaneous ventilation; use of the rigid bronchoscopic technique; continuous pulse oximetry during the procedure and in the immediate postoperative period.

Our current procedure uses intravenous propofol supplemented with midazolam and fentanyl. Atracurium is used as a muscle relaxant to allow for controlled, Venturi jet ventilation through the side-arm of the bronchoscope. Respiratory rate is controlled manually at approximately 20 per minute. In octogenarians and patients with severe tracheal obstruction, we always perform the initial intubation with the patient breathing spontaneously. Goldhill and co-workers[28] described an anesthetic practice very similar to ours except that a jet ventilator

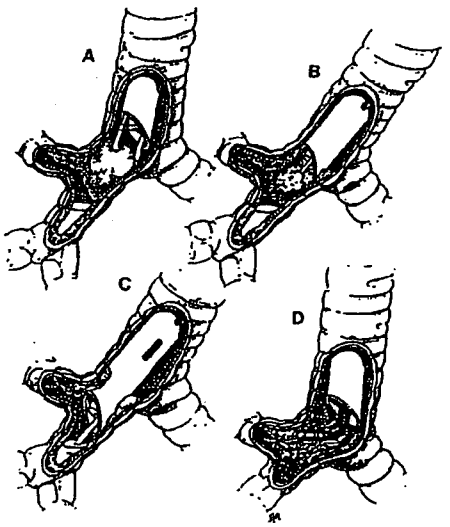

Figure 3. Technique of Nd:YAG laser bronchoscopy. A, Photocoagulation of lesion; B, lesion resected with tip of bronchoscope and delivered into barrel of scope; C, distal airway is suctioned clear of secretions; D, laser fiber is passed through the flexible bronchoscope within the rigid bronchoscope to treat tumor bed. (From the Lahey Clinic, Burlington, MA; with permission.)

is used at a respiratory rate of approximately 60 per minute. These investigators also confirmed the reliability and accuracy of pulse oximetry for monitoring patients undergoing laser bronchoscopy, and documented that significant concentrations of carboxyhemoglobin are not generated by laser smoke. High-frequency jet ventilation may also be used during laser bronchoscopy.[37, 38] Perrin and colleagues[39] prefer spontaneous-assisted ventilation using intravenous propofol or etomidate. Other investigators prefer inhalational anesthetics which require a closed system.[37, 39]

Regardless of the anesthetic and ventilatory technique, pulse oximetry is a must during any interventional bronchoscopy. Supplemental oxygen should be kept at a concentration of 50% or less during these procedures to limit risk of combustion. This places a patient with an already compromised ventilatory status at risk for significant oxygen desaturation. Use of oximetry has been demonstrated to detect these desaturations accurately[36, 37] allowing for rapid corrective measures.

Patients should be extubated immediately at the end of the procedure and allowed to breathe spontaneously. Propofol is an anesthetic agent that has been particularly helpful in achieving this goal. Several hours of close monitoring in a postanesthesia unit are indicated, as acute airway obstruction can occur secondary to clot formation or shifting of recently manipulated tissue. Re-expansion of previous atelectatic areas may lead to liberation of trapped mucus and secretions requiring aggressive pulmonary hygiene maneuvers.

Most patients are discharged the day following the procedure: an increasing number are discharged the same day.

OUTCOME

There have been no prospective randomized studies documenting the effectiveness of

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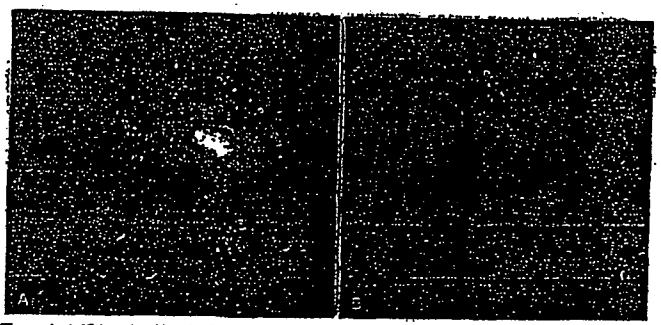

Figure 4. *A*, High-grade mid-tracheal obstruction from large cell carcinoma in an 85-year-old man. *B*, Recanalized tracheal lumen following laser bronchoscopy. The patient received external radiation therapy and is alive after 3 years.

laser bronchoscopy or its advantages over other therapies. To date, all studies have been retrospective descriptions of consecutive cases treated.[6] Four studies that compared results of laser therapy with historical controls suggest improved outcome with laser. In a small series, Jain and co-workers[9] compared patients with malignant tracheobronchial obstruction treated with laser bronchoscopy followed by radiation therapy with patients treated with radiation alone or with radiation followed by laser. The patients initially treated with laser bronchoscopy had a greater relief of airway obstruction and improvement in performance status, length of survival, and quality of life. Brutinel and colleagues[4] reported on 116 patients treated at Mayo Clinic and compared survival and quality of life results with 25 historical controls presenting with similar bronchial obstruction. All the historical control patients were dead within 7 months, whereas 60% of the laser bronchoscopy–treated patients were alive at 7 months and 28% were alive at 1 year. Dosel and associates[11] compared 47 patients treated with laser bronchoscopy with 53 historical controls and noted a significant improvement in survival for patients requiring emergency palliation of large airway obstruction. There was no improvement in survival in patients treated for nonurgent palliation of airway obstruction. Macha and colleagues[10] compared 75 patients treated with laser resection followed by radiation therapy for obstructing endobronchial tumors with 75 patients treated with radiotherapy alone for endobronchial occlusion by external compression. There was no difference in overall survival between the 75 matched pairs. In those patients who had successful recanalization of the obstructed airway by laser bronchoscopy, however, a 4-month increase in survival was noted compared with those who had unsuccessful laser therapy. Survival may not be a proper endpoint by which to judge the effectiveness of laser bronchoscopy. Most would agree that palliation of symptoms and improvement in quality of life are the most important goals of laser bronchoscopy. Few would argue that safe, rapid improvement of central airway obstruction, as in Figure 4, is not an effective therapy.

We have been performing laser bronchoscopy at Lahey Clinic since 1982. We reviewed our cases from 1992 through 1994 to illustrate a typical laser bronchoscopy experience. We treated 100 patients with 140 applications. The average age of the patients was 62 years. Sixty-four patients had bronchogenic carcinoma, 18 had metastatic endobronchial obstruction, and 18 had benign airway obstruction. Squamous cell carcinoma of the lung represented 54% of all bronchogenic tumors and 35% of the total cases. The most common

[6,7,9,13,15,18,21,29,33,64, and 65.

Table 1. LASER BRONCHOSCOPY AT LAHEY CLINIC BETWEEN 1992 AND 1994

Type of Obstructing Lesion	No. of Patients (%)	Total No. of Treatments
Benign	18	30
Tracheal stenosis	11 (61.1)	20
Neoplasms	7 (38.9)	10
Bronchogenic tumors	64	89
Squamous cell	35 (55.7)	44
Adenocarcinoma	7 (10.9)	18
Large cell	8 (12.5)	9
Small cell	5 (7.8)	8
Other	9 (14.1)	11
Metastatic	18	24
Colon	3 (16.7)	4
Renal cell	3 (16.7)	6
Other	12 (66.7)	16

nonmalignant indication was benign tracheal stenosis. Table 1 lists the causes of the airway obstruction and the number of treatments delivered. Over 87% of the procedures were performed at the level of the mainstem bronchi or above (Table 2). The procedure was believed to provide significant symptomatic relief or achieve its preoperative objective in 85.7% of the cases. No fatalities occurred during this series. We noted a complication rate of 6.5%. The complications included excess bleeding (1.43%), hypoxemia or hypercapnia resulting in premature termination of the procedure (1.43% and 0.71%, respectively), stridor (1.43%), cardiac arrhythmia (0.71%), and pneumothorax (0.71%). All these complications were considered minor and none altered the short- or long-term outcome. All patients were treated with rigid bronchoscopy under general intravenous anesthesia. The average length of the procedure was 42.7 minutes. In an earlier larger series of 269 patients undergoing a total of 400 procedures, we noted an anatomic improvement in airway caliber of 81.8% with an improvement in symptoms in

Table 2. SITE OF LESIONS

Trachea	40 (28.6)
Subglottic	5 (3.6)
Proximal trachea	12 (8.6)
Mid-trachea	19 (13.6)
Distal trachea	14 (10.0)
Carina	2 (1.4)
Right mainstem	40 (28.6)
Left mainstem	30 (21.4)
Bronchus intermedius	16 (11.4)
Left lower lobe	2 (1.4)

= 140.

78.3% of patients.[1] There was roentgenographic improvement of atelectasis in 70 of 130 patients with preoperative lung or lobar collapse. In our original series there was one intraoperative death due to a tension pneumothorax. In the largest series reported to date Cavaliere and associates[2] reported on 11 years of experience with 2253 applications in 1585 patients. In this series, squamous carcinoma made up 67% of the obstructing lesions. Radiographic and endoscopic improvement was noted in 93% of the patients with bronchogenic carcinoma. There was a complication rate of 2.3% with the most frequent complication being hemorrhage greater than 250 mL. A perioperative mortality rate of 0.44% was noted. One half of the deaths occurred during the procedure. The authors concluded that laser bronchoscopy should no longer be considered a therapy of last resort. This therapy currently has a distinct role in the management of lung cancer and often allows time for other therapies such as brachytherapy, endobronchial stents, external radiation therapy, and surgery.

Even patients in extremis may benefit from laser bronchoscopy. Stanopoulos and colleagues[16] described 17 patients with malignant airway obstruction presenting with respiratory failure requiring mechanical ventilation. Of these, 9 were successfully weaned from the ventilator after laser resection of obstructing endobronchial tumor. In 7 of the 9 patients, survival was sufficient enough to allow further treatment modalities. The improved outcome was related to the presence of obstructing endobronchial tumors; in the group that did not respond, the obstruction was primarily due to extrinsic compression of the airway.

COMPLICATIONS

Although a number of complications and hazards of laser bronchoscopy have been reported, this procedure has had a remarkable safety record considering the severity of central airway obstruction with which patients present and the frequent presence of comorbidities such as coronary artery disease and chronic obstructive lung disease. Operative mortality rate should be under 1%.[1,16] Early in our experience, cardiac events were the most common intraoperative and early postoperative complications. These have been virtually eliminated with the use of continuous

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Intraoperative pulse oximetry to assure adequate oxygenation.

Massive hemorrhage greater than 250 mL has been reported in 1% to 10% of cases.[16] This is usually because of a manipulation of a vascular tumor bed and often can be controlled with tamponade by the rigid bronchoscope. Fatal hemorrhage due to laser perforation of the pulmonary artery has been related to high laser power settings and the use of a flexible bronchoscope.[17] Other serious intraoperative complications include pneumothorax,[3] systemic and cerebral air embolism,[45, 46] and airway perforation. Dumon and co-workers[16] and Shapshay and Beamis[45] have outlined safety precautions for bronchoscopic laser surgery.

Postoperative problems include hypoxemia due to anesthetic respiratory depression, retention of secretions or debris, and hemorrhage from dislodged clots or inadequate tumor coagulation. Noncardiogenic pulmonary edema[47] and focal pulmonary hyperinflation[48] have also been reported in the immediate postoperative period. Immediate post-laser hemorrhage is uncommon if the tumor bed has been adequately photocoagulated. Macha and co-workers[49] noted that massive bronchial hemorrhage was the cause of death in 34.5% of patients treated with Nd:YAG laser bronchoscopy, but believed that the hemorrhage was caused by the natural history of the lung cancer rather than a direct sequela of the laser treatment.

Laser-related endobronchial fire is probably the most feared complication.[4] It should be noted that endobronchial fires have never been reported using the rigid bronchoscopic technique. Materials that ignite during laser bronchoscopy include the flexible fiberoptic bronchoscope sheath and endotracheal tubes. Endobronchial fire prevention and management techniques have been outlined by Denton and associates[50] and Krawitz and associates[51] and include the following: use of low oxygen concentrations during the procedure; laser pulses of 40 W or less; adequate spacing of laser pulses to allow dissipation of generated heat; keeping the tip of the laser fiber well separated from the endotracheal tube and the end of the bronchoscope; and rapid removal of the bronchoscope, tracheal tube, and laser fiber should a fire develop. The airway should be reinspected and any mucosal char or foreign material removed. Antibiotics, corticosteroids, and bronchodilators are usually administered. Granulation tissue and bronchial stenosis are often sequelae of endobronchial fires.[52]

SUMMARY

The worldwide epidemic of cancer of the lung has stimulated the development of therapies to relieve endobronchial obstruction. Table 3 lists a number of endobronchial therapies that might be used to treat malignant central airway obstruction. With over 15 years of worldwide experience, the Nd:YAG laser has proven to be the most important of these tools. Laser bronchoscopy can be performed with rigid or flexible instruments and produces a rapid recanalization of the airway with associated relief of symptoms. The treatment is repeatable and has acceptable immediate complications and infrequent delayed complications. To be effective, laser bronchoscopy can only be used for the treatment of intraluminal obstructions. Obstruction by submucosal infiltration and external compression require other endobronchial therapies. The performance of laser bronchoscopy requires an extra commitment by the bronchoscopist. A thorough understanding of airway and mediastinal anatomy is mandatory along with an appreciation of laser physics and tissue interaction. Attendance at specialized training courses may be required to satisfy local credentialing bodies.[2, 3] In the past 15 years, thousands of patients have benefited from the development of laser bronchoscopy techniques. No longer a therapy of last resort, laser bronchoscopy has proven to be an excellent tool to relieve the symptoms of central airway obstruction.

Table 3. ENDOBRONCHIAL THERAPIES

Tool	Scope Rigid/Flex	Rapid Effect	Repeatable	Comp: Immediate	Comp: Delayed	Lesion
Laser	R/F	+ + + +	- - + +	- +	+	endo
Brachytherapy	F*	+	-	-	+ + +	endo/sub
Cryotherapy	R/F	+ +	+ + -	+ +	- -	endo
Balloon Dilation	R/F	+ + - +	+ + + -	+ - -	-	extrinsic com
Photodynamic therapy	F*	+ + -	? + +	?	+ - -	endo/sub
Electrocautery	R/F	+ + +	+ - - -	+ +	+ -	endo
Stent	R/F†	+ + +	+ +	+ +	+ - -	ex com

R = rigid bronchoscope; F = flexible fiberoptic bronchoscope; endo = endobronchial, sub = submucosal, ex com = compression.
*Preferred method, might be performed with rigid scope.
†Dumon stent requires rigid scope; Wallstents and Ellerstovo stents require fluoroscopy.

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CRYOTHERAPY FOR TRACHEOBRONCHIAL DISORDERS

M. Omar Malwand, MD, and Jean-Paul Homasson, MD

Cryotherapy is the therapeutic application of extreme cold for local destruction of living tissue. Cold as a method of treatment has been used for centuries as evidenced by documents dating back to about 3500 BC.[1,2] A papyrus scroll of that time has documented that cold was used to treat inflammation and various war wounds, including those of the chest. Hippocrates, the father of medicine, described the use of cold to relieve the swelling and pain of trauma and other diseases affecting the bones and joints.[3] Baron Larrey, Chief Surgeon to the Imperial Guard of Napoleon, described in his *Memoires of Military Campaign Surgery* "It is obvious that the effect of cold has a sedative effect on the brain and nervous system. The part of body which is exposed to the cold is whiter than the rest of the body, all sensation is removed and the individual does not feel a sharp point. The fibres and capillary vessels become contracted, the fluids thicken and their circulation slows. The areas may remain in this stage of asphyxia without dying and if the cold is diminished by degrees, the equilibrium will easily be restored. There is a sharp line of demarcation between the soft area and the healthy part." Baron Larrey used this knowledge to perform amputation with minimal pain and hemorrhage on a large number of soldiers during the 1812 retreat from Moscow.[4]

James Arnott was the first physician to use the destructive effect of cold for the treatment of tumors. He designed special equipment for applying a mixture of ice and salt which achieved a local temperature of about −20°C at the tumor site. In 1848, he published results from 30 patients with carcinoma of the uterus.[5] Arnott was careful to claim no cure but reported a reduction in pain, discharge, odor, and histological regression of tumor.

By 1960, the advances in science, in particular the use of liquid nitrogen as a cooling agent, made the design of reliable and different cryoprobes and apparatus possible. Neurosurgeons were the first to use cryosurgery in Parkinson's disease.[6,7] Later this method was used extensively in skin disease. Zacarian[8] reported a 95% curative result for carcinoma of the skin in over 2000 patients. The technique has also been used during maxillofacial; ear, nose, and throat[9]; gynecologic[10]; and general surgery.[11]

The history of cryotherapy for tracheobronchial lesions has been relatively short due to the difficulty of anatomic accessibility. The use of cryotherapy for palliation of endobronchial tumor was renewed in the mid-1980s in France and the United Kingdom.[12,13]

Bronchogenic carcinoma is the commonest cause of death from malignant tumors in humans. Unfortunately, the majority of patients are not diagnosed until the disease is well advanced and not treatable surgically. Palliative therapy is the only possible treatment for these patients: chemotherapy and predomi-

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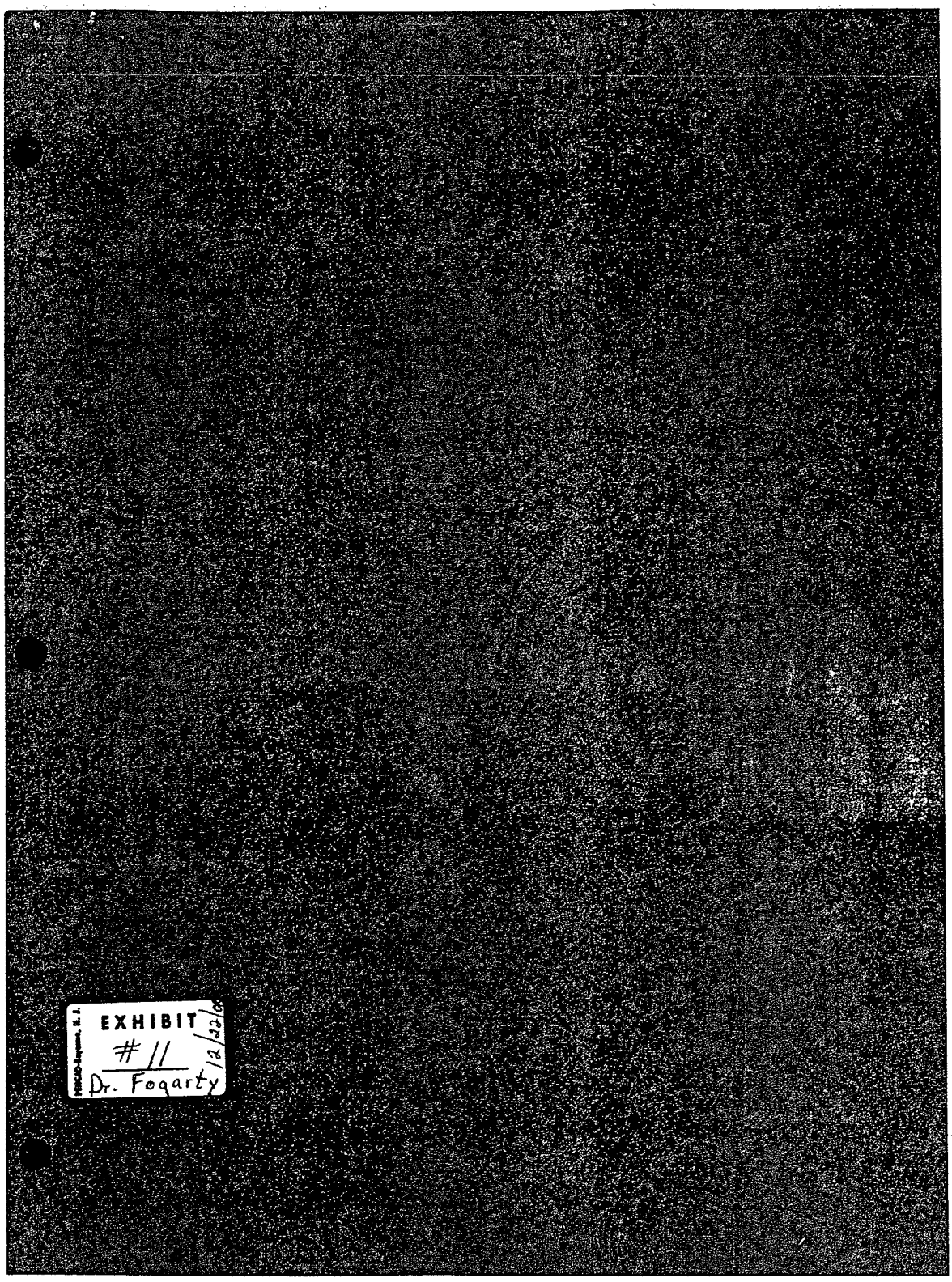

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Therapeutic Bronchoscopy

Endobronchial Laser Resection and Airway Stenting

Sandra Thomas, RN, CGRN
Antony Mathew, MD, FCCP

Lung cancer is the leading cause of cancer death among both men and women. About 30% of lung cancers cause obstruction of the major bronchus leading to severe complications such as postobstructive pneumonia, hemoptysis, and progressive dyspnea. Endobronchial laser treatment and airway stenting is an interventional pulmonary treatment offered to patients with lung tumors that obstruct the main airways. This article will provide an overview of endobronchial laser resection and airway stenting with a particular focus on procedural techniques and care of the patient.

Limited indication for LVL (RVL) Lcan

EXHIBIT #11 Dr. Fogarty

According to the American Cancer Society (www.cancer.org), lung cancer is the leading cause of cancer death among both men and women. There will be an estimated 154,900 deaths from lung cancer (89,200 among men and 65,700 among women) in 2002, accounting for 28% of all cancer deaths (American Cancer Society, 2002). About 30% of the lung cancers lead to obstruction of the major bronchus. Obstructive lesions of the airway cause severe complications such as postobstructive pneumonia, hemoptysis, and progressive dyspnea (Minna, Higgins, & Glatstein, 1989). Due to significant progress in equipment and techniques during the last few years, bronchoscopic endobronchial laser resection and stenting of the central airways has become possible. These procedures can be done as an out patient in the endoscopy lab. This article will highlight several important aspects of endobronchial laser resection and airway stenting including endoscopic techniques and patient care.

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Endobronchial Laser Resection and Airway Stenting

Endobronchial laser treatment and airway stenting is an interventional pulmonary treatment offered to patients with lung tumors that obstruct the main airways. Laser bronchoscopy was developed in the 1970s to early 1980s (Dumon, 1985). "Laser" is the acronym for Light Amplification by Stimulated Emission of Radiation. Lasers are identified by their wavelength, which also indicates their color. To date, only argon and Nd:YAG lasers have been used in endoscopy (Figure 1).

Laser light energy is transmitted through a flexible quartz waveguide that is usually protected by a plastic catheter that is passed through the endoscope. In order of decreasing wavelength and increasing frequency, electromagnetic radiation ranges from radio waves to gamma rays. The laser waves travel in parallel directions. It is important to note that laser light loses the property of traveling parallel when delivered through bare fibers, which have an irregular tip cross-section. As a result, aiming and control of power density become problematic. Fibers with metallic tips

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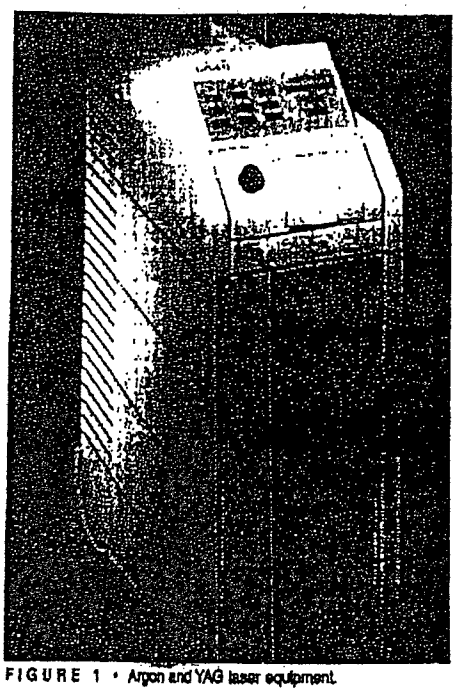

FIGURE 1 • Argon and YAG laser equipment.

should be used for endoscopic therapy. The metallic tip serves as an aiming guide to concentrate the energy. Only lasers that can be delivered through an optical fiber, i.e. the KTP, argon, dye, and YAG, are suitable for routine laser bronchoscopy.

Effects of YAG Laser Light on Living Tissue

The effects of a laser on living tissue depends on the temperature generated at the treatment site and the physical principles of light propagation (Dumon, 1990). Light can be transmitted, absorbed, diffused, or reflected. For instance, if the impact zone is white, the beam may be completely transmitted. In addition, transmission of YAG laser light is greater in pale tissues than in dark tissues. This is important because underlying dark tissue can be damaged during YAG laser treatment.

The laser light can be absorbed or converted into other forms of energy heat. The darker the tissue and the higher the power density, the greater the absorption. (Dumon, 1990). Tissue color depends mainly on tissue vascularization and on the laser charring. Photocoagulation creates a white blanched appearance with edema on the tissue while photovaporazation may cause charring of tissue and smoke.

Laser light can be diffused or spread over a certain circumference and depth. Laser light can also be reflected or bounced off the surface like a mirror. Reflection depends solely on the reflective power of the surface on which the light impinges (Dumon, 1990). Shiny and damp tissue are reflective. Metallic instruments are highly reflective. While reflection is not a major factor in YAG laser treatment, it can constitute a danger not only for tissues surrounding the operative site, but also for the unprotected eyes of the surgeon and endoscopy suite staff. The endoscope itself can also be damaged if laser energy is reflected from the target surface to the tip of the scope. To avoid damage from reflection, the endoscopist should make sure the laser fiber is advanced far outside the scope channel.

Power density (power/ spot diameter) depends on the power setting of the laser and the distance of the tip of the optical fiber from the tissue (Dumon, 1990). The duration of emission also determines energy density, the product of power density and time. Setting the laser in the discontinuous mode allows exact dosage of the amount of energy delivered to the treatment zone at each impact. The amount of energy and the spot diameter control the site and the depth of the laser treatment.

Procedural Indications

Mechanical dilation, laser, and stenting are essential components of endoscopic treatment. Any obstructive lesion in the main airway, trachea, and main stem bronchi is an indication for endoscopic laser resection and stent placement (Dumon,1990). For malignant lesions, surgery is the method of choice. Only patients ineligible for surgical resection should undergo endoscopic treatment.

Laser resection can be associated with radiation therapy and chemotherapy, but should be performed first. It is better to do the laser treatment first in order to relieve the airway obstruction by debulking the tumor, thereby preventing obstructive pneumonia. Chemotherapy also decreases the patient's resistance, which could potentially increase bleeding during laser treatment. Once radiation treatment is started, the tissue becomes hardened. This hardening interferes with how the laser beam is absorbed by the tissue and may also increase bleeding during endoscopy laser treatment.

Endobronchial carcinoid of typical histology is an indication for laser resection (Figure 2). Carcinoid tumors that are atypical in histology or have an extra bronchial extension are always surgical indications. Benign tumors such as hamartoma, chondroma, leiomyoma and papilloma can easily be removed endoscopically. Among tumors of uncertain prognosis, adenoid cystic carcinomas are rarely indications for surgery and can be treated by endoscopic techniques.

Procedural Contraindications and Cautions

Extrinsic compression of the trachea or main stem bronchus is a contraindication for laser resection due to the location of the tumor (Dumon, 1990). Even extrinsic lesions, however, can be treated now by using expandable stents (Figure 3). Carcinoid tumors of atypical histology should not be treated endoscopically because there may be extrabronchial extension of the tumor. An exception to this recommendation may be justified in patients with contraindications for surgery.

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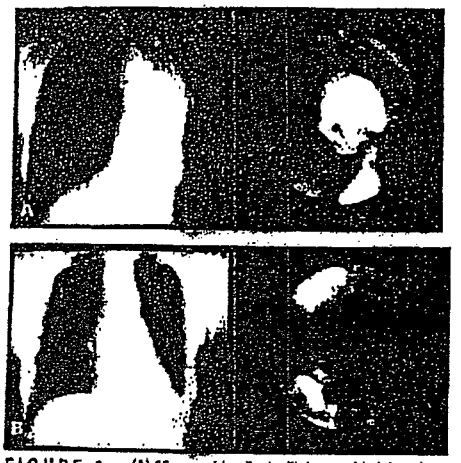

FIGURE 2 • (A) 65-year-old patient with inoperable left main stem obstruction, causing complete atelectasis of left lung. (B) Same patient after endobronchial laser resection.

Stenosis of the trachea and main stem bronchi requires a carefully planned association of resection, use of prosthetic devices, or transplant and medical treatment. Mechanical dilatation, laser, and stenting are essential components of endoscopic treatment for stenosis. Small peripheral lesions and lesions that do not compromise ventilation are theoretically not indications for laser resection or stent placement, but under certain circumstances exceptions may be made.

Laser Resection of the Airways

Anatomical Relationships

The trachea is easily accessible and its anatomical relationships are well known. Posteriorly, the esophagus is in permanent contact with the trachea. Anteriorly, the innominate artery crosses the lower third of the trachea. The aortic arch and the recurrent nerve are in contact with the left edge of the end of the trachea. The right main stem bronchus is in contact with the pulmonary artery anteriorly. The left main-stem bronchus is surrounded by the esophagus posteriorly, the aortic arch superiorly, and the pulmonary artery anteriorly.

FIGURE 3 • Expandable Schneider Wall Stent with and without Permalume covering.

Laser resection in the right and left upper lobe bronchi is difficult due to the lung anatomy. This is true even with a flexible fiberoptic bronchoscope because the rigidity of the laser fiber prevents angulation of the tip of the fiberoptic bronchoscope. Another danger in the upper lobe bronchi is close contact with the pulmonary artery, particularly on the left. For these reasons, indications for resection in the upper lobes are limited.

Access to the right lower and middle lobe bronchi and the left lower lobe bronchi is relatively easy. The main anatomic relations are the organs of the mediastinum, in particular the heart and pulmonary veins.

Physiologic Considerations

The volume of the tracheobronchial tree is only 150 cc (anatomical dead space). Even a minimal accumulation of blood or secretion can cause major hypoxia leading to dreaded cardiovascular risks: myocardial ischemia, arrhythmia, bradycardia, or cardiac arrest (Dumon, 1990). Maintaining a free airway and efficient ventilation at all times is essential to the prevention of complications. Proper precaution should always be taken when using oxygen in the presence of flammable materials such as a fiberoptic bronchoscope.

Endoscopic Techniques

Basic Principles of Endoscopic Resection

Safe endoscopic resection depends on maintaining ventilation, preventing hemorrhage, and minimizing laser exposure. To ensure ventilation, interruption of the resection to inspect the peripheral airways and perform aspiration should be initiated whenever necessary. To prevent hemorrhage, it is important to coagulate the lesion before resection. In this regard, it is essential to remember that at a given power setting, the closer the tip of the laser is to the target, the smaller the spot illuminated and, thus, the greater the power density. Power density can be changed simply by moving the tip of the laser closer to or farther from the surface. This rule constitutes one of the basic principles of laser resection.

Practically speaking, at a power setting of 30 to 45 watts with a emission duration of one second, the bronchoscopist can obtain tissue shrinkage and, therefore, devascularization by holding the fiber about one cm from the target. Charring and vaporization can be obtained by holding the fiber about 3 mm from the target.

Care of the Patient

Preprocedural Care

Preoperative evaluation includes assessing the patient's medical and pulmonary problems. It is important to obtain preprocedural arterial blood gases (ABGs), chest x-ray, and routine labs including a coagulation profile (PT, APTT, and platelets), particularly for those patients undergoing a laser resection. Clinical evaluation of the patient also includes identifying possible obstacles for intubation including evaluation of the cervical spine, since patients require hyperextension of the cervical spine for rigid bronchoscopy.

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Preprocedural teaching should include an explanation of the sequence of events during the procedure and the equipment that will be used. This information has been found in the authors' experience to relieve patient anxiety by enabling the patient to understand what is happening to them through each step of the procedure. The patient should also be advised they will not be allowed to eat or drink and that an intravenous line (IV) will be started. Medications (IV and topical) used for pain control and sedation should also be discussed.

Additional information should be provided about the patient's postprocedural routines. Patients should be prepared for frequent measurement of vital signs and continued restrictions on oral intake. Non-smoking status and the presence of a sore throat or hoarseness should be discussed. The patient should be taught they should avoid clearing their throat or coughing after the procedure. Any expectoration should be done in a sputum cup to allow the nurse to assess for unexpected bleeding.

Premedication

In the authors' practice setting, premedication for rigid bronchoscopy includes demerol 75 mg, phenergan 25 mg, and atropine 0.5 mg IM. For flexible bronchoscopy, premedication includes codeine 60 mg and atropine 0.5 mg IM. The preop medication is different in rigid and flexible procedures due to the difference in type of anesthesia used for the procedures.

For anesthesia, Diprivan has been found to be effective for rigid bronchoscopy because it counter-acts the laryngeal reflexes. With flexible bronchoscopy, the commonly used sedation is versed.

Intraprocedural Care

After obtaining consent, the patient is prepared for the endoscopic procedure. Rigid bronchoscopy (Figure 4) is usually done in the operating room setting under general anesthesia because of the need for further airway control. Flexible bronchoscopy can be performed with IV sedation in the endoscopy suite. Fluoroscopy is required for both procedures. Staff should wear masks with particulate filter respirators that provide fluid protection.

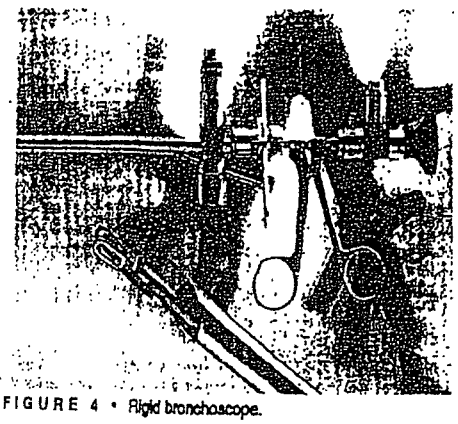

FIGURE 4 • Rigid bronchoscope.

Regarding staffing, the authors' practice is to utilize two registered nurses and one respiratory therapist during the endoscopic procedure. One registered nurse monitors the patient, including airway patency, the patient's level of consciousness, proper positioning of the patient, and patient vital signs including SAO2 and SMS. The second registered nurse supports the endoscopist's use of the laser, assuring that the laser and associated equipment are functioning appropriately throughout the procedure and that safety protocols are followed. The respiratory therapist assists the physician with technical support during the bronchoscopy.

Use of a large channel bronchoscope facilitates keeping a clear airway. The authors have found it is useful to use the regular gastroscopy forceps for debulking instead of the bronchoscopy forceps. A rat tooth forceps is helpful to clear a larger portion of debris at one time. Both types of forceps fit through the larger bronchoscope 2.8 channel. For dilation, a through the scope (TTS) 10 mm x 3 cm balloon filled with contrast is visualized under fluoroscopy.

Special Caution

Laser bronchoscopy is different from other types of laser cases in that work occurs in the airway and there is an increased chance of ignition. Using less than 50% FIO_2 is, therefore, recommended. The authors' practice is to turn the oxygen off when the laser is in use.

The laser power setting is also much lower for laser bronchoscopy compared to GI cases. A power setting of 30-45 watts with duration of one second is recommended for YAG laser bronchoscopy.

Because of airway involvement, laser bronchoscopy necessitates sequential steps. First the patient is well oxygenated. Next, the patient's external oxygen source is turned off. The laser is fired, the resulting smoke is evacuated from the airway, and the patient's oxygen source is turned back on. Scheduling of laser bronchoscopy must accommodate the additional time required to deliver this sequential care. Frequent removal of debris from the airway also requires additional time.

Postprocedural Care

Bronchial laser therapy requires an increased length of recovery time, generally two hours. Steroids may be necessary to control airway edema. A postprocedural chest x-ray is required after stent placement to rule out pneumothorax prior to the patient's discharge from the unit. Nursing assessment should also focus on monitoring for cardiovascular complications, pneumothorax, respiratory depression, hemorrhage, and perforation.

Complication and Accident Prevention During Therapeutic Endoscopy

Hemorrhage

Massive hemorrhage with resulting hypoxemia and perforation of surrounding structures is the most serious complication that can be encountered during laser endobronchial resection (Diaz-Jimenez, 1996). This complication can be avoided in the majority of cases with proper patient selection and technique. The most serious risk derives from poor

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ventilation. To aid in keeping the airway clear, a fire-resistant suction catheter made specifically for use with the laser can be used to provide continuous aspiration. For intubated patients, there are also specially made fire resistant endotracheal tubes.

Many patients have serious ventilatory insufficiency or failure consequent to the obstruction that has motivated the treatment. Therefore the principal objective is rapid tracheal or bronchial re-opening, that is enough to resolve the functional respiratory problem. A timid or insufficient attempt at re-opening can accentuate the obstruction.

When significant hemorrhage is produced during treatment, steps must be taken to control bleeding and keep the airways well ventilated. If bleeding is produced by a lesion situated in the trachea, the rigid bronchoscope should be passed through the lesion. The immediate aim is to compress the point of hemorrhage and ventilate the bronchial tree. The lesion should be then coagulated with laser. With bronchial lesions, the bronchoscope should be withdrawn into the trachea to ventilate the contralateral side as blood is aspirated out. The hemorrhage is simultaneously treated with local intervention such as laser coagulation.

Perforation

Perforation of surrounding structures is very rare, but usually catastrophic. It is best to avoid perforation by using good technique, avoiding direct laser shots to the tracheal or bronchial walls, and terminating the resection when the involved tissue does not absorb the laser beam well since this can be deeply damaging to the surrounding structures.

Complication

The mortality rate during treatment varies according to the reported series. It is lower among those using a rigid bronchoscope than those using a fiberoptic bronchoscope. (Diaz-Jimenez, 1996). Despite the fact that some authors find no difference in the results between the two methods, the authors believe that the rigid bronchoscope provides a better margin of safety than the flexible bronchoscope because of better visibility and the ability to introduce aspiration tubes and forceps. The time needed for the intervention is also less. The flexible bronchoscope can be introduced through the rigid bronchoscope to treat more distal areas.

Risks are further reduced using laser energies of no greater than 45 watts and by oxygen levels of less than 50% during laser emission. There have been several reports, like that of Casey et al. (1983) describing endotracheal ignition of the fiberoptic bronchoscope when using high energy laser bursts in the presence of high concentrations of oxygen.

Other infrequent complications have been reported including pneumothorax or pneumomediastinum, which usually occur in relation to mechanical ventilation during anesthesia, especially when jet ventilation is used (Dumon, 1990). There have been case reports, including an experience by the authors of the loss of the metallic protector of the distal end of the laser fiber because of excessive heating (Mehta, Golish, & Livingston, 1985).

Conclusions

In conclusion, laser bronchoscopy has made a significant contribution to the treatment of intraluminal airway disease. It can be used in conjunction with other forms of therapy. Laser bronchoscopy can provide significant palliation for patients with malignant or benign airway tumors who are not candidates for surgery. It may also spare some patients with tracheal stenosis the need for more invasive and risky surgery.

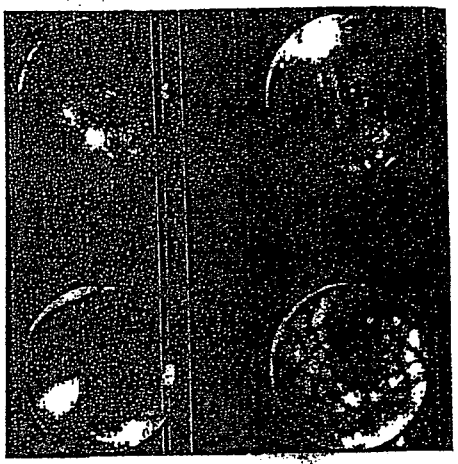

FIGURE 5 • 85-year-old postradiation therapy patient with diagnosis of inoperable non-small-cell carcinoma of lung who presented with increasing dyspnea. Bronchoscopy showed near compete obstruction of the right main stem. Patient underwent Wall Stent placement with a flexible fiberoptic bronchoscope as an outpatient. Note the improved lumen after the procedure. The patient had immediate improvement in symptoms.

The primary goal of airway stenting is to improve the patient's quality of life, though length of life may also be extended. The stent provides palliative treatment. Patients usually notice an immediate improvement in their airway after the procedure. One patient had such a remarkable improvement in her airway exchange after stent placement, she was able to return to her room on nasal cannula as opposed to her preprocedural status of endotracheal ventilation (Figure 5).

With appropriate patient selection and technique, laser photoresection represents a low risk option to achieve significant palliation for patients with benign and malignant conditions compromising the airway.

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CE TEST: Therapeutic Bronchoscopy: Endobronchial Laser Resection and Airway Stenting

Sandra Thomas, RN, CGRN, Antony Mathew, MD, FCCP

General Purpose: To provide gastroenterology nurses and associates with information on the use of endobronchial laser resection and airway stenting in the treatment of lung tumors that obstruct the main airways.

Objectives: After reading this article and taking the following test, the reader will be able to:
Describe the indications and procedure for endobronchial laser resection.
Discuss potential complications related to endobronchial laser resection.
Explain the management of the patient undergoing endobronchial laser resection.

CE Test

1. Which of the following patients is the best candidate for endobronchial laser resection?
   a. a patient who has a tumor with extrabronchial extension
   b. a patient who has a small peripheral papilloma lesion
   c. a patient who has a carcinoid tumor of atypical histology
   d. a patient who has a lung tumor that is obstructing the airway

2. Which of these strategies should be incorporated during a laser bronchoscopy procedure?
   a. use a metallic tip to aim and concentrate the energy
   b. aim the laser at the darker, internal tissues
   c. ensure that the laser light travels in a criss-cross motion
   d. protect the laser light energy with a rubber catheter

3. Which of these measures will prevent damage related to reflection during a laser bronchoscopy procedure?
   a. aiming the laser beam at shiny, deep tissues
   b. allowing the laser energy to bounce from the target surface to the tip of the scope
   c. ensuring that the laser fiber is advanced far outside the scope channel
   d. reducing the circumference of the diffused area

4. Performing laser resection prior to administering either chemotherapy or radiation treatments is likely to produce
   a. increased tissue fragility and bleeding.
   b. reduced incidence of obstructive pneumonia.
   c. decreased patient immunity.
   d. increased hardening of local tissues.

5. Which of these measures is essential to prevent complications related to laser resection?
   a. increasing the anatomical dead space
   b. using minimal anesthesia
   c. maximizing the laser exposure time
   d. removing accumulated secretions

6. Which of these actions will result in tissue shrinkage and devascularization during laser resection?
   a. holding the fiber about 1 centimeter from the target
   b. administering anticoagulant medications
   c. increasing the emission duration to 10 seconds
   d. reducing the power density of the laser to 55 watts

7. Routine preprocedure evaluation of a patient scheduled for laser resection includes all of the following except
   a. arterial blood gases (ABGs)
   b. pulmonary function test (PFT)
   c. chest x-ray
   d. platelet count

8. Treatment side effects of laser resection can include
   a. sore throat.
   b. facial swelling.
   c. aphasia.
   d. hearing loss.

9. Which of these activities should you instruct a patient to avoid after a laser resection procedure?
   a. swallowing his saliva
   b. brushing his teeth
   c. extending his neck
   d. clearing his throat

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10. Which of the following safety precautions do the authors recommend during a laser bronchoscopy procedure?
   a. maximize the laser power setting
   b. administer 100% FIO2
   c. turn off oxygen during laser use
   d. use a duration of 5—10 seconds

11. Untreated bleeding during therapeutic endoscopy is likely to result in which of these potentially fatal complications?
   a. hypertension
   b. hypoxemia
   c. renal failure
   d. tracheal stenosis

12. Which of these measures can reduce the possibility of perforation during therapeutic laser resection?
   a. using a fiberoptic bronchoscope
   b. avoiding direct laser shots to the tracheal wall
   c. prolonging the laser exposure time if the tissues are not absorbing the laser beam
   d. increasing the laser energy to promote visibility

13. During a laser resection for a tracheal lesion a large amount of bleeding is noted. Which of these actions should the clinician take?
   a. withdraw the bronchoscope
   b. insert an endotracheal tube
   c. pass a rigid bronchoscope through the lesion
   d. direct the laser shot to the bronchial wall

14. Which of the following types of drugs should you expect to administer after a laser resection to control airway edema?
   a. NSAIDs
   b. steroids
   c. sedatives
   d. anticholinergics

15. Cardiovascular complications as a result of major hypoxemia during a laser bronchoscopy include
   a. arrhythmias.
   b. congestive heart failure.
   c. cardiac tamponade.
   d. pulmonary embolus.

16. Which of these steps should be taken first during a laser bronchoscopy procedure?
   a. oxygenate the patient
   b. turn off all external oxygen sources
   c. evacuate airway smoke
   d. fire up the laser

17. Which of these actions is appropriate one-half hour after a laser resection?
   a. assess expectoration for signs of bleeding
   b. offer sips of clear liquids
   c. administer codeine and atropine intramuscularly
   d. encourage deep breathing and coughing

18. Which of these laser techniques will help reduce treatment complications?
   a. slowly re-opening the trachea and bronchi
   b. maximizing the temperature generated at the treatment site
   c. setting the laser in the discontinuous mode
   d. rapidly expanding the treatment circumference of the laser

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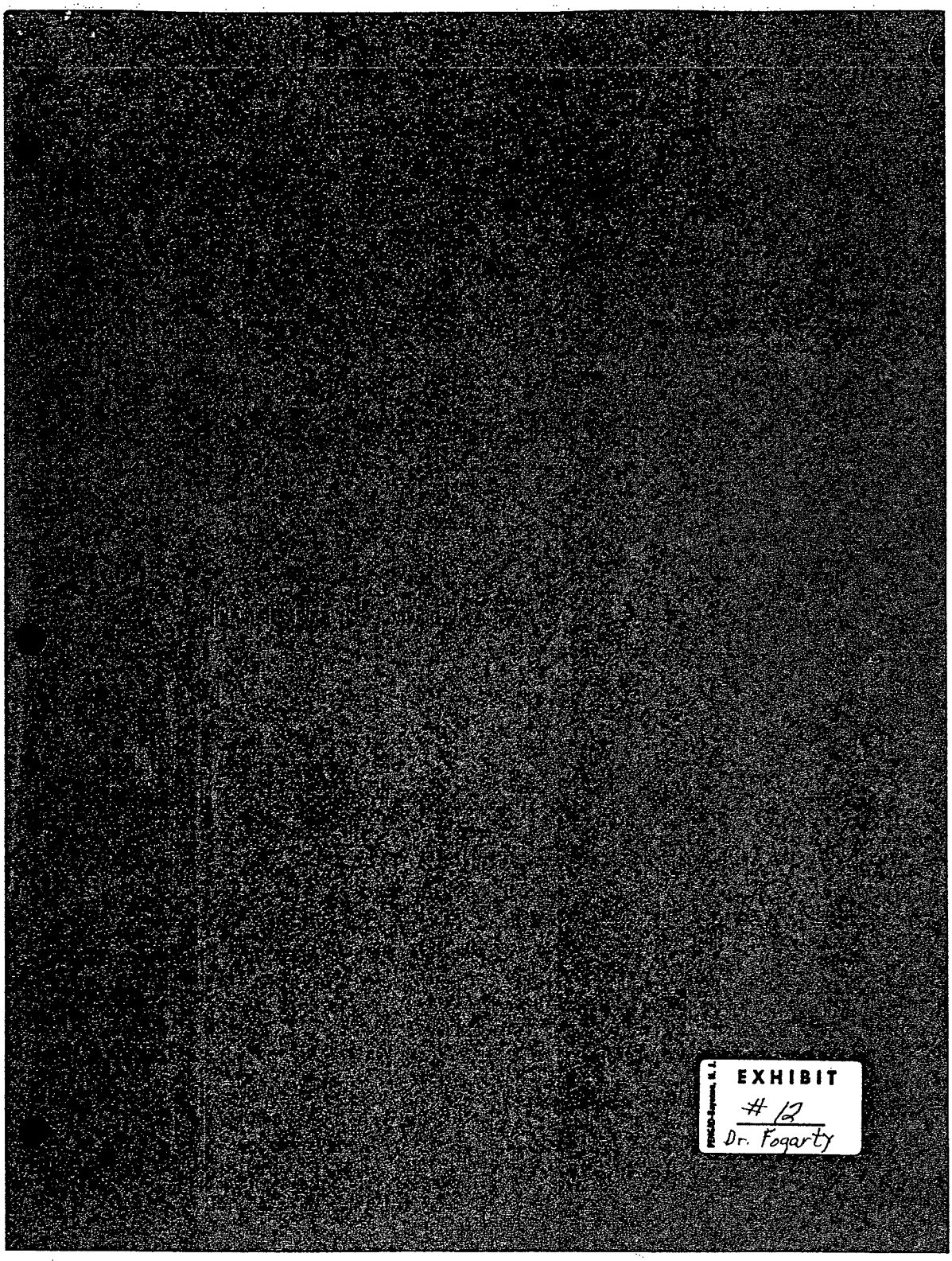

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Lasers in Surgery and Medicine 29:70–72 (2001)

Laser Resistance of Expandable Metal Stents in Interventional Bronchoscopy: An Experimental Evaluation

Hubert Hautmann, MD,* and Rudolf M. Huber, MD
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Background and Objective: Nd-YAG non-contact laser therapy is used to eliminate recurrent tumor tissue within airway stents. This study was performed to determine maximum exposure time until the stent wire is destroyed as well as exposure time necessary to deliberately fracture the wire mesh.
Study Design/Materials and Methods: Strecker stents, Wallstents, and Nitinol Accuflex stents were implanted into pig bronchi. Then Nd-YAG laser light was directed to the stent wires at different power levels. Portions of the stent surrounded by bronchial tissue as well as bare wires were investigated.
Results: The Strecker stent and the Wallstent revealed a considerably higher laser resistance than did the Nitinol Accuflex stent. At 15 W, minimum exposure time until wire destruction was 4.6 and 6.8 s for the Strecker stent and the Wallstent respectively. In contrast, the Nitinol Accuflex stent tolerated only 1.7 s.
Conclusions: Laser therapy with bronchial wire stents can be carried out at low power levels. It should, however, be avoided in the case of Nitinol Accuflex stents due to their low heat tolerance. Lasers Surg. Med. 29:70–72, 2001. © 2001 Wiley-Liss, Inc.

Key words: bronchoscopy; expandable metal stents; laser therapy; laser surgery; Nd-YAG laser; non-contact laser; laser safety; bronchial carcinoma

INTRODUCTION

Endobronchial stent insertion is a well-accepted option in the palliative treatment of bronchial carcinoma. Over the past decade, its application has greatly increased among bronchologists. Besides silicone prostheses, metallic stents are widely used since they can be implanted by flexible bronchoscopy [1]. The most common models are the Tantalum Strecker stent, the Wallstent, and the Nitinol Accuflex stent [2,3]. Typical complications are the ingrowth of tumorous tissue through the interstices of the wire mesh or recurrent tumor at the proximal or the distal ends of the stent. Non-contact Nd-YAG laser therapy is then the treatment of choice recommended by various authors [4–6], although it has been shown that even low laser energy may lead to immediate fracture or vaporization of the metal strands [7,8]. Stents can traverse the orifice of a functioning bronchus without causing obstruction [4], but in individual cases it may be advantageous to remove the overlapping portion of the stent to prevent incrustation of secretions. Therefore, laser energy that is applied to the stent has to meet specific criteria. In the first place, it should be as low as possible to prevent stent damage. Secondly, it should not exceed the amount necessary to fracture the metal wire since this may cause unnecessary injury to the surrounding tissue. This study was designed to assess critical power levels and exposure times in an experimental setting using isolated pig tracheas in order to reduce the risk of unintentional stent damage when Nd-YAG laser therapy is performed.

MATERIALS AND METHODS

Three common stent models were used: the Nitinol Accuflex stent (Boston Scientific Co., Watertown, Massachusetts) with a nominal diameter of 12 mm, the Wallstent (Schneider, Zurich, Switzerland) with a nominal diameter of 12 mm, and the Tantalum Strecker stent (Boston Scientific Co., Watertown, Massachusetts) with a nominal diameter of 11 mm. The metal composition of the stents is shown in Table 1. The laser was a Nd-YAG type with a wavelength of 1064 nm (Medilas, Dornier Co., Germering, Germany), which is predominantly used in interventional bronchology [9,10]. To test the laser resistance, the stents were implanted into isolated pig bronchi adjusted to the size of the prostheses and carefully aligned with the bronchial wall. A circular hole was then cut into the bronchus to simulate the orifice of a branching bronchus (Fig. 1). In experiment A, the laser was applied to the portion of the stent surrounded by the bronchus, taking into consideration the transmission of heat to the surrounding bronchial tissue. In experiment B, the laser was applied to the bare wires which were located directly over the cutout area. The laser light was transmitted by a Teflon-coated air-cooled flexible quartz fiber (600 μm) of 2.1 mm outer diameter. This is normally introduced through the working channel of the flexible bronchoscope, but in the experiment the laser fiber was mounted to a clamping fixture. The distance from the laser tip to the stent wire was adjusted to 5 mm, with the light directed tangentially to the stent at an angle of 30° to the horizontal.

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TABLE 1. Metal Composition of the Wire Stents

Stent	Composition
Strecker stent	Tantalum
Wallstent	Cobalt/chromium
Nitinol Accuflex stent	Nickel/titanium

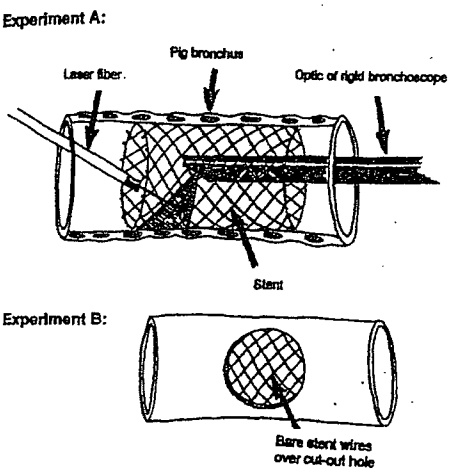

Fig. 1. Experimental setup to measure the laser resistance of airway stents. Experiment A: Stent surrounded by bronchial tissue; Experiment B: Bare stent wires over cut-out hole.

axis, simulating the configuration in clinical practice. The power settings were 15, 20, 25, and 30 W. The optic of a rigid bronchoscope was placed near the target area in order to videotape the procedures. Image sequences from the videotape were digitized for computerized evaluation to determine the exact time between initiation of laser energy and fracture or vaporization of stent wire. Each experiment was performed five times. Data are given in mean ± standard deviation (SD).

RESULTS

The time thresholds at which breakage or vaporization of a wire occurred in the different stent types and at the different power settings are displayed in Table 2 and in Figure 2. The Nitinol Accuflex stent was found to show extremely low resistance to the applied laser energy. Even with power settings as low as 15 W, immediate vaporization of the stent wire occurred. This was uniformly observed in both experiments. In contrast, the Strecker stent and the Wallstent exhibited a markedly higher resistance. However, exposure time until the stent wire was destroyed in experiment A was still limited to a few seconds. To avoid damage to the stent wire at 15 W, exposure time must not exceed 4 s (Strecker stent) or 6 s (Wallstent), respectively. In experiment B, with the wire mesh not in contact with the bronchial tissue, exposure time at which damage of the stent wire was incurred was lower, as expected. At a power level of 30 W, a maximum exposure time of 220 ms was required to destroy all different types of stent wire.

DISCUSSION

Endobronchial Nd-YAG laser therapy inside metal wire stents is often indicated since recurrent tumor frequently obstructs the stent lumen. It is therefore essential to define maximal exposure times of laser light at different power adjustments that can be applied to the stent under non-contact conditions without destroying the wire mesh. A differentiated model is now presented to describe the physical behavior of three different common stent types when exposed to laser energy. We chose isolated pig bronchi to meet realistic experimental conditions with special regard to heat conduction from the stent to the surrounding tissue within the airway. As previously shown [8], laser light has the potential to destroy metal wire stents at low power settings. But, as our data demonstrate, Nd-YAG laser therapy seems feasible for the Strecker stent and for

TABLE 2. Exposure Time to Laser Light Until Breakage or Vaporization of the Stent Wire is Induced (mean values ± SD, in seconds)

Experiment	Stent type	Power setting (W)			
		15 W	20 W	25 W	30 W
A[a]	Strecker stent	4.64 ± 1.78	3.46 ± 1.35	2.08 ± 1.03	1.02 ± 0.42
	Wallstent	6.34 ± 1.94	4.66 ± 1.56	2.86 ± 1.26	1.96 ± 0.90
	Nitinol Accuflex stent	1.76 ± 0.94	0.97 ± 0.68	0.63 ± 0.41	0.32 ± 0.25
B[b]	Strecker stent	1.56 ± 0.54	1.02 ± 0.44	0.58 ± 0.32	0.20 ± 0.10
	Wallstent	2.56 ± 0.54	1.26 ± 0.51	0.58 ± 0.35	0.22 ± 0.13
	Nitinol Accuflex stent	0.52 ± 0.19	0.28 ± 0.17	0.17 ± 0.15	0.12 ± 0.13

[a]Laser light applied to the portion of the stent surrounded by bronchial tissue.
[b]Laser light applied to the bare portion of the stent located directly over the cut-out hole, simulating the orifice of a branching bronchus.

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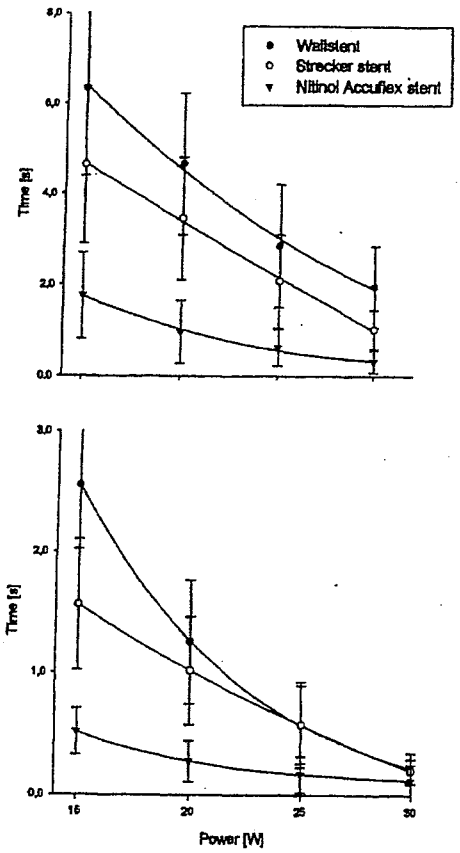

Fig. 2. Relation between power setting and exposure time as specified in Table 1. A = Experiment A, B = Experiment B, Error = Error bars represent SD.

the Wallstent at power levels below 20 W, provided that the exposure duration stays below the critical value. This is best ensured by restricting the duration of the single laser impulse. In contrast, the Nitinol Accuflex stent, which has not been studied previously, is extremely heat-sensitive. Due to the physical properties of the nitinol wire, exposure to laser light leads to immediate thermal damage even at low energy levels. Therefore, direct contact of the laser beam with the nitinol wires must be avoided. This is of particular interest since the Nitinol Accuflex stent is now very frequently used for the restoration of malignant airway stenoses. The given exposure times apply to direct contact between laser light and stent wire. With tumor tissue in between, which is normally the indication for laser therapy, stent damage will only set in at higher power levels.

To resect a portion of the stent at orifices of branching bronchi, the laser energy needed to fracture the different stent wires is considerably lower since there is no underlying tissue directly absorbing heat. The Nitinol Accuflex stent only requires half a second of exposure duration at 15 W, short enough to not significantly injure surrounding tissue when this is accidentally hit. However, it has to be considered that modifying the design of a stent by the use of laser may cause a loss of integrity and function. Nitinol Accuflex and Stecker stents consist of a single wire which could unravel when fractured.

Covered versions of the Nitinol Accuflex stent and the Wallstent are also available. Although no study data is available for covered models, no significant resistance of covers to laser energy can be expected since these are made of thin synthetic material. When the integrity of the cover is of primary importance, the use of lasers is not recommended.

CLINICAL IMPLICATIONS

1. The Nd-YAG laser can reasonably be used for tumor resection inside metal wire stents (Wallstent, Strecker stent). Since metallic stents can be easily damaged by laser energy, exposure duration must be limited in relation to the selected power setting.
2. Of all metallic stents, the Nitinol Accuflex stent is most susceptible to damage and laser therapy should be avoided whenever possible.

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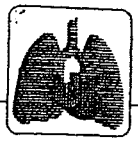

laboratory & animal investigation

Nd-YAG Laser Damage to Metal and Silicone Endobronchial Stents*

Delineation of Margins of Safety Using an *In Vitro* Experimental Model

↑ Risk of fire & Laser to metal

Julius J. Dalupang, MD; Thomas G. Shanks, MPH; and Henri G. Colt, MD, FCCP

Study objective: To identify margins of safety within which bronchoscopic Nd-YAG laser resection can be performed without damaging indwelling tracheobronchial stents.
Design: Experimental *in vitro* study simulating a patient-care environment.
Methods: Uncovered and covered metal Wallstent (Schneider; Zurich, Switzerland) and Dumon (Bryan Corporation; Woburn, MA) silicone stents were deployed in the tracheobronchial tree of a ventilated and oxygenated (fraction of inspired oxygen, 40%) heart-lung block of a dead canine. Rigid bronchoscopic Nd-YAG (1,064 nm) laser procedures were performed in order to deliver laser energy using fiber-to-target distances of 10 mm and 20 mm, and noncontact, continuous-mode, 1-s pulses at power settings of 10 W, 30 W, and 40 W. The major outcome measure was laser-induced stent damage, defined as discoloration, ignition, or breakage. This was assessed using six power densities: 75 W/cm^2, 172 W/cm^2, 225 W/cm^2, 300 W/cm^2, 518 W/cm^2, and 690 W/cm^2.
Results: The uncovered Wallstent and the silicone stent remained intact at power densities of 75 W/cm^2 (10 W, 20 mm) and 172 W/cm^2 (10 W, 10 mm), but were damaged at power densities > 225 W/cm^2 (30 W, 20 mm). The covered Wallstent was damaged at all power densities tested.
Conclusion: Uncovered Wallstent and silicone stents are not damaged when Nd-YAG laser energy is delivered using power densities ≤ 172 W/cm^2 (10 W, 10 mm). Covered Wallstents, however, had a high likelihood of ignition at all power densities studied. *(CHEST 2001; 120:934–940)*

Key words: bronchoscopy; complications; laser physics; laser/tissue interactions; metal stents; Nd-YAG laser resection; power density; silicone stents

Abbreviations: FIO_2 = fraction of inspired oxygen; IACUC = Institutional Animal Care and Use Committee; UCSD = University of California-San Diego

Tracheobronchial stents are increasingly used to palliate benign or malignant airway disease. Although recommendations exist to ensure safe bronchoscopic Nd-YAG (1,064 nm) laser resection for central airways obstruction, guidelines for laser usage in patients with indwelling endobronchial stents have not been established.

The paucity of data pertaining to laser/stent interactions is increasingly important because recurrent obstruction from either granulation tissue or tumor occurs in 9 to 67% of patients with metal stents[1–8] and in 6 to 15% of patients with silicone stents.[9–11] In these patients, laser-induced stent damage may cause substantial morbidity from airway burn injury in case of stent ignition, or airway wall and vascular perforation in case of metal stent rupture.

In patients without indwelling stents, it is generally recommended that laser resection be performed using laser pulse durations of 1 to 2 s, a power output of ≤ 40 W, and a fraction of inspired oxygen (FIO_2)

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0.40.[12] Using these recommendations as a starting point, the purpose of this study was to identify margins of safety defined by the classic measures of power density and pulse frequency within which Nd-YAG laser energy could be delivered without damaging indwelling silicone and metal stents.

Materials and Methods

Theoretical Basis for Study Design

When a laser beam reaches a target material, radiant energy is absorbed, reflected, and transmitted. This distribution of energy, defined by Beer's law,[13] is dependent on the optical properties of the material and the wavelength characteristic of the laser light (1,064 nm in the case of Nd-YAG laser). As absorbed energy is converted into heat, a rise in the temperature of the target material occurs. Based on Fourier's law of heat transfer[14] and on laws of thermodynamics, the temperature of the material will rise above threshold levels only if the absorbed power density exceeds the capacity of the material to conduct heat away from the impact site. Power density, therefore, is directly proportional to the power setting of the laser (in watts) but inversely proportional to spot size (in centimeters squared) of the laser beam. The relationships between these optical and thermal phenomena can be mathematically represented as[15]:

$$\kappa t_P - \rho C_V (T_i - T_o) \approx (1 - R) I_o t_P$$

where κ is the thermal conductivity, t_P the duration of irradiation, ρ the density of the material, C_V the specific heat per unit volume, R the reflectivity, and I_o the laser intensity. The expression $\kappa t_P^{1/2}$ is the thermal diffusivity or penetration depth of the laser beam, while (1-R) is the absorption coefficient.

For example, at low power densities, the poor absorption of the Nd-YAG laser and its pronounced Mie and Rayleigh scattering result in slow homogeneous heating of a large volume of tissue without serious mechanical damage to the tissue surface.[16] At high power densities, however, the temperature 2 to 3 mm below the tissue surface rises rapidly, prompting vaporization of water content and a pocket of steam with a pressure high enough to rupture overlying tissues.[17] Based on these principles, we hypothesized that certain quantities of laser energy, defined by power density, would cause local heating without the extreme temperature elevation required to disrupt stent integrity or prompt stent ignition.

FIGURE 1. The heart-lung block, including the tracheobronchial tree, harvested from an dead adult canine.

In Vitro *Experimental Model*

In order to enhance applicability of our results to the clinical setting, the following experimental environment simulating a rigid bronchoscopic intervention in patients was designed. An intact heart-lung-tracheobronchial tree was harvested from a dead adult canine and cleaned thoroughly. The entire structure was suspended at a slope of 60° (Fig 1). Throughout the experiment, this lung-tracheobronchial model was intubated with a rigid bronchoscope (EFER-Dumon Rigid Bronchoscope; Bryan Corporation; Woburn, MA) and connected to a Harvard respirator pump for animals (Harvard Apparatus; Holliston, MA) delivering a tidal volume of 400 mL per breath. Respiratory frequency was set at 12 cycles per minute, and oxygen delivery through the system was set at an FIO_2 of 40%. The rigid telescope, laser fiber, and suction catheters were introduced through sealed rubber obturator caps, maintaining a closed system so that two-lung ventilation was maintained throughout the intervention. This protocol was reviewed and approved by the University of California-San Diego (UCSD) Institutional Animal Care and Use Committee (IACUC) [IACUC tissue request No. T 99154]. No animals were killed for the sole purpose of this study; tissue was transferred from a previously killed animal in a separate IACUC-approved protocol.

Experimental Protocol

Under direct bronchoscopic guidance, stents were sequentially inserted into the central bronchi. In three series of experiments, stents studied were as follows: (1) uncovered 10-mm by 30-mm Wallstents (Schneider; Zurich, Switzerland) made of cobalt-based superalloy Elgiloy filaments braided into a cylindrical mesh; (2) 10-mm by 30-mm Wallstents (Schneider) covered with 1.0-mm thick polyurethane (European model stent); and (3) 10-mm by 30-mm stents made of molded silicone with external surface studs (Bryan Corporation). A new stent was used for each individual experiment.

For all experiments, a 100-W–capacity Nd-YAG laser (model 813; Laserscope; San Jose, CA) and saline solution-cooled, 0.6-mm–diameter coaxial fiber (Endostat; Laserscope) were used. The fiber was placed through the rigid bronchoscope and directed tangentially toward the inner side of the proximal extremity of each indwelling stent. The helium-neon focusing laser beam was used to ensure that the laser was fired parallel to the airway wall in the direction of the target surface.

Using noncontact, 1-s duration, and continuous mode, laser

Table 1—*Power Densities at Each Power Setting and Fiber-to-Target Distance

Power	Distance	Power Density
10 W	20 mm	75 W/cm^2
10 W	10 mm	172 W/cm^2
30 W	20 mm	225 W/cm^2
30 W	10 mm	518 W/cm^2
40 W	20 mm	300 W/cm^2
40 W	10 mm	690 W/cm^2

*Computed based on the following formula: power density = 0.8635 power (watts) + spot size (centimeters squared).

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energy was delivered at power settings of 10 W, 30 W, and 40 W. At least 1 s separated each pulse of laser energy delivered. The distance between the distal aspect of the laser fiber and the target was precisely measured and maintained by fixing the fiber to a ruler attached to the obturator cap of the rigid bronchoscope. For each of the three power settings, laser fiber-to-target surface distances of 10 mm and 20 mm were used.

The average power density delivered for each setting was computed based on the formula[18]: PAW = 0.8635 × power (watts)/πr^2 where πr^2 is the spot size, and PAW is average power density. Because the laser beam diverges 11° around the fiber core, the spot size at a distance was calculated using the following equation: spot size = π [(fiber radius in centimeters) + (distance in centimeters) × tan 5.5°]^2. Using fiber-to-target distances of 10 mm and 20 mm, therefore, spot sizes were 0.05 cm^2 and 0.155 cm^2, respectively. Computed power densities for each experimental condition are shown in Table 1.

Outcome Measures and Statistics

Laser energy was delivered until stent damage occurred or a total of 60 impulses were delivered. Stent damage was defined as visualization of blackish discoloration, blister formation, perforation, actual ignition, or rupture of the integrity of the stent. Rupture of integrity of the metal stent was defined as a spontaneous break in the continuity of the metal mesh during laser application.

The total number of pulses and the total energy required to damage a stent during each experimental condition were recorded and expressed as mean ± SD. Comparisons of mean number of pulses and mean total energy delivered were made using paired Student's *t* test at a level of significance of 0.05.

RESULTS

The uncovered Wallstent was not damaged despite 60 pulses at power densities of 75 W/cm^2 (10 W, 20 mm) and 172 W/cm^2 (10 W, 10 mm). The wire mesh broke, however, at power densities ≥ 225 W/cm^2 (30 W, 20 mm; Table 2).

The covered Wallstent was damaged using a power density of only 75 W/cm^2 (10 W, 20 mm), prompting a black discoloration at the impact site. This occurred after delivering a mean of 36 pulses (Table 2). Black discoloration of the stent was also observed at 172 W/cm^2 (10 W, 10 mm). At power densities of ≥ 225 W/cm^2, black discoloration was immediately followed by perforation of the covering of the Wallstent (Fig 2). This occurred after a mean of only 2.6 pulses were delivered. At the highest power density tested, 690 W/cm^2 (less than two pulses at 40 W, 10 mm), the stent abruptly burst into flames.

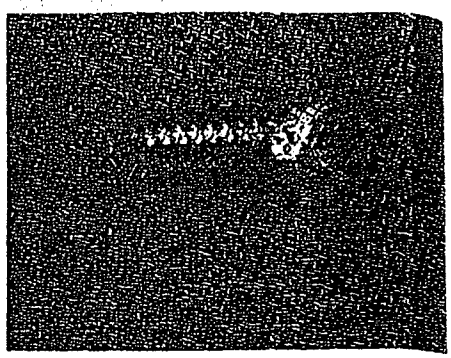

FIGURE 2. The perforated and discolored covered Wallstent after application of laser energy at 518 W/cm^2 (30 W, 10 mm).

The silicone stent was not damaged despite 60 pulses at power densities of 75 W/cm^2 (10 W, 20 mm) and 172 W/cm^2 (10 W, 10 mm). At power densities of ≥ 225 W/cm^2, a slight discoloration was noted at the impact site after a mean of ≤ 3.6 pulses (Table 2). A blister formed, accompanied by focal black discoloration at the impact site at a power density of 690 W/cm^2 after less than two pulses were delivered, although the stent did not ignite (Fig 3).

When distance was maintained constant at 10 mm or 20 mm ($p < 0.05$; Table 2), the mean number of pulses and mean total energies (in joules) at which stents were damaged significantly decreased as

Table 2—*The Total Number of Pulses and Total Energy Required To Damage the Uncovered Wallstent, Covered Wallstent, and Silicone Stents**

		Stent Type					
		Uncovered Wallstent		Covered Wallstent		Silicone Stent	
Power/Distance	Power Density	Total Pulses	Total Energy, J	Total Pulses	Total Energy, J	Total Pulses	Total Energy, J
10 W/20 mm	75 W/cm^2	60	592 ± 2†	36 ± 4.3	359.3 ± 43.1	60	594 ± 2.5†
10 W/10 mm	172 W/cm^2	60	589.3 ± 3.5†	35.6 ± 4.0	355.3 ± 45	60	591 ± 3.6†
30 W/20 mm	225 W/cm^2	3.3 ± 0.5	94.3 ± 26.5	2.6 ± 0.5	79.3 ± 13	3.3 ± 0.5	103 ± 19.9
30 W/10 mm	518 W/cm^2	3.3 ± 0.5	96.6 ± 17	2.6 ± 0.5	77 ± 18	2.6 ± 0.5	79 ± 18.9
40 W/20 mm	300 W/cm^2	1.6 ± 0.5	56.3 ± 18.5	1.6 ± 0.5	61.3 ± 17	2.3 ± 0.5	78.6 ± 8
40 W/10 mm	690 W/cm^2	1.3 ± 0.5	54.3 ± 21.8	1.3 ± 0.5	40 ± 6.2	1.3 ± 0.5	48 ± 9.1

*Data are presented as No. or mean ± SD.
†Not affected.

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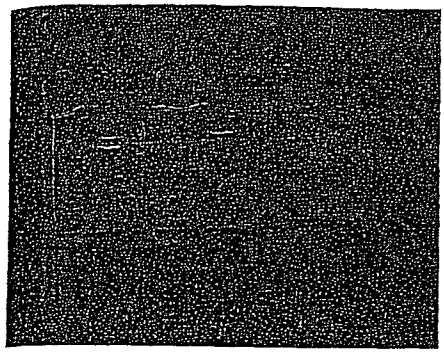

FIGURE 3. The discolored studded silicone stent after application of laser energy at 690 W/cm² (40 W, 10 mm).

power settings were increased. The mean number of pulses and mean total energies at which stents were damaged were not significantly different, however, when fiber-to-target distance increased from 10 to 20 mm while maintaining power settings constant. Consequently, no definite relationship was found between power density and total energy at which stent damage occurred (Fig 4).

DISCUSSION

This experimental study realistically simulates a patient-care setting in which rigid bronchoscopic laser resection is performed in the presence of an indwelling stent while using an $FIO_2 \leq 40\%$. Results clearly identify a margin of safety for laser resection when power density is ≤ 172 W/cm², or when a power setting of 10 W is applied with a laser fiber-to-target distance of at least 10 mm.

Our observation that 60 pulses at 10 W applied 10 mm from the target did not damage either the uncovered Wallstent or the silicone stent reinforces that of Witt et al,[19] who found that uncovered Wallstent, Strecker, and Palmaz metal stents were destroyed when noncontact Nd-YAG laser was used at power settings > 10 W. In fact, these investigators[19] found that metal stents were destroyed after just one 25-W pulse delivered 4 mm from the target, prompting them to conclude that Nd-YAG laser should never be used in patients with indwelling metal stents.

A few researchers might contend that lower power densities are not frequently used in bronchoscopic practice in which some operators are accustomed to higher power settings and shorter laser fiber-to-target distances. We suggest that the effects of laser resection using these settings should be further investigated. For example, in an Nd-YAG dosimetry study performed in porcine bladder, Cos and Di Sant'agnese[20] demonstrated that 10 W applied for 10 s produced far more effective penetration of laser energy than 100 W for 1 s. Although these investigators[20] used a fiber-to-target distance of only 2 mm, it is possible that the effect would be similar if applied at a greater distance because of the dynamic change of absorption with repetitive irradiation.[16,21,22]

Although spectroscopic studies[23,24] have shown similar alteration in optical properties of organic polymers with repetitive irradiation, the paucity of adverse effects from prolonged irradiation at 10 W may be related to the cooling times of the stent materials. Before metals and organic polymers are uniformly heated, absorbed laser energy is equitably partitioned among electrons. Expressed as "cooling time," this equipartition may be as short as 10^{-13} s in metals, and between 10^{-12} to 10^{-6} s in nonmetals.[25,26]

In our study, it is noteworthy that the covered Wallstent was damaged at an even lower power density (75 W/cm²; 10 W, 20 mm). The covering of the original model of the self-expanding Wallstent is a thermoplastic elastomer made with a urethane backbone. This material does not have the high-temperature resistance of conventional vulcanized rubber and cannot tolerate temperatures of 88°C to 100°C.[27] This is probably why the covered Wallstent ignited immediately at a power setting of 40 W.

We also found that uncovered Wallstents, covered Wallstents, and silicone stents were all damaged at power densities > 225 W/cm² and at power settings > 30 W. The thermal conductivity of most metals ranges from 0.66 to 4.180 W/cm²/°C/cm,[28] while that of silicone rubber is 6 to 12 W/cm²/°C/cm.[27] Comparatively, the thermal conductivity of water, a major constituent of biological tissues, is only 0.005 W/cm²/°C/cm.[28] A radiant power density of 1460 W/cm² is required to vaporize biological tissues.[22] Despite their greater thermal conductivities, all stents were damaged at power densities commonly used to coagulate rather than to vaporize tissues. This might indicate that stent materials have greater absorptivity of Nd-YAG laser energy than biological tissues. Sainte-Catherine and coworkers[29] observed, for example, that metal surfaces had greater absorptivity for Nd-YAG laser energy than CO_2 laser energy. This finding is contrary to the known behavior of Nd-YAG and CO_2 laser systems in human tissues.

We believe the potential for increased absorptivity of laser energy by stents is real because, as in the case of the covered Wallstent, temperatures rise rapidly, prompting stent ignition without warning. Obviously, the presence of dark pigment such as

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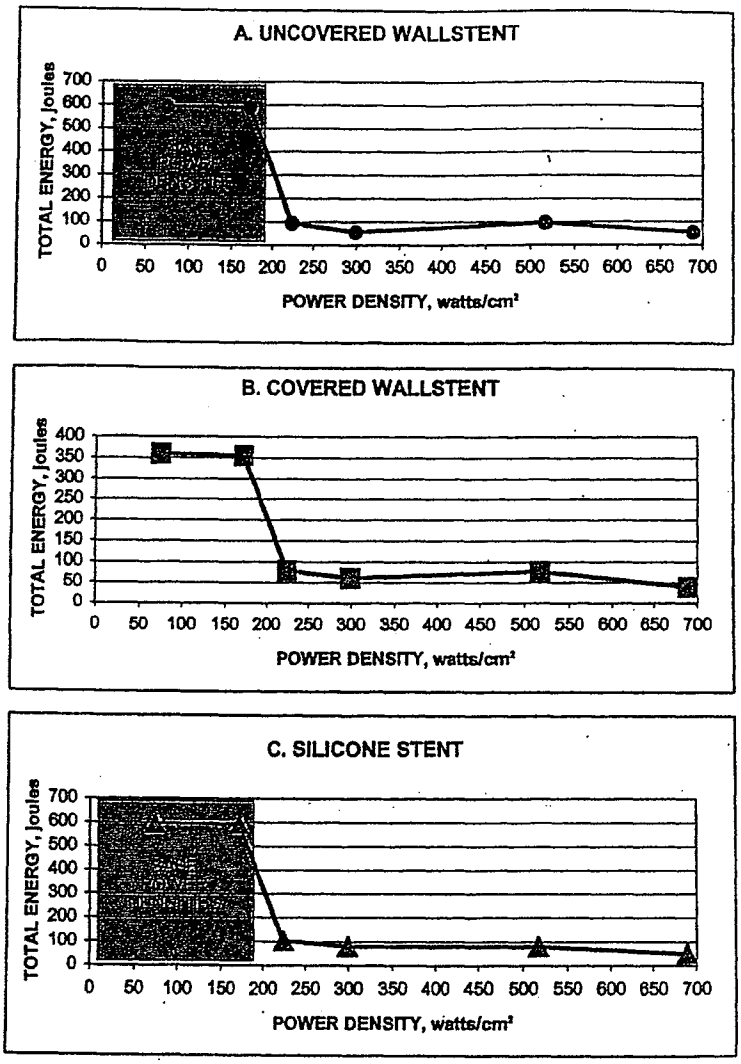

FIGURE 4. The relationship of power density (watts/centimeters squared) and the total energy (joules) required to destroy the stents. Prolonged irradiation using the safe power densities (shaded area) can be performed in uncovered Wallstent and silicone stents without stent destruction. The uncovered Wallstent was destroyed at all power densities applied.

blood in or around the stent would further increase the absorption of Nd-YAG laser radiation, precipitating stent ignition and airway burn injury.

The silicone stent, although becoming discolored, never ignited. Perhaps this is because the polydimethylsiloxane chain, the basic skeleton of the silicone stent, can withstand temperatures ranging from − 70°C to + 250°C.[27] We ceased laser firing, however, the moment we saw discoloration rather than continuing until stent ignition. The reason for this is that in actual clinical practice, the severely grave consequences of air-

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ıy burn injury must be avoided, and it is well ›ognized that Nd-YAG laser irradiation of darkly gmented or charred material increases surface absorption.[30]

Although our study suggests parameters that might allow granulation or tumor tissue surrounding a silicone stent to be resected without removing the stent, careful attention must be paid to these parameters and to the rules governing safe bronchoscopic laser resection. The importance of laser/tissue interactions was well demonstrated by Scherer,[31] who, in a recently published *in vitro* study, was able to ignite blood or soot-covered silicone stents using multiple laser power settings, whereas clean silicone stents could not be ignited regardless of power density or oxygen concentration.

Our study might raise a question pertaining to the effect of local temperature on laser/tissue interaction. The threshold temperature at which materials are damaged by laser energy is more easily reached when the baseline temperature of a target material is higher and nearer the threshold temperature. The laser energy delivered in our study was applied to tissues residing within an experimental model at less than true body temperature, but greater than room temperature. Predictably, the stents placed in our model were also at higher baseline temperature, and hus more easily damaged by laser energy than if operated on at room temperature.

Another potential concern about our study is that the laser beam was focused on each stent, rather than on surrounding tissues. During tissue removal of granulation tissue, the laser beam is usually focused on the tissue itself, which may or may not be directly adjacent to the indwelling stent. Because laser energy is easily scattered and reflected, however, collateral absorption is frequent. Laser energy delivered onto surrounding tissues, therefore, will also be frequently absorbed by adjacent foreign bodies. In our study, stents were frequently damaged after only one or two impulses at higher power densities, suggesting that substantial variation of target points during bronchoscopic laser resection would be necessary to prevent inadvertent stent damage.

Because uncovered Wallstent and silicone stents were damaged after just a few pulses at 30 W and 40 W, but were not affected by prolonged irradiation using 10 W, questions are raised pertaining to the concept of energy density per pulse (defined as power density [watts/centimeters squared] multiplied by pulse duration in seconds) as a defining factor of laser safety. We cannot address this issue, however, because we did not vary impact duration times in our study. In the study by Scherer,[31] impact duration significantly contributed to the likelihood of silicone stent ignition, prompting that author's recommendation to maintain impact duration to ≤ 1 s when using power settings of ≥ 40 W.

Finally, both in our study and in that of Witt et al,[19] there is an absence of a significant relationship between power density and total energy (in joules) delivered before stent damage occurs. Probably, this is related to the lack of influence of distance on total energy delivered. It is tempting to presume that the total energy needed to damage a stent decreases as power density increases. As shown in Figure 4, however, at various power densities damaging all three stents, the total energies delivered were similar. For instance, at power densities of 300 W/cm^2 (40 W, 20 mm) and 690 W/cm^2 (40 W, 10 mm), differences in total energy delivered to damage an uncovered Wallstent were not statistically significant (54.3 ± 21.8 J vs 56.3 ± 18.5 J, $p < 0.85$). Similar observations were made for silicone stents damaged at power densities > 225 W/cm^2, and covered Wallstents, which were damaged at all power densities.

One reason why total energy may be an inconsequential measure of outcome for any given power density is that power density involves not only the time rate at which energy is expended but also the spatial extent of that energy.[18] In biological tissues, for example, a wide range of power densities can achieve similar macroscopic effects (*ie*, tissue blanching). Although total energies delivered to achieve these effects might be similar, each power density will be different in terms of tissue margins and depth of coagulation. Energy delivered from a site near the target tissue, for instance, achieves narrower lateral margins and a deeper depth of coagulation than energy delivered from a site far from the target tissue (dependent on wavelength absorption characteristics).

In summary, our results suggest that a wide range of power densities can be damaging to an airway stent, and that total energy alone should not be used to delineate margins of safe laser resection. Applying our findings to the clinical setting, bronchoscopists should be most aware of power density, rather than concerned with power settings or total energy only, when contemplating laser/stent interactions.

At an $FIO_2 \leq 40\%$, a margin of safety exists for Nd-YAG laser applications onto or around an uncovered Wallstent or silicone stent using power densities ≤ 172 W/cm^2, or a power setting of 10 W with a fiber-to-target distance of 10 mm. The common practice of removing these stents, specifically the silicone stent, prior to laser resection may in this case be unnecessary. A margin of safety is not as readily apparent for covered Wallstents, which at higher power densities ignite easily and without warning.

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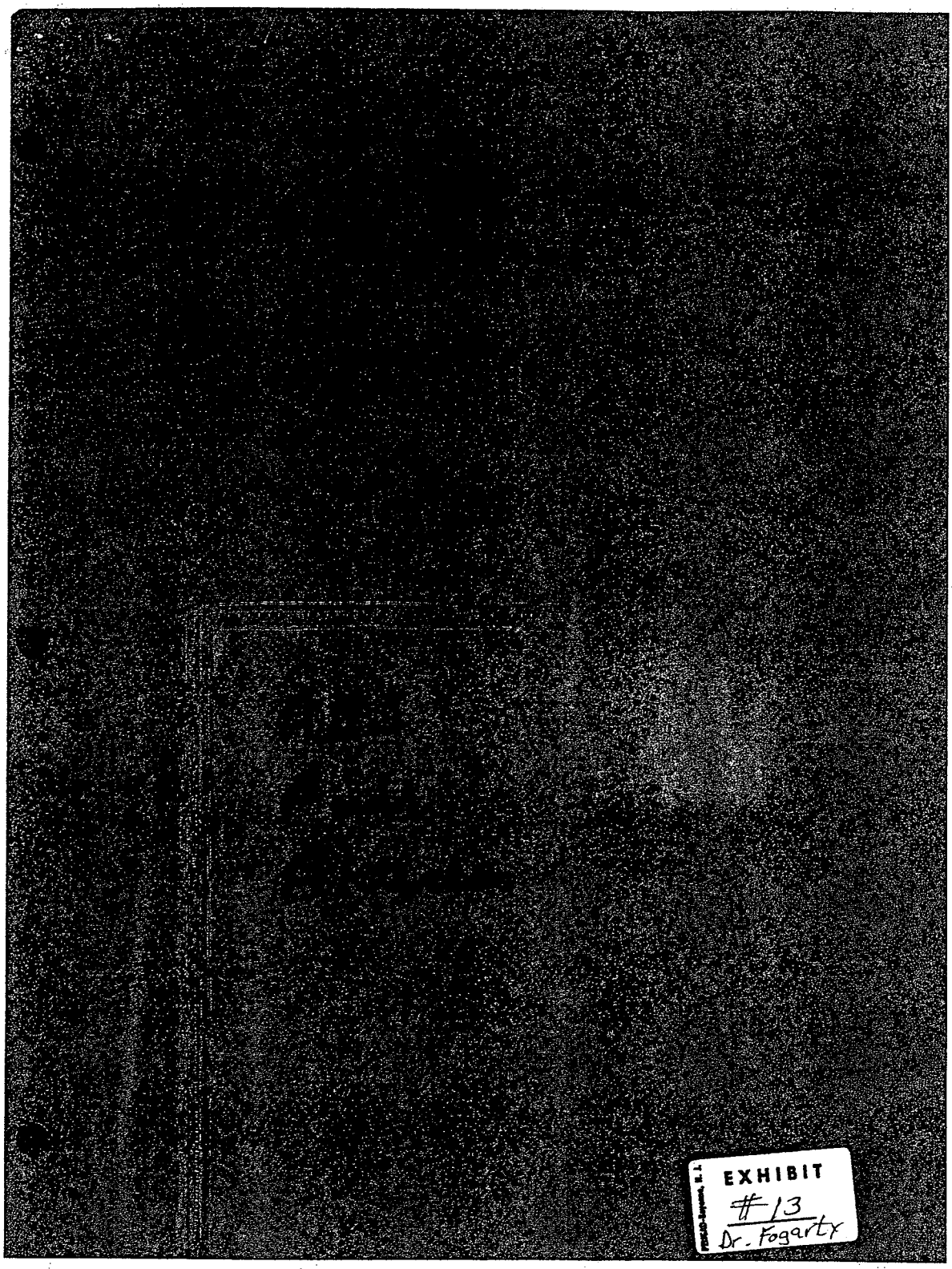

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Laser Treatment of Endobronchial Lesions

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THE neodymium:yttrium-aluminum-garnet (Nd:YAG) laser is used for palliative and therapeutic management of endobronchial lesions. The authors report three cases of what appear to be pulmonary venous gas emboli (PVGE) during endobronchial Nd:YAG laser therapy.

Case Reports

Case 1

A 75-kg man, aged 55 yr, with a scarred fibrotic residual left lung after a severe childhood infection that resulted in complete collapse of the left lung presented with a bronchopleural fistula after a stump infection. The patient was asymptomatic until aged 54 yr, at which time he developed a *Pseudomonas* infection of the remaining lung tissue that caused the formation of a bronchopleural fistula and an empyema. The empyema was drained, and the infection resolved with intravenous antibiotics. Nd:YAG laser therapy was proposed to develop an endobronchial tissue reaction so that a sealant plug could be set permanently in the bronchial stump, thereby occluding the fistula.

After placement of standard monitors and a radial arterial catheter, anesthesia was induced with propofol and mivacurium. The patient's trachea was intubated with a standard 9.0-mm endotracheal tube. Anesthesia was maintained with a propofol infusion (150-200 $\mu g \cdot kg^{-1} \cdot min^{-1}$) and intermittent doses (0.2 mg/kg) of mivacurium to facilitate initial insertion of the rigid bronchoscope. Topical anesthesia was applied to the airway. An initial assessment of the bronchial stump was performed using a fiberoptic bronchoscope passed through an adapter attached to the endobronchial tube. The endotracheal tube was then replaced with a rigid ventilating bronchoscope with side ventilation slits (Shapshay Universal Ventilating Laser Bronchoscope Karl Storz, Endoscopy-America, Inc., Culver City, CA).

Ventilation was provided using a Venturi system with a modified Sanders injector attached to the side arm of the bronchoscope.[1] The inspired oxygen concentration was kept as low as possible while maintaining the oxygen saturation at greater than 95%. An air-to-oxygen mixture was delivered by attaching the anesthesia circuit to the entraining side port of the bronchoscope. The inspired oxygen concentration delivered was approximately 25-35%. During the course of the laser treatment, moderate bleeding occurred. The rigid bronchoscope was advanced into the bronchial stump, and additional laser treatments were delivered. During one pulse of the laser, the patient was noted to have an acute decrease in blood pressure to 40/20 mmHg, severe bradycardia to 20 beats/min, and ST segment elevation in lead II of the electrocardiogram. The oxygen saturation was 95% immediately before the event. The procedure was terminated, but a cardiac arrest followed. The patient was quickly resuscitated within 2 min using standard advanced cardiac life support protocol.

The patient awoke but was noted to be confused and to exhibit a left hemiplegia. Computerized tomography scan of the brain revealed a gas embolus in the region of the right middle cerebral artery. Postoperatively, the patient recovered cognitive function but continued to exhibit a residual left hemiplegia.

Case 2

A 59-kg man, aged 61 yr, with a history of a rapidly progressing bronchogenic carcinoma presented for palliative management of an endobronchial tumor occluding his right mainstem bronchus, causing severe dyspnea and complete collapse of the right lung. After placement of routine monitors and a left radial artery catheter, anesthesia was induced and maintained with intravenous propofol (150-200 $\mu g \cdot kg^{-1} \cdot min^{-1}$) and mivacurium (0.2 mg/kg), and topical anesthesia was applied to the airway. The surgeon assessed the lesion by using a flexible bronchoscope; the endotrachial tube was then removed, and a rigid ventilating bronchoscope with Sanders injector attachment was placed into the trachea. Baseline hemodynamics were pulse rate, 75-81 beats/min; blood pressure, 120/60 mmHg-110/55 mmHg. The lungs were ventilated with an air-to-oxygen mixture that provided 40% oxygen entrained from an anesthesia circuit to maintain an oxygen saturation of 96%.

Approximately 90 min into the procedure, the surgeon encountered bleeding and stopped using the laser. Ventilation was continued through the bronchoscope, which was advanced into the right main stem bronchus. The patient rapidly developed profound bradycardia to 40 beats/min, hypotension to 60/20 mmHg, and ST segment elevation in lead II of the electrocardiogram. There was marbling of the skin of the upper extremities. The oxygen saturation initially remained at 96%. The procedure was terminated; the rigid bronchoscope withdrawn, and an endotracheal tube placed. Resuscitation was initiated, and inspired oxygen was increased to 100%. The patient responded to resuscitation efforts within 1 min. Initially on emergence, the patient followed simple commands but was encephalopathic and had a left-sided weakness.

A grand mal seizure occurred 15 min after arrival to the postanesthesia care unit. Computerized tomography of the brain demonstrated intraparenchymal gas bubble present in the right frontopa-

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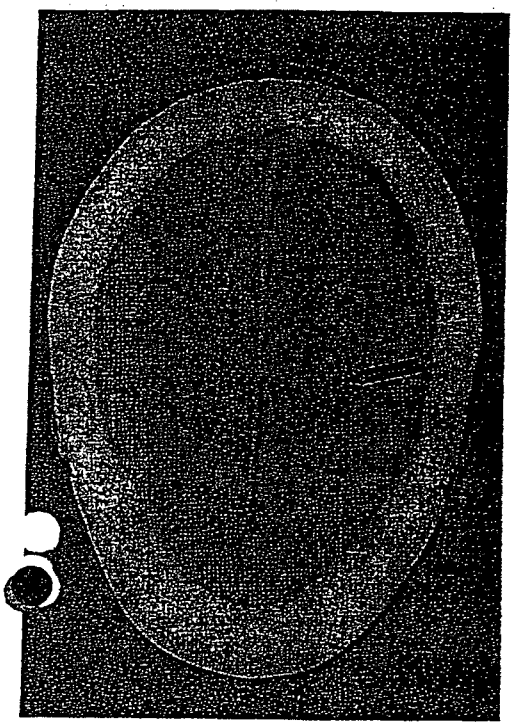

Fig. 1. Postoperative computerized tomography scan showing intracerebral gas after Nd: YAG laser bronchoscopy of patient #2.

rietal region (fig. 1). The neurologic deficits slowly resolved, with only a slight residual weakness in the left upper extremity. The patient returned to the operating room on postoperative day 11 for repeated ablation of the tumor, which was found to be extending across the carina into the left main stem bronchus. The same anesthetic plan was implemented without incident.

Case 3

A 60-kg woman presented with a metastatic neoplasm to the left main stem bronchus. Palliative therapy was planned to debulk the tumor and open the bronchus using the Nd:YAG laser. After placement of standard monitors and an arterial catheter, the patient was induced with propofol and mivacurium. The trachea was intubated a 9.0-mm endotracheal tube. Anesthesia was maintained with a ...opofol infusion (150–200 $\mu g \cdot kg^{-1} \cdot min^{-1}$), and spontaneous ventil... was allowed to return and was assisted as necessary.

The surgeon first evaluated the tumor with the fiberoptic bronchoscope. The endotracheal tube was then removed, and the rigid ventilating bronchoscope was inserted. Spontaneous ventilation was maintained with intermittent, gently assisted hand ventilation via a circle circuit attached to the side arm of the bronchoscope, using air and oxygen to maintain oxygen saturation above 95%. Laser resection proceeded with removal of a large amount of tumor tissue. Significant bleeding was encountered, and the patient had a transient decrease in oxygen saturation to 85%. Hand ventilation with 100% oxygen returned the oxygen saturation to 95%, but the patient suddenly became bradycardic to a rate of 30 beats/min and hypotensive to a blood pressure of 40/20 mmHg, with ST segment elevation noted in lead II of the electrocardiogram. The patient was resuscitated within 2 min; the ST segments returned to baseline after 15 min, as did the blood pressure and pulse rate.

On recovery, the patient was noted to be confused and exhibited a left hemiplegia. The neurologic deficit returned to normal after 20–30 min, and a brain computerized tomography scan obtained after symptom resolution was normal.

Discussion

Two reviews reported several deaths during Nd:YAG laser therapy in 1,951 patients with endobronchial tumors who underwent 3,428 procedures.[2,5] These deaths resulted from "cardiovascular decompensation," described as episodes of severe bradycardia, shock, infarction, and cardiac arrest. The descriptions of these episodes are very similar to the cases of possible PVGE reported here and to those described previously in the literature.[4–6]

In 1929, Van Allen[7] performed extensive studies in dogs given pulmonary venous gas emboli. These dogs experienced one of two responses, either 1) acute hypertension and dysrhythmias, followed by hypotension and cardiac arrest, or 2) blindness, seizures, hemiplegia, and death. The distribution of gas introduced into the pulmonary vein of the anesthetized dogs was dependent on body position. In the horizontal, supine position, air was distributed mainly to the coronary arteries, and in the vertical or standing position, to the cerebral circulation.

Evans *et al.*,[8] in a study involving upright ventilated cats, found that air infused into the left ventricle caused one of two responses, either 1) the cat exhibited an acute increase in blood pressure, pulse rate, and left ventricular contractile force and developed arrhythmias, or 2) the cat exhibited an immediate decrease in blood pressure and pulse and no arrhythmias. They concluded from this study that gas embolism to the cerebral circulation resulted in the hyperdynamic responses, whereas emboli to the coronary circulation

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resulted in a depressed response. A follow-up study was performed, and this confirmed that air infused into the cerebral circulation caused an increase in blood pressure, increased left ventricular contractility, and arrhythmias.[9]

In the cases reported here, patients were in a supine position with a 20° head-up tilt and exhibited symptoms of coronary and cerebral emboli. The elevated ST segment in lead II could be the result of a gas embolus to the right coronary artery, the most superior coronary artery in a supine patient. All three patients described presented initially with a left-sided hemiplegia on emergence, which would correspond to an embolus entering the right carotid artery and traveling to the right brain, resulting in left-sided neurologic symptoms.

The diagnosis of PVGE in the three patients was based on the following signs: acute onset of bradycardia, hypotension, ST segment elevation on the electrocardiograph, maintenance of oxygen saturation before cardiac decompensation, and a new neurologic deficit on emergence.

The incidence of PVGE with endobronchial use of the Nd:YAG laser may be a more common complication than has been previously recognized and may have multiple etiologies. The proposed cause of gas embolism in the first case report is continued laser treatment after bleeding was encountered. The Nd:YAG laser has a coaxial gas channel that delivers compressed helium to the tip for cooling purposes. The laser treatment caused an opening in a pulmonary vein, and continued treatment with the laser with coolant gas flows of 800 ml/min resulted in a helium gas embolus. The pressure generated by the coolant gas flow at 400 ml/min has been found to be in excess of 500 mmHg measured at the tip of the the coaxial gas channel of the laser.[6] This pressure gradient could force gas into an open pulmonary vein when the laser tip is wedged into position. The entrance of gas follows a direct path to the left heart, coronary arteries, aorta, brain, and systemic circulation. This patient's neurologic deficit was a permanent one, probably because the physical properties of helium, an insoluble inert gas, limited its reabsorption from the cerebral circulation.

In the second case report, bleeding was encountered, and laser treatment was stopped, but ventilation was continued using a modified Sanders injector attached to a rigid bronchoscope. The surgeon advanced and wedged the bronchoscope into the right main stem bronchus to tamponade the bleeding; cardiovascular decompensation occurred immediately. The proposed etiology of PVGE in this case is that a distal, high-pressure system developed in the obstructed bronchus resulting in the direct passage of air and oxygen into the open pulmonary venous circulation. A Sanders injector can deliver 28 cm of H_2O inspiratory pressure with an inspiratory flow rate of 140 l/min.[10] The rigid ventilating bronchoscope has side-ventilation slits to allow pressure dissipation and bilateral lung ventilation to occur when the tip of the bronchoscope is advanced into a main stem bronchus.[11] These vents may have been partially obstructed and failed to adequately decompress the pressurized lung. This patient was noted to have marbling of the skin immediately after cardiac decompensation began. Marbling is a sign associated with systemic gas emboli when air bubbles present in subcutaneous tissues cause venous stasis.[4,5] The gas embolism in this incidence was thought to be an air-to-oxygen mixture. The oxygen absorbed rapidly, resulting in a small, residual deficit caused by the slower absorption of the air component of the gas bubble.

In the third case report, the patient was allowed to breathe spontaneously, with occasional gentle assistance and hand ventilation with an air-to-oxygen mixture. During a brief desaturation, the patient was more aggressively hand ventilated with 100% oxygen, and the oxygen saturation returned to 95%; however, cardiac decompensation occurred immediately. This gas embolus was probably 100% oxygen; therefore, the neurologic sequelae resolved quickly and completely as the oxygen was rapidly absorbed.

On the basis of these three case reports, our preliminary conclusion of methods to decrease the incidence of PVGE during endobronchial laser therapy when bleeding is encountered is that airway pressure should be minimized and the bronchoscope withdrawn above the carina. A spontaneous ventilation technique may reduce the extent of PVGE. However, lung tissue involved with extensive neoplasm may lose its normal elasticity, and any abnormal communication formed between the pulmonary venous system and the airway may be held open and air entrained, even during spontaneous ventilation.[7,8] The standard practice of laser surgery has been to use minimal concentrations of oxygen to reduce the risk of an airway fire.[12] The use of high concentrations of inspired oxygen should be considered when bleeding is encountered, and the risk of airway combustion should be weighed against the risk of possible PVGE.

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Perioperative Acute Renal Failure Associated with Preoperative Intake of Ibuprofen

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NONSTEROIDAL antiinflammatory drugs (NSAIDs) inhibit prostaglandin synthesis. Because renal blood flow depends on prostaglandin, particularly when circulating blood volume is decreased, a recommendation has been made that NSAIDs be withheld before surgery because of the risk of renal dysfunction.[1] However, there has been no report of perioperative renal dysfunction attributable to preoperative administration of NSAIDs, and a recent review has endorsed preoperative administration of NSAIDs for minor outpatient procedures and a combined multimodality drug therapy including NSAIDs after surgery.[2] The authors report a case of perioperative acute renal failure after lumbar discectomy in a young patient who was taking ibuprofen preoperatively.

Case Report

A 94-kg man, aged 38 yr, with a 10-yr history of back pain and a herniated nucleus pulposus compressing the L5 nerve root was admitted for lumbar discectomy. Past medical history revealed alcohol abuse and drug-seeking behavior with claims of recovery and abstinence in the past year. The patient admitted to taking acetaminophen-codeine (300 mg-30 mg) tablets and meperidine (50 mg) tablets that were prescribed to him at 6-h intervals until the day before surgery. Physical examination revealed no systemic abnormalities. Complete hemogram and urinalysis were within normal limits, and on the eve of his operation, concentrations of blood urea nitrogen (BUN) and serum creatinine were 17 mg/dl and 0.7 mg/dl, respectively. A lumbar laminectomy using general anesthesia was planned.

After uneventful induction of anesthesia and orotrachael intubation

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Key words: Nonsteroidal antiinflammatory drugs. Renal dysfunction, perioperative.

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3 PTS

I thogenesis of Systemic Air Embolism During ronchoscopic Nd:YAG Laser Operations

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Background. The occurrence of systemic air embolism during bronchoscopic neodymium:yttrium-aluminum garnet laser operations has been suspected. Here we describe its mechanism.

Methods. Two patients with embolic cardiac and neurologic complications after bronchoscopic neodymium: yttrium-aluminum garnet laser tumor ablation are described. A subsequent third patient was monitored for intracardiac and aortic air by transesophageal echocardiography. A review of the literature and safety recommendations are discussed.

Results. The appearance of systemic air emboli was related to the use of the laser fiber air coolant at high flow and resolved by decreasing the air flow. The presence of intracardiac and aortic air was associated with hypotension and inferior ischemic electrocardiographic changes.

Conclusions. Systemic air embolism during bronchoscopic laser operations is a potentially catastrophic complication and is related to the use of gas-cooled laser fibers and contact probes. We recommend using the noncontact mode whenever possible and maintaining the coaxial coolant air flow at the minimum level or using a fluid coolant if contact is necessary.

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The excellent palliative results and relative safety of onchoscopic neodymium:yttrium-aluminum garnet (Nd:YAG) laser ablation of obstructive malignant t[illegible]s of the tracheobronchial tree have been well bed in large series of patients [1–3]. Hypoxemia, hemorrhage, airway perforation, pneumothorax, cardiovascular morbidity, and anesthetic complications are reported as the major complications [1–5]. More than 100 bronchoscopic Nd:YAG laser operations have been performed at our institution since 1989 with minimal morbidity [6]. Recently, 2 patients suffered severe intraoperative arrythmias and hypotension during laser therapy for endobronchial tumors. Despite rapid resuscitation, seizures and major strokes developed in both patients. The cardiac and neurologic complications were characteristic of systemic air embolism for numerous reasons. The patients had no history of cardiovascular or cerebrovascular disease. The arrhythmias and hypotension were temporally associated with laser therapy and not with anesthesia induction or preliminary bronchoscopy. There was no significant hypoxia or hemorrhage before the cardiac events. The cardiovascular collapse was rapidly resuscitated in the operating room, and the duration of hypotension was unlikely to have resulted in anoxic brain injury. Finally, the manifestations of early seizures and focal neurologic deficits were typical of the clinical presentation of cerebral air embolism [7]. To investigate the pathogenesis of the complications, we monitored the possible presence of systemic air emboli in the left cardiac chambers and aorta by transesophageal echocardiography in a third patient undergoing endobronchial tumor laser ablation.

Material and Methods

Endobronchial laser operations were performed under general anesthesia with endotracheal intubation using an SLT Contact Laser System (CL MD/DUAL Nd:YAG Laser, 600-μm gas cooled FEF small flexible fiber, SMTR 1.5 contact probe; Surgical Laser Technologies, Oaks, PA) inserted through the suction channel of a flexible fiberoptic bronchoscope (Olympus BF-1T2Od, New Hyde Park, NY). Power settings ranged from 25 to 35 watts in 0.5-second intermittent pulses, and a continuous air flow of 0.8 to 1.5 L/min through the coaxial fiber channel cooled the laser fiber tip and contact probe. Blood pressure, electrocardiogram, pulse oximetry, and end-tidal carbon dioxide were continuously monitored. Transesophageal echocardiography was performed with a two-dimensional probe (Imaging System 77020; Hewlett-Packard Corp, Andover, MA) and real-time video recording.

Results

The first patient was a 68-year-old woman with progressive shortness of breath and no significant past medical history. She presented with acute dyspnea and hypoxemia. A chest radiograph showed atelectasis of the left lower lobe and partial aeration of the left upper lobe.

[illegible]cepted for publication Nov 20, 1997.

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Bronchoscopy revealed an endobronchial lesion almost completely obstructing the left main bronchus, and biopsies documented a histology of squamous cell carcinoma. She underwent bronchoscopic Nd:YAG laser ablation therapy using a contact probe at a power setting of 25 watts in single 0.5-second pulses. The air coolant flow was not recorded. After a total energy delivery of 125 joules within a 5-minute period, bradycardia abruptly developed and then deteriorated into pulseless ventricular tachycardia. Chest compressions, cardioversion, and pharmacologic resuscitation were successful, and the procedure was aborted. Postoperatively, she had stable hemodynamics with no ischemic electrocardiographic changes, but remained comatose with frequent right-sided seizure activity for 2 weeks. Serial brain computed tomographic scans showed no organic lesions, and a transthoracic echocardiogram revealed no abnormalities. Her neurologic status gradually improved, although a left hemiplegia persisted. Palliative irradiation was administered to the mediastinum and left hilum. She was transferred to a skilled nursing facility after 10 weeks.

The second patient was a 45-year-old woman who presented with a productive cough, shortness of breath, and fevers that persisted despite antibiotic therapy. Her history was significant for a left upper extremity malignant melanoma resected 3 years previously with metastasis to the axillary lymph nodes. Chest radiographs and a chest computed tomographic scan revealed right middle lobe atelectasis and mediastinal lymphadenopathy. Flexible bronchoscopy revealed a large endobronchial lesion in the bronchus intermedius, and bronchial washings confirmed metastatic malignant melanoma. Palliative Nd:YAG laser tumor ablation was attempted using a contact probe and a power setting of 25 watts in 0.5-second intermittent pulses. The coolant air stream was set at 1 L/min. A total energy of 324 joules had been delivered over 4 minutes, when bradycardia abruptly developed with a brief episode of asystole. She was treated with atropine and epinephrine. Laser therapy was resumed. After a further delivery of 37 joules she became hypotensive, requiring phenylephrine and epinephrine, and the procedure was aborted. Postoperatively, she was comatose with right-sided seizures. A right frontal infarct was demonstrated by a computed tomographic scan and magnetic resonance imaging of the brain. Electrocardiograms, serum cardiac enzyme measurements, transthoracic echocardiogram, and carotid duplex studies showed no abnormalities. After 3 weeks her neurologic status gradually improved, although a left hemiplegia persisted. Palliative irradiation was administered to the right hilum and mediastinum. She was transferred to a skilled nursing facility after 8 weeks.

The third patient was a 60-year-old man with a history of a pyriform sinus squamous cell carcinoma diagnosed 3 years previously. He underwent external beam radiation therapy, left radical neck dissection, and brachytherapy seed placement. Eighteen months later, metastatic disease to the right lung, mediastinum, and pelvis was documented, and he received chemotherapy and mediastinal irradiation. Despite the palliative therapy, his recurrent disease continued to progress, and an increase in the size of the right upper lobe mass and hilar adenopathy was shown by serial chest computed tomographic scans. Pleuritic chest pain and shortness of breath developed. Chest radiographs and a chest computed tomographic scan revealed right upper lobe atelectasis and tumor invading the right upper lobe bronchus. An exercise tolerance test with thallium revealed no electrocardiographic or perfusion abnormalities. Fulguration of the endobronchial tumor was planned, using intraoperative transesophageal echocardiography to detect any systemic air emboli. Bronchoscopy revealed a right upper lobe tumor invading and almost completely obstructing the right main bronchus. Neodymium: yttrium-aluminum garnet laser therapy was performed using a contact probe and a power setting of 35 watts in 0.5-second intermittent pulses. The coolant air stream was initially set at a flow rate of 1.5 L/min. Care was taken not to bury the contact probe into the tissue. After 7 minutes of laser therapy, air bubbles were visualized in the left atrium, left ventricle, and ascending aorta (Fig 1A). Electrocardiographic monitoring showed associated ST segment depressions in lead II of 1.68 mV, compared with a baseline of 0.12 to 0.48 mV. There were no changes noted in lead V_6. The blood pressure dropped temporarily to 90/60 mm Hg from 140/70 mm Hg, and the oxygen saturation decreased to a low of 93%. The air coolant flow was immediately decreased to 0.8 L/min, with abrupt cessation of air accumulation (Fig 1B), resolution of lead II ST depression to 0.44 mV, and subsequent improvement of the blood pressure to 130/70 mm Hg and the oxygen saturation to 98%. Laser therapy was continued, and after a total of 400 pulses with an energy delivery of 6,103 joules, the patency of the right main and upper lobe bronchi was restored. Postoperatively, there were no apparent cardiovascular or neurologic sequelae. The right upper lobe was reinflated on chest radiograph, and the patient was discharged home after 5 days.

Comment

Systemic air emboli were suspected as the cause of intraoperative arrythmias, cardiac arrest, postoperative seizures, and strokes in 2 patients undergoing endobronchial Nd:YAG laser tumor ablation. This suspicion prompted us to monitor the next scheduled patient with a transesophageal echocardiogram. The presence of air bubbles in the left atrium, left ventricle, and aorta was documented during use of the Nd:YAG laser, with concurrent signs of inferior myocardial ischemia. Reduction of the laser fiber coolant air flow resulted in resolution of the intracardiac air, hypotension, and ischemic electrocardiographic changes, confirming the pathogenesis of the systemic air emboli. The inferior but not anterolateral ischemic changes were consistent with the fact that in the supine position the anterior, least dependent position of the right coronary artery ostium is susceptible to air

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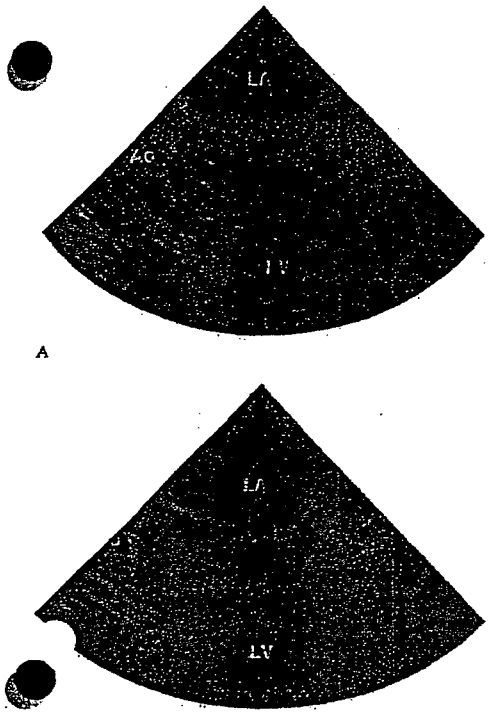

Fig 1. Transesophageal two-dimensional echocardiographic images depicting the left atrium (LA), left ventricular outflow tract (LV), and proximal aorta (Ao). (A) Prominent intracardiac air bubbles with the laser gas cooling system set at 1.5 L/min. (B) Resolution of the systemic air emboli with the laser fiber coaxial air flow decreased to 0.8 L/min.

emboli, in contrast to the posterior, dependent position of the left main artery ostium. These 3 patients add to the growing literature of air emboli complications after Nd:YAG laser operations.

Air embolism associated with Nd:YAG laser operations has been reported after procedures for endometrial ablation [8–11], hepatic metastasis ablation [12], laparoscopic cholecystectomy [13], congenital choanal stenosis [14], and endobronchial tumor ablation [15–18]. The diagnosis of air emboli was clinically suspected in the majority of cases, although definitive evidence of air emboli in some patients was by aspiration of intravascular air [8–10], documentation of retinal artery bubbles on fundoscopy [15], and demonstration of intravascular air by radiographs [9, 14] or computed tomographic scan [1[illegible]ne case report demonstrated increases in end-tidal C[illegible]hat were temporally related to Nd:YAG laser activation using a CO_2-cooled laser fiber and documented a moderately increased arterial carbon dioxide tension that may have been due to absorption or embolization of the coolant gas [19].

Introduction of air into systemic veins may result in cardiovascular collapse due to right heart and pulmonary emboli. Air entry into the pulmonary veins may result in myocardial ischemia and strokes due to systemic emboli to the coronary and cerebral circulations. Left ventricular and aortic air has been documented after endometrial ablation operations even in the absence of a patent foramen ovale on postmortem examination [9]. The complication of air emboli after an Nd:YAG laser operation may be catastrophic, with 9 fatalities reported from the 21 cases in the literature (2 reports were duplicated from a total of 11 deaths in the literature). Seven deaths occurred after venous embolization [8–10, 12, 14], and 2 deaths after systemic embolization [15, 17]. A further 2 patients sustained permanent strokes [10, 17], and the remaining 10 patients made full recoveries after sustaining cardiac and neurologic complications [11, 13, 16–18]. The treatment of choice for air emboli is hyperbaric oxygen therapy. Three patients with strokes after systemic air emboli during endobronchial Nd:YAG laser operations were treated early with hyperbaric oxygen and had complete resolution of their neurologic deficits [16–18], although 1 patient treated with hyperbaric oxygen after laser endometrial ablation and venous air emboli had residual neurologic deficits [10]. The common denominator in the 3 patients described in this report and 19 of 21 patients in the literature who suffered air emboli during Nd:YAG laser operations was the use of a gas-cooled laser fiber tip. In the remaining 2 patients, the type of laser fiber and coolant mechanism were not mentioned [15, 16]. In the majority of cases artificial sapphire contact probes were attached to the fiber tips, and none of the reports specify that a noncontact mode was used. Air, carbon dioxide, and nitrogen were used as coolants at flows ranging from 0.5 to 5 L/min.

Light energy emitted by the laser source is transmitted to the target tissue through flexible quartz fibers. The radiant energy absorbed by the tissue is converted to thermal energy with various tissue effects. At temperatures between 60 and 100°C the tissue is denatured and coagulated, and at temperatures greater than 100°C the tissue is vaporized with cutting or ablation results. The thermal tissue effect depends on factors such as the laser wavelength and the power or duration of the laser energy. Neodymium:yttrium-aluminum garnet lasers result in effective coagulation and are preferred in airway operations because of their hemostatic effect and efficient application with flexible quartz fibers. Increasing the power setting of the Nd:YAG laser can result in tissue vaporization rather than coagulation, and both effects can be used for ablation of endobronchial tumors [1, 3]. Alternatively, artificial sapphire probes attached to the laser fiber tips can alter power densities and thermal gradients, and thus decrease the dependence of tissue effect on the particular laser wavelength used [8, 10]. Specific probes of various shapes, sizes, and finishes can achieve predictable tissue effects of coagulation or vaporization with the Nd:YAG laser. The laser fiber tips and

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probes can be used in contact or noncontact modes with the tissue. Direct contact results in a greater efficiency of energy utilization and more precise control. Cooling of the laser fiber and contact probe is required to prevent thermal damage. Gas or fluid coolant is delivered to the fiber tip through a coaxial channel provided by a polyethylene sheath around the laser fiber. Gas such as compressed air, carbon dioxide, or nitrogen is preferred over fluid because of improved visibility. The delivery of gas is variable, but inadequate flows lead to frequent charring and fracturing of the contact probe from the fiber tip. The pressure of air exiting the distal coaxial sheath can be excessive and has been measured at greater than 500 mm Hg when the flow rate was set at 0.4 L/min [17].

Our observations indicate that a high flow of coolant gas during use of the contact probe leads to vascular air emboli. This is consistent with the hypothesis that air emboli during endobronchial laser operations result either from direct air flow from the coaxial cooling sheath into open pulmonary venous tributaries or from occlusion of the proximal recanalized bronchus by the bronchoscope with distal high pressures forcing gas into vascular channels [17]. Transesophageal echocardiographic monitoring did not document systemic air emboli at lower coolant air flow rates or when the laser was not engaged. These findings do not support an alternative hypothesis that positive-pressure ventilation under conditions of pulmonary instrumentation with limited vision, superatmospheric pressure of intrathoracic gas, and pathologic consolidation processes encircling the pulmonary veins are responsible for systemic air emboli during laser bronchoscopy [15]. However, these mechanisms may be operative under certain circumstances, and fatal systemic air embolism has been reported after transbronchial lung biopsies where gas cooling is not used [20, 21]. Because the major risk factor for air embolism during laser operations appears to be inherent to the use of gas-cooled laser fibers, the risk of air embolism is not limited to the Nd:YAG laser but could occur with lasers of other wavelengths. A further mechanism for air dissection and embolism during laser operations is related to the use of gas for insufflation or ventilation, and reports of this complication range from subcutaneous emphysema and hypercapnia in a patient undergoing knee CO_2 laser arthroscopy [22] to cardiac arrest in patients undergoing urethral Nd:YAG laser operations [23].

Systemic air emboli have not been reported as a cause of mortality or morbidity in many of the major series of bronchoscopic Nd:YAG laser operations, although all reports describe cardiovascular complications, including arrhythmias and cardiac arrest, attributed to cardiac disease [1–5]. One reason may be that the clinical diagnosis of air emboli is difficult to differentiate from other causes of cardiac and neurologic dysfunction. Nevertheless, the largest series of 2,710 bronchoscopic Nd:YAG laser procedures by Cavaliere and colleagues [3] reported very few complications that could be attributed to systemic air embolism, with no strokes and 17 episodes (0.6%) of heart failure and myocardial infarction resulting in 7 deaths (0.3%). Another possible reason is that minor systemic air embolism may result in subclinical or subtle cardiac and neurologic sequelae that are not diagnosed. Our third patient had no obvious complications despite documented systemic air emboli. Finally, differences in experience and technique such as the use of noncontact modes and rigid bronchoscopy may account for differences in embolic complications. Retrospective studies that have systematically investigated the frequency of Nd:YAG laser-associated cardiovascular and cerebrovascular events during treatment for endobronchial cancer have found a much higher incidence of complications. Lang and colleagues [17] reported that 8 of 62 patients undergoing 111 bronchoscopic Nd:YAG laser operations had serious cardiac and cerebral complications. Bradycardia developed in 5 patients, 4 of whom progressed to intraoperative cardiac arrest and were resuscitated, and 1 patient sustained a postoperative myocardial infarction and died. Four patients had both strokes and electrocardiographic changes, which resolved in 3; 1 had persistent neurologic deficits. The procedural incidence of cardiovascular and cerebrovascular complications was 8.1% and 3.6%, respectively. Hanowell and associates [24] studied the frequency of cardiovascular complications associated with general anesthesia in 73 patients undergoing 87 Nd:YAG laser endobronchial tumor resections. The procedural incidence of cardiovascular complications was 27.6%, consisting of arrythmias, hypotension, hypertension, myocardial ischemia, and infarction. A more accurate assessment of the incidence and clinical relevance of systemic air emboli during bronchoscopic Nd:YAG laser operations would require a prospective study with transesophageal echocardiographic monitoring and detailed perioperative studies of cardiac and neurologic function.

The details of laser cooling systems and coolant flow rates can be of critical importance and are not discussed in many reports of Nd:YAG laser operations [1–5]. It is essential that thoracic surgeons be familiar with the risks of gas-cooled fibers and contact probes, as the indications for the Nd:YAG laser are increasing to include ablation of benign bronchial lesions [25] and thoracoscopic resection of pulmonary lesions [26]. In addition to the warning issued by the Food and Drug Administration regarding the danger of air embolism during the intrauterine use of gas-cooled laser fibers [27], we caution that this hazard can occur in any part of the body. Fatal embolic complications have been reported after laparoscopic, otolaryngologic, and bronchoscopic procedures as well as gynecologic operations. The use of contact probes with high-flow gas cooling systems in enclosed areas of the body should be abandoned in all surgical specialities. We believe that the major mechanism of systemic air embolism during bronchoscopic Nd:YAG laser operations is as follows: capillary integrity is disrupted by laser energy, the laser fiber is partially buried in the tumor, coolant air enters the tumor from the distal coaxial sheath, and the air is forced through disrupted capillaries into the pulmonary venous circulation, and subsequently to the left

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heart. We conclude that systemic air emboli are not narily related to tissue vaporization or the total mount of heat energy delivered. The complication of air nboli can be avoided by using endobronchial lasers in the noncontact mode. Our experience has led us to change our technique, and we use the noncontact mode whenever possible, maintaining the laser fiber coolant air flow at the minimum level. If direct contact between the probe and tissue is necessary, then a fluid coolant should be considered. Surgeons who continue to use gas-cooled contact probes should take particular care to avoid burying the probe into the tissue, to avoid obstructing the proximal recanalized bronchus with the bronchoscope, and to maintain the coolant air flow at the lowest possible level.

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LINKS

Venous air embolism during the use of a Nd YAG laser.

Agil M, Ulhaq A, Arafat A, Hussain A, Rasheed A, Turkistani A.

Department of Anaesthesiology, College of Medicine, King Saud University, Riyadh, Saudi Arabia. mansooraqil@yahoo.com

We report a case of a 47-year-old female who suffered a cardiac arrest during sub-mucosal diathermy of the inferior turbinate using a Nd YAG laser. The possible causes of the cardiac arrest are discussed. Venous air embolism due to Nd YAG laser was thought to be the most likely cause in this case. Although venous air embolism has previously been reported during nasal sinus surgery and choanal atresia when using a Nd YAG laser, the occurrence of this complication during a relatively minor surgical procedure has not previously been reported. It is important, therefore, to raise the awareness of this life threatening complication during use of a Nd YAG laser regardless of the duration of surgery. We recommend the use of appropriate methods and techniques to avoid this life threatening complication during the use of Nd YAG laser even for relatively short procedures.

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Cardio-Cerebrovascular Complications From Nd:YAG Laser Treatment of Lung Cancer

Nicholas P. Lang, MD, Gerald M. Wait, MD, Raymond R. Read, MD, Little Rock, Arkansas

The laser palliation of patients with unresectable lung cancer has an acceptable complication rate. Perforation, bleeding, and pneumothorax are the main complications described. Cardiovascular morbidity has been reported to be 1% in six surgical series and has been attributed to general anesthetics or hypoxia. However, one very recent anesthesia study described a 25% incidence, and two case reports inferred an air embolism. We reviewed 62 patients who have undergone 111 treatments for endobronchial carcinoma. Eight manifested perioperative cardiac or cerebral events. Five of the eight developed bradycardia; four experienced progression to intraoperative cardiac arrest. Other electrocardiographic abnormalities appeared and resolved within 24 hours. Four patients developed stroke and electrocardiographic changes. Two of these resolved spontaneously within 1 month. Early computed tomography in one patient showed intracerebral air. These data indicate that patient disease or hypoxemia is not sufficient to explain intraoperative cardiac and postoperative cerebral changes. Air embolism to the cerebral circulation occurs during laser bronchoscopy. Reduced cooling air flow, return to helium fiber cooling, or reversion to photodynamic therapy is indicated.

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Presented at the 43rd Annual Meeting of the Southwestern Surgical Congress, Las Vegas, Nevada, April 21–24, 1991.

The neodynium:yttrium-aluminum-garnet (Nd:YAG) laser is an effective tool in the palliation of unresectable endobronchial tumors, opening bronchi and controlling hemorrhage. Hypoxia, bleeding, pneumothorax, and perforation are frequently listed as the major complications of this procedure. Cardiovascular morbidity in 6 surgical series totaling 3,892 procedures was less than 1% [*1–6*]; however, a very recent anesthesia study (1991) reported a 25% incidence of morbidity [*7*] and two case reports inferred air embolism [*8,9*]. The use of Nd:YAG laser therapy and other operative procedures such as hysteroscopic intrauterine endometrial ablation and laser resection of hepatic metastasis can produce cardiovascular complications secondary to systemic venous air embolism [*10–12*]. To define the frequency of Nd:YAG laser-associated cardiovascular-cerebrovascular events during treatments for endobronchial cancer, we reviewed our experience with 62 patients.

PATIENTS AND METHODS

Each patient was evaluated preoperatively by history and physical examination, chest radiograph, measurement of arterial blood gas, pulmonary function tests, hematologic studies, electrocardiogram (ECG), computerized tomography (CT), and preoperative bronchoscopy with biopsy. Inoperability was determined after staging by tumor location (bronchial involvement within 2 cm of the carina or tracheal or bilateral bronchial involvement) or physiologic performance (forced expiratory volume in 1 second [FEV_1] less than 1.5 L for lobectomy or FEV_1 less than 2.0 L for pneumonectomy). Symptoms on presentation were dyspnea, chronic cough, hemoptysis, and recurrent pneumonia. Eighty-six percent of these patients were found to have squamous cell carcinoma. The most common site of tumor involvement was the right main stem bronchus, followed by the left main stem bronchus. The upper lobe bronchi were the commoner lobar bronchi involved. All patients gave a history of smoking. Intraoperatively, patients underwent general endotracheal anesthesia with monitoring of blood pressure, pulse oximetry, end tidal carbon dioxide, and ECG. Patients were initially maintained on forced inspiratory oxygen (FIO_2) less than 50%. All patients were treated by the same surgical endoscopist. For all laser treatments, a Nd:YAG laser (Molectron 8000 N1, Cooper Lasersonics, Inc., Santa Clara, CA) with a coaxial quartz fiber (Model #G56DW) and a high air flow (3 L/min) cooling system was used. A Pentax FB-19D or FB-19H (Pentax, Orangeburg, NY) flexible fiberoptic bronchoscope was employed. Photoresections were performed using standard settings of 0.5-second bursts (range: 0.4 to 0.6 seconds) with power settings of 50 watt-seconds (range: 40 to 70

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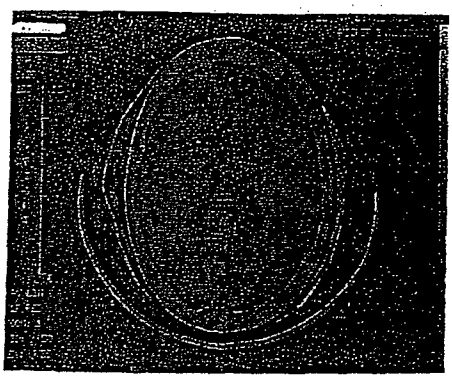

Figure 1. Postoperative CT scan showing intracerebral air after Nd:YAG laser bronchoscopy.

watt-seconds). The average amount of energy delivered was 2,800 J (range: 138 J to 11,500 J). After photoresection with subsequent recanalization of the airway, a guidewire was placed to allow positioning of a nylon sheath for subsequent high-dose remote afterloading brachytherapy utilizing the Gammamed IIi Iridium^{192} (Mallinckrodt Diagnostica, B.V. Patten, Dusseldorf, Germany) radiation source.

RESULTS

Eight patients manifested cardiac or cerebrovascular events during or immediately after laser photoresection. There was no cardiac or cerebrovascular disease that would have predisposed these patients to the subsequent perioperative events. Several had undergone prior laser treatments (range: 1 to 7) without complications. Only one patient had a complication with his initial procedure. There were no intraoperative deaths. Five of the eight patients developed bradycardia, with four experiencing a rapid progression to intraoperative cardiac arrest. Only three had a drop in oxygen saturation before bradycardia. Other electrocardiographic abnormalities that appeared (ST segment depression and secondary and tertiary atrioventricular block) resolved within 24 hours. Four patients had postoperative strokes and ECG changes. All strokes were apparent after the patients recovered from the anesthesia. Two strokes resolved within 1 month with supportive care; one resolved after treatment with hyperbaric oxygen; and the fourth one did not resolve (patient was left with a permanent deficit). Delayed CT (72 to 120 hours) of the head in three patients showed no change (1 patient), infarct (1 patient), and metastatic tumor (1 patient). Early CT (6 hours) in one patient showed intracerebral air (Figure 1). There was no correlation with the amount of energy delivered (197 to 4,017 J) or the patient's age (41 to 69 years). Only one patient was found to have permanent ECG changes suggesting infarction. He died 24 hours later.

COMMENTS

Since most patients undergoing palliative laser bronchoscopy for advanced lung cancer require general anesthesia, are hypoxic, prone to aspiration of blood or mucus, and need repeated treatments, it is surprising that intraoperative cardiovascular complications are rarely reported. Thus, the incidence of cardiovascular complications in 6 large series totaling 2,359 patients having undergone 3,892 procedures was less than 1% (0.9%) [*1–6*]. Morbidity was attributed to the anesthetic agent or aspiration [*6*]. The authors did not mention stroke. However, one very recent study (1991) by Hanowell *et al* [*7*], which systematically reviewed the incidence of cardiovascular complications associated with general anesthesia and Nd:YAG laser endobronchial tumor resection, noted the following complications and their incidences in 24 procedures: hypotension (9%), hypertension (5%), ventricular ectopy (5%), supraventricular tachycardia (5%), ventricular tachycardia (1%), heart block (1%), myocardial infarction (1%), and myocardial ischemia (1%). Prolonged anesthesia and age were reported as predictive variables. There was no correlation between intraoperative hypoxemia and the development of cardiac complications. Our own considerable experience with patients undergoing palliative laser treatment agrees with this later study since it shows a disturbingly high incidence of serious cardiovascular problems (7%) or cerebrovascular incidents (3%) consistent with and, even in one case, proven to be the result of air embolism. Because of the morbid condition of many of our patients who were referred for palliative treatment, we too believed, initially, that intraoperative cardiovascular manifestations were due to patient debility, hypoxia, or anesthesia. However, our thinking changed radically when a 42-year-old man with no history of cardiac or cerebrovascular disease sustained intraoperative bradycardia, convulsed in the recovery room, and woke up with a left-sided hemiplegia that took 6 weeks to resolve. A CT scan of the head, obtained 6 hours after the procedure, showed intracerebral air within the right hemisphere (Figure 1). Because of this tragedy, we reviewed our experience and that of others.

In 1929, Van Allen *et al* [*13*], in extensive canine experiments, studied the effects of air embolism to the pulmonary venous circulation and reported two physiologic responses: neuromuscular (cerebrovascular) or cardiovascular. Cerebrovascular manifestations included blindness, convulsions, hemiplegia, and death. Cardiovascular events began with acute hypertension followed by dysrhythmias and circulatory collapse. In 1947, Durant and co-workers [*14*] showed that as little as 0.025 mL of air injected into the anterior descending branch of the left main coronary artery, could elicit cardiac dysfunction and 0.05 mL could result in death. In 1953, Geoghegan *et al* [*15*] described the mechanisms of death due to intracardiac air during open heart surgery as being occlusion of the coronary arteries, ventricular failure, and cerebral air embolism with infarction. All the results from the aforementioned canine studies were then confirmed in patients with the appearance of the pump oxygenator and open heart surgery [*16*]. Intraoperatively and postopera-

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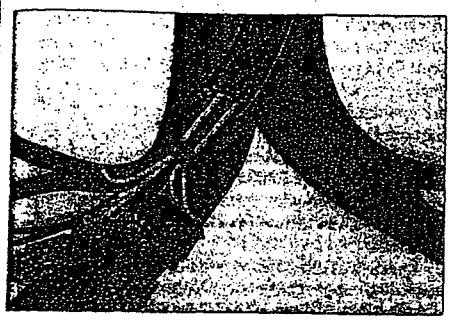

Figure 2. Air introduced directly into the pulmonary venous system by the laser coaxial fiber.

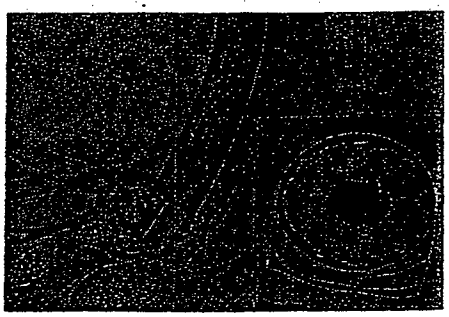

Figure 3. Distal postobstructive pressure generated by the occlusion of the recanalized bronchus.

tively, patients manifested the same physiologic response as animals to air embolism.

Two case reports in the literature document air embolism as the mechanism of stroke and death after bronchoscopic Nd:YAG laser therapy [7,8]. One patient developed a left cerebrovascular accident after laser resection of an endobronchial carcinoid [7]. The second experienced massive systemic arterial air embolism manifested by hypertension, tachycardia, circulatory collapse, and death following resection of an obstructing endobronchial squamous cell carcinoma [8].

Peachey *et al* [8] concluded that there were three risk factors for systemic arterial air embolism during laser therapy: (1) pulmonary instrumentation under limited vision; (2) intrathoracic gas at superatmospheric pressures induced by positive pressure ventilation during endotracheal anesthesia; and (3) postobstructive pneumonia or cancer consolidating the lung and encasing the pulmonary vasculature preventing collapse and contracture after surgical disruption, thereby opening an avenue for the passage of air into the pulmonary venous circulation.

In addition to ventilatory gas flow, we believe that two other potential mechanisms, intrinsic to the Nd:YAG laser, exist by which air can be introduced into the pulmonary venous system. The pressure of the high air flow (400 mL/min) measured at the tip of the coaxial fiber was found to be greater than 500 mm Hg. Air under pressure can thus be introduced into an open pulmonary vein during resection of a tumor, either by direct flow from the coaxial fiber (Figure 2) or when the tip of the bronchoscope is advanced into the recanalized orifice of an obstructed bronchus, occluding the airway and forming a distal closed high-pressure system. The postobstructive pressure generated may force air directly from the alveoli into the pulmonary venous system, as was described almost 200 years ago [13] (Figure 3). In the perioperative period when cardiac complications occurred in our cases, the laser procedure was terminated; however, positive pressure ventilation was continued until the patient recovered from anesthesia. If positive pressure ventilation was the sole etiology, then the condition of the patients should have worsened instead of improving, as happened with our patients.

The importance of this report is illustrated by the comment made by Durant *et al* [14] in 1947: "Although pulmonary air embolism is relatively infrequent in medicine practice, it is so catastrophic when it does occur that further investigation into its etiology, pathologic physiology, prophylaxis and treatment is fully warranted. Moreover, ... its importance from the standpoint of frequency may be much greater than has been recognized, since very few of these accidents are likely to be reported and ... death may be attributed erroneously to heart disease or some other condition."

This review of our experience and of the literature has led to three changes in technique that we believe will reduce these complications: (1) Reduce cooling air flow to very low levels (less than 50 mL/min); (2) Do not advance the bronchoscope until it completely occludes the bronchus; (3) Do not push the fiber tip into or through obstructing tumor.

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DISCUSSION

William F. Sasser (St. Louis, MO): These are critically ill patients and usually the surgeon is operating in a desperate situation. The patient, the family, and the other physicians involved in the care should be aware of the many complications that can occur. Air embolism can now be added to the list of cardiovascular problems. In the surgical literature, the complication rate is cited as 1% to 2%; however, in the anesthesia journals, the complications from laser bronchoscopy run as high as 25%. I use general anesthesia and do not paralyze the patient. There are spontaneous respirations with minimal assists from the anesthesiologist. Is this the type of anesthesia you use? How do you regulate the length of time that you use the laser? Do you monitor the build-up of carbon dioxide? Is there a time limit that you do not exceed? Please elaborate on the helium fiber cooling technique that you described.

Carey P. Page (San Antonio, TX): Have you used precordial esophageal or transcranial ultrasound monitoring to detect these emboli intraoperatively? This approach would permit early diagnosis and use of hyperbaric oxygen.

Gerald Walt (closing): We do maintain the patients under a minimal paralysis during this procedure and try to have them spontaneously breathe. Carbon dioxide is constantly monitored throughout these procedures as is pulse oximetry. Helium fiber cooling was found to be a better conductor of heat; however, it is expensive, and air is a much cheaper commodity. Dr. Page, the anesthesiologists do monitor with precordial leads; however, I do not have any data as to whether we were able to record any information. Usually when a catastrophic event occurs, we terminate the procedure and we attempt to resuscitate the patient.

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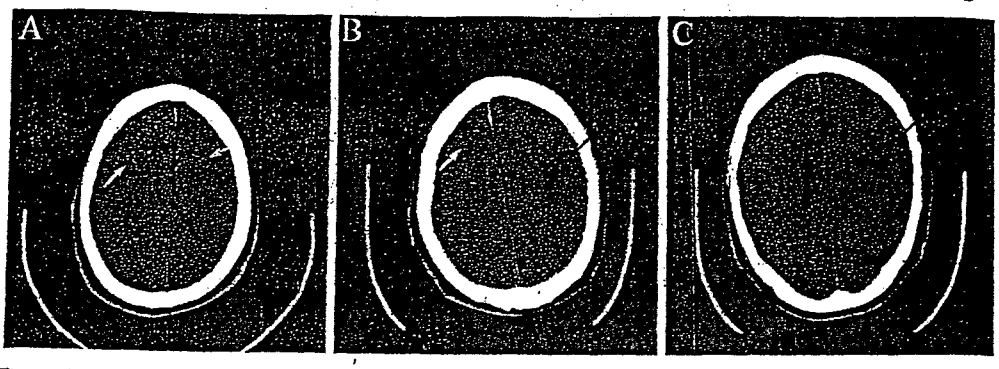

Figure. Axial CT imaging of brain shortly post-event (A) shows multiple punctate, hypodense foci (air bubbles) at the gray/white junction bilaterally (white arrows); 20 hours post-event (B) shows resolution of most hypodensities, but residual hyperdensities likely representing hemorrhage (black arrow); 5 days post-event (C), only small hyperdensities remain.

Cerebral air embolism during transbronchial biopsy

Stephen M. Maricich, PhD, MD, Ronald A. Rauch, MD, Perry J. Foreman, PhD, MD, Houston, TX

A 55-year-old man with a history of prior rectal carcinoma underwent elective bronchoscopy and transbronchial biopsy for evaluation of a new lung mass. At the precise point of biopsy, he had a short tonic-clonic seizure followed by irritability, disorientation, and hemiparesis of his left face, arm, and leg. The timing of the event and appearance on CT (figure) suggested the diagnosis of cerebral air embolism (CAE). Although rare, CAE can be a potentially life-threatening complication of this procedure.[1,2] Our patient returned to his normal neurologic baseline within 48 hours of the event without intervention.

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Anaesthesia, 1988, Volume 43, pages 872–875

ASE REPORT

Systemic air embolism during laser bronchoscopy

T. PEACHEY, J. EASON, J. MOXHAM, D. JARVIS, AND M. DRIVER

Summary

We report a case of massive, fatal, systemic gas embolism which occurred during the course of laser bronchoscopic resection of a bronchial carcinoma. The clinical features of systemic air embolism are discussed.

Key words

Complications; air embolus.
Surgery; laser.

In the first half of this century, when induction of artificial pneumothorax was employed frequently in the treatment of pulmonary tuberculosis, systemic air embolism by way of the pulmonary vein was a well recognised hazard.[1] We suggest that this hitherto extremely rare surgical complication may be seen more often, as a result of increased use of laser bronchoscopic resection for the relief of airways obstruction in cases of advanced bronchial carcinoma. Laser bronchoscopy brings together three risk factors for the entry of gas into the pulmonary vein, namely pulmonary instrumentation under conditions of limited vision, intrathoracic gas at superatmospheric pressure and a pathological process which consolidates the lungs and encircles the pulmonary veins.

Case history

A female patient, aged 68 years, who had been a lifelong smoker and who was known to have a poorly differentiated squamous bronchial carcinoma, for which she had received a course of radiotherapy, presented with a 6-week history of haemoptysis and increasing breathlessness. On examination she was dyspnoeic at rest and had a loud wheeze audible in both inspiration and expiration. Her chest radiograph revealed an opacity in the superior mediastinum which extended into the right upper zone; there was partial collapse of the right upper lobe. Bronchoscopy confirmed the presence of a tumour at the carina, which narrowed the right main bronchus to a pinhole and the left to approximately 50% of its normal calibre. It was decided to undertake laser bronchoscopic resection of this tumour in the hope of palliating the patient's obstructive symptoms.

The patient was premedicated with oral temazepam 20 mg and atropine 0.6 mg one hour before the procedure. ECG monitoring was instituted on her arrival in theatre; a pulse oximeter was placed on her finger and a radial artery cannula inserted using local anaesthetic. An intravenous cannula was inserted into each arm and anaesthesia induced with fentanyl 100 μg and propofol 150 mg and maintained by an infusion of the latter at a rate of 10 mg/minute. An 8-mm Portex cuffed tracheal tube was inserted with the aid of suxamethonium 100 mg and paralysis was maintained with atracurium 25 mg; further doses were given as indicated by a peripheral nerve stimulator. A fibre-optic bronchoscope was inserted through an airtight port in the catheter mount and the patient's lungs were ventilated manually with a 10 litre/minute flow of oxygen-enriched air using a non rebreathing circuit (Fig. 1). A smoke absorption device (made from two Pall gas filters between which a layer of granular activated charcoal was sandwiched) was connected to the expiratory limb of the system. The first half hour of the procedure was uneventful from the anaesthetic point of view; the mean arterial pressure was maintained between 100 and 120 mmHg, the pulse rate 90–100 beats/minute and the haemoglobin saturation never decreased below 97%.

Bronchoscopy revealed a mass of tumour which widened the carina and obstructed both main bronchi, the left partially and the right completely. The tumour was largely necrotic and its surface coated with mucopus and old blood. A Messerschmidt Nd. YAG laser operating at 50 watts output was used to widen the right main bronchus sufficiently to permit passage of the bronchoscope into the right lower lobe bronchus.

Torrential bleeding occurred as further tumour was burnt off the medial wall of the right main bronchus. The patient becam
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T. Peachey, MB, BS, Registrar, J. Eason, FFARCS, MRCP, Senior Lecturer, Department of Anaesthesia, J. Moxham, MD, FRCP, Consultant Physician, D. Jarvis, MB, BS, Registrar, Department of Thoracic Medicine, M. Driver, FRCPath, Consultant, Department of Pathology, King's College Hospital, Denmark Hill, London SE5 9RS.

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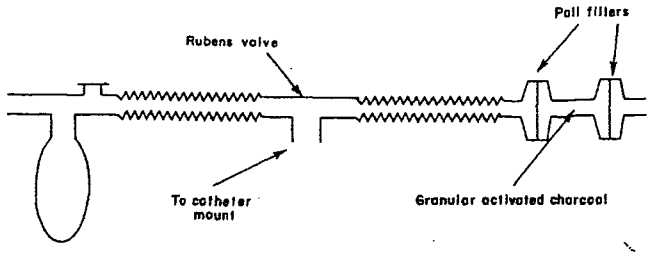

Fig. 1. Diagram of anaesthetic system used for manual ventilation during bronchoscopy.

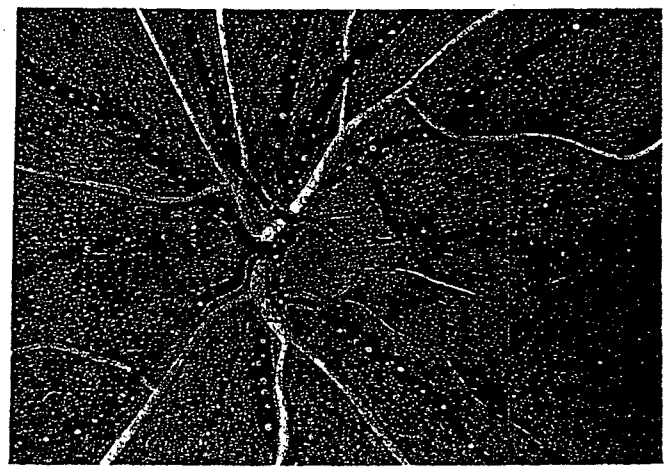

Fig. 2. Artist's impression of retinal appearance after massive systemic air embolism.

patient became acutely hypertensive (mean arterial pressure 180 mmHg) and bradycardic (40 beats/minute). Both pupils became fixed and dilated and marked patchy facial pallor was noted. It was impossible to identify a bleeding point as a result of profuse haemorrhage (500 ml of blood were aspirated by way of the bronchoscopic suction channel over a period of a few minutes). Ventilation became increasingly difficult and in view of suspected hypoxia, the inspired oxygen was increased to 100%; atropine 0.6 mg was given intravenously and an attempt made to pass a left-sided Robertshaw double lumen bronchial tube. It was apparent immediately that this could not be passed beyond the tumour which obstructed the left main bronchus so the tracheal tube was replaced. The patient's bradycardia became worse despite intravenous adrenaline, calcium chloride and further atropine. The hypertension gave way, after 2 minutes, to profound hypotension and external cardiac massage was instituted.

In the course of withdrawing an arterial sample for blood gas analysis (the Pa_{O_2} was 57 kPa and Pa_{CO_2} 7 kPa), it was noticed that copious bright red froth was issuing spontaneously from the arterial cannula. Systemic air embolism was suspected; the patient showed generalised intense but mottled pallor, crepitus could be felt along the course of the brachial, femoral and carotid arteries, and a loud millwheel or 'squelchy boot' murmur was audible throughout the chest (although this seemed loudest over the left ventricle). Ophthalmoscopy revealed that the entire retinal arterial tree was outlined with air and bubbles could be seen moving centripetally along the retinal veins (Fig. 2).

The appearance of the fundi was extremely striking; it was as if the arteries had been injected with mercury so that the retina resembled a silver spider's web. It was clear to us that massive systemic air embolism had taken place, presumably because the tumour in the medial wall of the right main bronchus was in continuity with a branch of the pulmonary vein. This had been breached by the laser with the result that air was forced from the bronchus into the systemic circuit by positive pressure ventilation. The patient was tipped head-down; ventilation and cardiac massage were continued for 30 minutes but the bradycardia gave way to asystole refractory to all treatment and our rescusitative efforts had to be discontinued.

Postmortem examination revealed the presence of a mass of tumour tissue which encircled and obstructed both main bronchi and involved the oesophagus and one of the right

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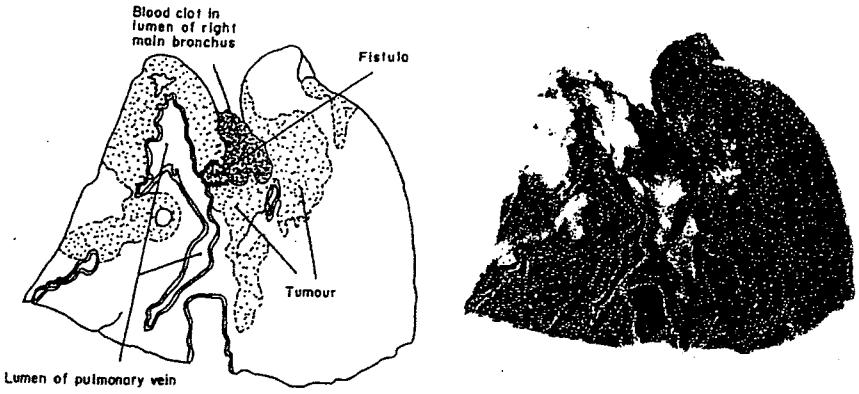

Fig. 3. Posterior aspect of coronal section through upper part of right lung.

pulmonary veins (Fig.3). Dissection revealed a fistula through the tumour, which connected the medial wall of the right main bronchus with a branch of the pulmonary vein. Tumour deposits were also identified in the hilar and mediastinal lymph nodes and in the cervical vertebrae.

Discussion

Systemic air embolism by way of the pulmonary vein has been reported as a complication of pneumonectomy,[2] needle lung biopsy,[3] penetrating lung injury,[4–6] blunt lung injury,[4] high-pressure artificial ventilation in neonates[9] and in particular, the induction of artificial pneumothorax.[7,10–12] Pressure within the pulmonary vein may be intermittently subatmospheric so air can be entrained if the vessel wall is torn in such a way that its lumen is brought into continuity of the atmosphere. This can occur either directly as a result of a penetrating chest wound or indirectly through the airway.

The risk of systemic air embolism is increased considerably if tissues adjacent to the vessel are consolidated, as may occur with a bronchogenic carcinoma or tuberculous process. Normal elasticity of the lung is lost and any abnormal communication, however formed, between the vein and air passages is held open for a longer period than would otherwise be the case. Where such a communication involves the airways, the risk of embolism is greater if the airway pressure is artificially increased, by intermittent positive pressure ventilation, for example. If the communication is with the pleural cavity, a tension pneumothorax would constitute a greater danger than, say, a sucking wound of the chest. It is not surprising therefore that a majority of earlier reports of systemic air embolism concern the creation of artificial pneumothoraces to treat extensive pulmonary tuberculosis, in which two risk factors—an airspace at super atmospheric pressure and abnormally rigid lung tissues coexisted.

Situations most likely to give rise to systemic air embolism by way of the pulmonary vein, in current medical practice, are penetrating lung injuries and surgical procedures on patients with extensive neoplastic or inflammatory pulmonary consolidation in whom intermittent positive pressure ventilation has to be employed. These dangers, during thoracotomy, are usually appreciated and so avoided by the surgeon, but when access is limited severely, as in endoscopic procedures such as laser bronchoscopy, the risk is inherent in the procedure and is therefore largely unavoidable.

Some authorities recommend that laser treatment should be carried out in the spontaneously breathing patient[13–15] (in whom systemic air embolism is less likely to occur), although a majority favour assisted ventilation[16–23] since it provides a more tranquil operating field, avoids hypoxia as a result of respiratory depression and only rarely causes complications.[24]

Systemic air embolism is probably an extremely rare event; few clinicians have seen it and its clinical signs are not well known. Clarke[25] lists four pathognomonic signs: marbling of the skin (which was present in our patient), pallor of half or a portion of the tongue (Leibermeister's sign, because of embolism of all or part of a lingual artery), air bleeding (which was illustrated dramatically by the froth which issued from the radial arterial line in our patient) and bubbles of air in the retinal blood vessels. Clarke goes on to state that the millwheel murmur characteristic of venous air embolism is absent in systemic embolism. This murmur was obviously present in our case: we believe that this may have been because of the relatively large volumes of gas which entered the left side of the heart, as evidenced by the total replacement of retinal arterial blood by gas. Air has been demonstrated to pass from the arterial to the venous circulation[5,26] as is borne out by our observation of bubbles which moved centrally along the retinal veins. However, we consider that in the case described the total volume of gas that passed through the left ventricle must inevitably have exceeded that which reached the right heart. Clinically, the millwheel murmur was louder over the left ventricle.

Systemic air embolism is only rarely diagnosed antemortem.[8] The dramatic, albeit brief, episode of hypertension which marked its occurrence in our patient has only once been commented on in the literature.[12] Van Allen and co-workers noted, in their elegant experimental study of pulmonary venous air embolism in dogs, that brief, extreme hypertension preceded circulatory collapse. It is unlikely that we would have observed the phenomenon had we not

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employed direct intra-arterial pressure monitoring. The signs of air embolism disappear within a few hours of death and are easily missed at postmortem examination.[9,25]

The principal clinical manifestation of systemic air embolism is circulatory collapse followed by pupillary dilatation. Unless the initial hypertension is noticed, or evidence of intra-arterial air is sought (by skin incision to detect air bleeding or ophthalmoscopy to check for retinal intravascular air) or the episode occurs during thoracotomy (when intra-coronary air may be seen), systemic air embolism may remain unrecognised and death will be attributed to other causes, such as hypoxia, haemorrhage or dysrhythmia.

Treatment remains a problem after the diagnosis. Earlier authors recommend that the patient should be allowed to remain 'in the original position quietly and fight his own battle'.[12] However, a more aggressive approach to management, as described by Yee *et al.*[4] has led to a favourable outcome in the surprisingly large number of cases they have encountered. Immediate thoracotomy should be performed if an episode of systemic air embolism is suspected (by the occurrence of acute hypertension and/or haemoptysis followed by circulatory collapse on commencement of intermittent positive pressure ventilation in a patient with chest trauma). Yee *et al.* advise left ventricular aspiration, if air is found in the coronary arteries, and either cross clamping the hilum of the affected lung or its prompt isolation with a double lumen tracheal tube. The patient should be tipped head down (to encourage any intra-arterial air to migrate to the lower half of the body), ventilation should be with 100% oxygen at minimal inspiratory pressures and surgical isolation of the site of air entry should then be attempted. There may be a place for vasopressors (to increase pulmonary venous pressures) and rapid institution of cardiopulmonary bypass.[27,28] Regrettably, we believe that systemic air embolism had occurred on a massive scale in the case we describe, and that definitive treatment would have been hopeless by the time we had realised what had happened.

Acknowledgments

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Microbubbles*

Pathophysiology and Clinical Implications

Michal Barak, MD; and Yeshayahu Katz, MD, DSc

Gas embolism is a known complication of various invasive procedures, and its management is well established. The consequence of gas microemboli, microbubbles, is underrecognized and usually overlooked in daily practice. We present the current data regarding the pathophysiology of microemboli and their clinical consequences. Microbubbles originate mainly in extracorporeal lines and devices, such as cardiopulmonary bypass and dialysis machines, but may be endogenous in cases of decompression sickness or mechanical heart valves. Circulating in the blood stream, microbubbles lodge in the capillary bed of various organs, mainly the lungs. The microbubble obstructs blood flow in the capillary, thus causing tissue ischemia, followed by inflammatory response and complement activation. Aggregation of platelets and clot formation occurs as well, leading to further obstruction of microcirculation and tissue damage. In this review, we present evidence of the biological and clinical detrimental effects of microbubbles as demonstrated by studies in animal models and humans, and discuss management of the microbubble problem with regard to detection, prevention, and treatment. *(CHEST 2005; 128:2918–2932)*

Key words: dialysis; lung; pulmonary hypertension; surgery

Abbreviations: DCS = decompression sickness; HBO = hyperbaric oxygen; PMN = polymorphonuclear leukocyte

The earth has bubbles, as the water has, and, these are of them. Whither are they vanished?

Banquo

Into the air; and what seem'd corporal melted as breath into the wind. . . "

Macbeth, Act I, Scene III William Shakespeare

The rapid advancement of technology in the past few decades has brought new areas to medical practice. One recent development is the detection of microbubbles by ultrasound. Using this updated technique, clinicians and researchers have found that the phenomenon of microbubbles is widespread. Microbubbles originate mainly in extracorporeal lines and devices, such as cardiopulmonary bypass and dialysis machines, but may be endogenous in cases of decompression sickness or mechanical heart valves. Circulating in the blood stream, microbubbles lodge in the capillary bed of various organs, causing local reactions. Our natural tendency is to overlook minute particles, some of which are invisible, believing them to be harmless. However, solid data show that microbubbles are of clinical importance. In this review, we present evidence of the biological and clinical effects of microbubbles, as demonstrated by studies in animal models and humans, and discuss the management of the microbubble problem with regard to detection, prevention, and treatment.

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Definition

Gas embolism is an iatrogenic event in which gas enters the circulation and can result in serious morbidity and death.[1] Animal studies[2,3] have shown that rapid infusion of a large volume of air may be fatal. Our knowledge of the consequences of small-quantity air emboli is lacking. The cutoff point between the occurrence of a major catastrophic episode and subtle but unequivocally important symptoms is yet undefined. An arbitrary definition of microbubble size may be erroneous since only a bubble of a diameter smaller than the capillary can travel through the circulatory system without leaving an imprint and be accepted as safe.[4] Furthermore, in the biological setting, there is a dynamic, constant process of small bubbles fusing to create large bubbles, and large bubbles splitting into many small ones; thus, a few "harmless" microbubbles could coalesce into one injurious large bubble.

The composition of a gas bubble is usually air or

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oxygen, although the medical use of carbon dioxide, nitrous oxide, and nitrogen can also result in gas emboli.[5–7] Gas composition affects bubble elimination time in the body, since each gas has its own solubility coefficient and diffusion coefficient in a given fluid.[8] It is reasonable to believe that gas composition also affects local tissue reaction and systemic response, although research on this subject is limited.[9]

Gas bubbles usually originate in extracorporeal tubing, infusing with the fluids into the blood stream. The bubbles may be present while priming and preparing the lines for use, or newly formed as a result of turbulent flow in the tubing and at the vascular access. Differences in temperature is another possible cause for bubble generation in lines, since warming initiates bubble formation, such as when an active blood warming system is used.[10] The course of the bubble in an extracorporeal infusion set is affected by many factors, principally two opposing forces: firstly, the buoyant force of a bubble, which takes it upward in a standard drip chamber; and, secondly, the driving force of the fluid flow, by which the bubble is carried into the patient's body. For illustration purposes, assuming a flow rate of $8.33 \cdot 10^{-6}$ m^3 s^{-1} (500 mL/min^{-1}) [flow rate of a rapid infusion system], these forces are equal to a $441 \cdot 0^{-6}$ m (441 μm) diameter air bubble in the blood, which means that a smaller bubble will be carried into the patient's blood stream and a larger bubble will remain in the drip chamber.

Microbubbles may be created *de novo* in a patient without connection to the extracorporeal system. One example is the decompression sickness (DCS) of divers, and another is the mechanical prosthetic heart valve, generating microbubbles that are demonstrated *in vivo*.[11–13] Both conditions will be discussed later in this review. There is a spectrum of scenarios in which the extremes are a single exposure to very high volumes in contrast to recurrent chronic exposure to small volumes of microbubbles. The clinical implications of the microbubble phenomenon depends on the extent and cumulative effect of such an event.[14]

Dynamics of Microbubble Elimination

The fundamentals for the dissolvance of a gas bubble in a solution have been formulated by Epstein and Plesset.[15] The formula takes into account several parameters, including the gas-liquid diffusion constant, universal gas constant, saturation concentration of the given gas, temperature, surface tension, ambient pressure, and the radius of the bubble (Appendix). When using the equation for elimination of air microbubbles in the bloodstream, some of these parameters can be regarded as constants since, in most clinical settings, changes in temperature, ambient pressure, and gas composition (almost always air) are negligible.[16] An exception is the cardiopulmonary bypass procedure, in which body temperature is significantly lowered.[17] Alterations in the physiologic steady state can also be detected in DCS, where ambient pressure rapidly decreases on returning to the water surface,[18] and in the hyperbaric chamber, where ambient pressure is high.[19]

Bubble dissolvance occurs when the surface tension sets off diffusion of the gas to the surrounding liquid phase as it generates an overpressure inside the bubble.[20] According to the Epstein-Plesset equation, dissolution times for an air bubble in water are 1 s for a 10^{-6} m^3 (1 μm) radius bubble, 1 to 6 s for 10^{-5} m (10 μm), 100 to 600 s for 10^{-4} m (100 μm), and 1 to 6 million s (11 to 70 days!) for 10^{-3} m (1 mm) bubble. It is important to note that these numbers refer to a spherical bubble in water. In the human body, the shape of the bubble changes during its journey in the circulation, becoming more elongated and slender as it floats further into the periphery. As the bubble is entrapped in the vessel, it is remodeled into a cylinder with hemispherical end cups.[21] In a typical entrapped bubble, the length of the cylindrical bubble is greater than its radius. Therefore, the dissolution time is increased by at least 50% compared to the calculated absorption time for a spherical bubble with the same initial volume.[21] Regarding the liquid composition, a layer of denaturated proteins has been seen at the bubble-blood interface,[21,22] further slowing down the bubble disappearance process *in vivo*. When the gas composition is not air, bubble elimination time may be changed as well.[21,23,24] It could be concluded that the theoretical model derived from the Epstein-Plesset equation underestimates the actual life span of a gas bubble in the body, hence its possible harmful effects.

There have been studies[25,26] that demonstrate the beneficial effect of surfactant on bubble elimination. It seems that by changing the bubble surface tension, a surfactant promotes bubble absorption. It also reduces bubble adhesion forces and, in this way, protects the endothelium from additional injury.[27] The beneficial effect of surfactants has been demonstrated *in vitro*, although it has not been tried in humans for microbubble elimination.

Mechanisms of Microbubble Tissue Damage

The immediate and more rapid event following microbubble injection is the obstruction of blood

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flow in the capillary distal and proximal to the occluding particle. This causes antegrade and retrograde tissue ischemia along with changes of pressures in the circulation and interstitium around the affected blood vessel. Instantaneously, the inflammatory response and complement activation takes place since the body reacts toward the bubble as a foreign substance (Table 1). We discuss each of these processes separately in the following chapters, although these events are inseparable in the biological situation. Nearly all research regarding microbubble-induced tissue damage was done in lung models, since the lung is the main organ exposed to venous emboli.

Mechanical Tissue Damage

The microbubble travels in the blood stream until it is lodged in the microcirculation. During its course, the bubble is compressed against the endothelial capillary wall, causing functional stripping of endothelial cells and an increase of large-pore radii.[28] In addition, gaps between endothelial cells are created both in pulmonary and bronchial microvessels following air embolism.[29] Normally, endothelial cells are tightly joined, preventing intravascular fluids from pouring out into the surrounding tissue. Gap formation allows leakage and resultant interstitial edema. The hydrostatic pressure upstream to the bubble increases, causing further fluid passage into the interstitium. Studies[30,31] using an animal model of air emboli in the sheep lung found sustained elevation in pulmonary artery pressure and pulmonary vascular resistance. Repeated episodes of air embolism have been shown to cause an increase in thickness of the muscular pulmonary arteries and some structural changes of pulmonary hypertension.[32-34] Downstream to the obstructing bubble, tissue ischemia takes place depending on its sensitivity to hypoxic conditions. The endothelium may be protected by surfactant, as was established by Suzuki and colleagues.[27] In their study on microvessel preparation injected with microbubbles, surfactant reduced the bubble adhesion force and preserved basic endothelial structure and vasodilatory function.

Inflammatory Response

Our understanding of microbubble-induced inflammatory response originates from early studies[35,36] of pulmonary edema in animal models. Neutrophils play a central role in mediating air embolism-induced lung injury. They aggregate around the bubble to produce clumps. A local destructive process takes place, probably by superoxide and hydroxyl radical production and proteolytic enzyme release. These molecules increase membrane permeability to fluids and proteins and facilitate interstitial pulmonary edema.[30] A study[37] of leukopenic animals showed that leukocyte depletion attenuated the increased microvascular permeability that follows venous air embolization. The pathophysiologic process is independent of bubble composition and starts as the circulating bubble is trapped in a small arteriole (diameter 10^{-4} to 10^{-3} m) [100 to 1,000 μm] or in a capillary.[38] Although evidence for the inflammatory response to microbubbles is solid, our understanding of the pathophysiologic process is incomplete and awaits further investigation.

The Complement

Activation of complement by circulating microbubbles commences at the air-liquid interface that surrounds gas-filled particle.[39,40] Ward et al[41] demonstrated that prior depletion of complement proteins with a cobra venom factor reduced the occurrence of complement activation and lowered the incidence of decompression sickness in rabbits. In humans, Stevens et al[42] reported that increased levels of activated plasma proteins, C3a and C5a, correlated with the occurrence of DCS after saturation diving. C3a and C5a trigger polymorphonuclear leukocytes (PMNs) and stimulate mast cells to release histamine, which increases vascular permeability. Activated PMNs further augment tissue damage by releasing cytotoxic substances, such as active oxygen metabolites and arachidonic acid products.[43,44] PMN-derived oxygen metabolites cause lipid peroxidation in endothelial cell membranes. The arachidonic acid products such as prostaglandins

Table 1—*Mechanisms of Microbubble Tissue Damage*

Mechanical	Inflammatory Response	Complement	Clotting Activation
Compression against vessel wall	Neutrophils sequestration around bubble	Increased levels of C3a and C5a	Platelet aggregation
Gap formation	Increased permeability	Triggering PMNs	Thrombin production
Fluid leakage	Radical species production	Histamine release	Thrombus generation
Muscular hypertrophy	Clot deposition	Radical species production	
		Prostaglandin, leukotriene synthesis	

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and leukotrienes are vasoactive factors, and all alter microvascular permeability. In order to attenuate the complement-mediated endothelial damage resulting from gaseous microemboli, Nossum et al[45] used anti-C5a monoclonal antibodies preparation. They showed reduced PMN infiltration in pretreated rabbits compared with the control group and concluded that anti-C5a protects the endothelium against injury caused by small amounts of gas bubbles. It is therefore concluded that complement activation is involved in microbubble-induced tissue damage.

The Clotting System

Microbubbles affect clotting through both activating coagulation and inducing platelet aggregation. The result is clot formation at the bubble proximity. Later, fibrinolysis and local reaction to the thrombus occurs. The bubble surface acts as a foreign substance and activates the coagulation cascade.[46] Microbubble gas-blood interface adsorbs macromolecules that are normally present in the blood. The adsorption provokes molecular conformational changes, such as unfolding, and exposes regions of proteins that trigger blood coagulation.[22] Using thrombin production assay, sparging (microbubble embolization) increases thrombin production 2.1- to 3.7-fold compared with bubble-free blood.[47] The addition of surfactants to the coagulation assay attenuated thrombin production in sparged samples by 30 to 70%, probably due to occupancy of the gas-blood interface.

Early studies[48,49] have shown that platelets adhere to the bubble surfaces, where the bubbles act as platelet agonists with respect to aggregation. Additionally, microbubble-induced endothelial damage causes tissue factor expression and subsequent platelet activation and thrombus generation.[49,50] Platelets accumulation around air bubbles in the blood occurs due to cellular reaction, but also as a result of the physicochemical flotation process, as Ritz-Timme et al[51] demonstrated. In their study, attachment of particles (cells) to flowing air bubbles in an aqueous medium (blood) was demonstrated. By plugging blood vessels, the thrombus causes hypoxic local damage.[52] Indeed, prophylactic heparinization had been shown to reduce neurologic impairment after cerebral arterial air embolism in the rabbit,[53] verifying that some of the damage is due to thromboinflammatory responses at sites of air-injured endothelium. Another direction may be preventing platelet accumulation using antiplatelet drugs. Moon et al[54] proposed that antiplatelet drugs, combined with other pharmacologic agents, may be useful adjuncts to recompression therapy in cases of decompression sickness and iatrogenic gas embolism, although this treatment "requires further study."

Clinical Consequences of Circulating Microbubbles

The clinical outcome of air embolism depends on the size of the bubble, location (organ/tissue), general status, and comorbidity of the patient, plus many known and unknown factors.[55] Large air embolism is usually disastrous, both in the venous and arterial circulation.[56–58] The natural course of a large venous embolism is migration into the pulmonary circulation and obstruction of the right ventricular outflow, acute increased resistance to the right ventricle and diminished left ventricular preload, followed by cardiovascular collapse.[1,59] Air emboli in arterial vessels cause symptoms of end-artery obstruction and tissue ischemia and necrosis. Although arterial air emboli could reach any organ, occlusion of cerebral and cardiac circulation is particularly deleterious because these systems are highly vulnerable to hypoxia and go through irreversible cellular damage. The result of such an event may be massive brain ischemia and stroke or myocardial ischemia and infarction. Both could be fatal. The detection of such catastrophic events and resuscitative measurements are well known.[1,60,61] Less is known about the results of small air emboli in the venous or arterial circulation. A small quantity of microbubbles may be clinically silent, while recurrent exposure to microbubbles causes a slow smoldering chronic effect that is difficult to detect but has important consequences.

The patient's comorbidity may also influence the outcome of circulating air emboli. When there is a right-to-left shunt, venous air emboli may traverse to the arterial circulation and cause organ ischemia. Such a course of events is termed *paradoxical air embolism*,[62] and there are a few mechanisms by which it may occur. One is passage of gas through a cardiac right-to-left shunt into the systemic circulation. The prevalence of a cardiac right-to-left shunt ranges between 15 to 40% in various studies,[63,64] usually as a result of patent foramen ovale but may be caused by other cardiac anatomic anomalies. Neonates are vulnerable to developing arterialization of venous air since the foramen ovale may remain patent for some time after birth.[65] A right-to-left shunt might also be extra-cardiac, mostly from dilatation of pulmonary vessels, causing an intrapulmonary shunt in ARDS. In many cases the existence of such a shunt is unknown to the patient or physician, and the risk of paradoxical emboli is not taken into account. The passage of air emboli from the venous to the arterial circulation occurs also when the

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volume of air is vast. The pulmonary circulation filtration capability had been studied by Butler and colleagues[3,66,67] in animal models. They found that when a volume of venous air emboli was $> 3.5 \cdot 10^{-7}$ $m^3 kg^{-1}$ (0.35 mL kg^{-1}) the filtration threshold was exceeded, leading to arterial spillover of bubbles in 50% of the animals, and increased to 71% for an air dose of $4 \cdot 10^{-7}$ $m^3 kg^{-1}$ (0.40 mL kg^{-1}). These studies draw attention to the possibility of each venous air embolism turning into an arterial one, depending on gas volume and injection time. The lung itself is injured by performing the nonrespiratory function of filtering the venous blood, while protecting the arterial system from microemboli. Researchers have simulated microembolic conditions in animal models in order to examine the resultant changes in the lungs. Various models have been used. One model applied starch microemboli (diameter [63 to 74] $\cdot 10^{-6}$ m [63 to 74 μm]) to investigate blood gas alterations following embolism.[68–70] In another animal model, glass beads (diameter [1 to 5]) $\cdot 10^{-4}$ m [100 to 500 μm]) were injected into lambs[37,71,72] or dogs.[28] A model of air emboli was used as well.[30–32] All studies clearly demonstrated that pulmonary edema is the end point of venous embolism and, when repeated, the structural pathologic changes in the lung resemble those seen in pulmonary hypertension.[33,34]

Scientific evidence from humans is limited; nevertheless, it supports most of the laboratory findings. The inflammatory response following pulmonary microemboli has been reported in a few cases.[73,74] CT scan and pulmonary function tests demonstrated the effect of pulmonary emboli on the lung to cause air trapping and mosaic perfusion.[75,76] These publications refer to cases of macroscopic pulmonary emboli and not microbubble events. Investigations on human lungs following microbubble injury are found mainly in the diving medicine literature and are discussed below.

Procedures and Events Generating Microbubbles

Almost every invasive procedure may cause the introduction of microbubbles into the blood stream.[77] Of course, the more invasive and interventional the procedure, the greater is the risk of microbubble generation. There have been an increasing number of reports[78,79] about air microemboli in some procedures, such as cerebral angiography and left-heart catheterization. Admittedly, most microembolic events are silent,[80] but some are symptomatic and the phenomenon cannot be ignored. We concentrated on procedures in which the bubble load is high and affect critical organs, including the brain and the lung (Table 2).

Cardiopulmonary Bypass

Major and minor CNS complications following open-heart surgery are frequent difficult clinical problems.[81–84] The American College of Cardiology/American Heart Association guidelines[85] have classified postoperative neurologic deficits into two types. Type 1 deficits include a major focal neurologic deficit, stupor or coma. Type 2 deficits are deterioration of intellectual function, confusion, memory deficits, agitation, or seizures without evidence of focal injury. The incidence of cerebral complications after cardiac surgery varies widely according to age, sex, type of procedure, atherosclerotic disease of the aorta, and other factors.[86,87] Stroke, for example, ranges from 5% in patients after coronary artery bypass graft surgery to almost 9% in patients > 75 years of age who undergo the same operation, and up to nearly 16% in patients following valve surgery.[82,86] The incidence of apparent cognitive damage, such as deterioration of memory, may reach 60% 1 week after open-heart surgery, falling to 25 to 30% from 2 months to 1 year postoperatively.[88] The incidence of cognitive dysfunction at 1 week following cardiac surgery is approximately twice that of noncardiac surgery.[89] In addition to patient morbidity, adverse cerebral outcome is associated with increased mortality, prolonged hospitalization, and excessive use of intermediate or long-term care facilities.[81,90] Roach and colleagues[81] calculated the additional cost of in-hospital neurologic morbidity after cardiac surgery as approximately $400 million annually. They estimated that true costs, including long-term out-of-hospital medical and rehabilitative services, probably result in additional expenditures ranging from 5 to 10 times narrow in-hospital costs, or $2 to $4 billion annually.[81]

There are several factors that contribute to the adverse neurologic outcome after open-heart surgery, such as reduced cerebral blood flow, local or systemic inflammatory response, cellular edema, and the effect of anesthetic drugs. These factors along

Table 2—*Sources of Microbubbles*

Procedures generating microbubbles
Cardiopulmonary bypass
Hemodialysis
High-flow lines
Others, invasive procedures.
Endogenous sources of microbubbles
Mechanical heart valves
DCS

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with gas and solid emboli from the cardiopulmonary bypass set and from endovascular origin produce cumulative effects on brain function during and after surgery.[83,17] Cardiopulmonary bypass machines are used in most open-heart surgeries to oxygenate and pump the blood while the heart is arrested. Solid or gas emboli from various sources in the extracorporeal set and tubes may drift into the aorta and systemic circulation.[91,92] To minimize embolization, a screen filter is installed on the arterial line that returns blood to the aorta. The filter pores are 28 to $40 \cdot 10^{-6}$ m (28 to 40 μm), allowing smaller emboli to pass through. Nevertheless, larger air and fat emboli also pass through and enter the circulation downstream to the filter whenever their load is high.[89,17] Microbubbles that traverse the filter join and become large bubbles. Air, atherosclerotic debris, and fat microemboli that enter the systemic circulation and arrive at the brain cause neuronal necrosis by blocking small cerebral vessels.[93] It has been established that postoperative adverse neurologic deficit correlates positively with numbers of emboli to which the patient is exposed during surgery.[94–96]

Several methods have been suggested, aimed at reducing the risk of neurologic complications following open-heart surgery. One of the main strategies to avoid brain injury is reducing emboli load during surgery.[97–99] Other means to improve the neurologic outcome include modification of surgical techniques[100,101] and the use of neuroprotective anesthetic techniques and drugs to enhance cerebral oxygenation and decrease cellular metabolism.[102–104] None of the above measures resulted in complete brain protection, but practicing a few together may be beneficial. Further protective means are warranted to improve outcome in the clinical scene.

Hemodialysis

As far back as 1975, there was evidence of pulmonary microembolization during hemodialysis.[105] The subject of dialysis-induced microemboli has been revisited, mainly as a consequence of better detection technology, raising major concerns as to whether their presence can be overlooked or if practical means of emboli elimination must be developed. In 2000, Woltmann et al[106] used B-mode and spectral mode ultrasound to detect microemboli occurring in the hemodialysis access of two patients. The authors postulated that these microemboli developed from turbulent blood flow around the venous access. A prospective study[107] of 25 patients published that year showed microemboli in the subclavian vein (downstream from the arteriovenous fistula); the authors concluded that gas microemboli are formed by the blood pump of the hemodialysis machine. In 2002, Droste and colleagues[108] used pulsed-Doppler ultrasound to demonstrate a continuous shower of microemboli into the pulmonary vasculature during dialysis and hypothesized that this may explain the high pulmonary morbidity in long-term dialysis patients. Those microemboli are most probably gaseous, as suggested by the ultrasound high relative intensity signal. The origin of these microbubbles may be in air bubbles already in the hemodialysis tubes and filter before the procedure, or entering the blood stream during connection and disconnection of the lines, or formation of gas bubbles as the result of pressure gradients and turbulent flow in the tubes and access. In a follow-up study,[109] a significant reduction of microembolization was found when prefilled instead of dry dialyzers were used. The majority of these studies imply that the composition of microemboli detected during dialysis is gas.

Today, hemodialysis devices are equipped with ultrasonic detectors of air larger than $850 \cdot 10^{-6}$ m (850 μm) and alarms that announce the occurrence of an extremely large air bubble event. Smaller emboli, however, even in large numbers, do not activate the alarm. In the past, two cases of dialysis equipment recall were enforced by the US Food and Drug Administration. In the first, in 1992, approximately 4,000 devices were rejected due to failure of the ultrasonic bubble system, which resulted in air observed in the venous line that reached the patients.[110] The second US Food and Drug Administration recall included approximately 3,000 hemodialysis devices in which air bubbles were detected in the extracorporeal system.[111] These cases illustrate the shortcomings of current ultrasonic bubble detectors, which are set to discover relatively large bubbles but allow the entrance of smaller but significant microbubbles.

The patient with end-stage renal failure undergoes approximately three sessions of hemodialysis a week, 150 sessions yearly. Each session takes a few hours, in which the patient is exposed to a microbubble shower. Microbubbles originate from the dialysis tubes or filter flow in the venous vasculature and are trapped in the pulmonary circulation. Thus, the hemodialysis patient may suffer both acute and chronic lung injury due to a microbubble shower. Regarding the acute effect, the main clinical indication for respiratory insult is hypoxemia, which is a well-known symptom during hemodialysis.[112] Several theories have been suggested to explain this event, such as hypoventilation due to changes of pH, direct effect of acetate on the central respiratory center, and increased alveolar-arterial oxygen gradient due to complement activation.[113] Nevertheless,

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the damage caused by exposure to loads of microbubbles should not be overlooked in explaining acute hypoxemia during hemodialysis. Chronically, the recurrent ongoing microbubble lung injury may explain the high pulmonary morbidity, manifested as increased pulmonary artery pressure, of long-term dialysis patients,[114,115] and is "a mimic of pulmonary thromboembolism."[116] It has been established that > 30% of hemodialysis, but not peritoneal dialysis, patients had pulmonary hypertension that normalized when kidney transplantation was performed.[117,118] The occurrence of pulmonary hypertension as a result of recurrent events of air emboli was demonstrated decades ago in animal models.[33,34] Studies in hemodialysis patients focusing on the connection between microbubble load and development of pulmonary hypertension are warranted.

The damage caused by microbubbles may be more detrimental in case of cardiac or extracardiac right-to-left shunt, which may be found in up to 40% of the population.[64] In those cases, air emboli may enter the cerebral circulation and cause varying degrees of neurologic damage.[119] Indeed, the above-noted clinical studies[106–109] that described microemboli during dialysis had either no patient with a shunt[108,109] or did not report that detail in the study.[106,107] Nevertheless, it is reasonable to believe that a patient with a right-to-left shunt is at higher risk for neurologic morbidity as a result of venous air embolism during hemodialysis. Cerebral atrophy and deterioration of neurocognitive functions in chronic hemodialysis patients is a recognized problem that correlates with the duration of dialysis treatment.[120–122] Various factors may promote cerebral atrophy in these patients, such as uremic neuropathy, aluminum intoxication, impaired cerebral circulation, and hypertension. The additional risk of cerebral damage due to microbubbles has not been investigated yet.

High-Flow Lines

The use of high-flow lines is prevalent in almost every operating room where major surgery is performed, in ICUs, emergency shock-trauma departments, and whenever massive blood loss is predicted.[123,124] Most current devices use large-bore, low-resistance fluid sets that enable the administration of a large volume and, at the same time, warming the infused solution or blood. The devices are equipped with an "air eliminator" designed to vent air from the line before entering the patient. Nevertheless, these eliminators are ineffective when large volumes are administered[125,126] and in eliminating microbubbles. The air in the system originates from three sources: it may be in the line before its priming and flushed in with the fluids; it may come from newly formed bubbles caused by turbulent flow (the amount of air detected in high flow lines correlates with flow rates[10]); and, finally, as one of the manufacturers of these devices warns, microbubbles are released from the fluid as it is warmed.[127] These microbubbles are formed continuously within the system and present a constant source of air. It is hard to evaluate the damage caused to the patient from microbubble exposure. In the scenario of massive bleeding and an unstable patient, the physician who resuscitates the patient cannot pay attention to each air bubble. Furthermore, some of these bubbles are small and, in the viscous transfused blood, are practically invisible. Therefore, new and effective air eliminators are needed to improve our detection and prevention of microbubbles in high flow systems.

Mechanical Heart Valves

In the early 1990s, a phenomenon of spontaneous endogenous ultrasound signals was reported in patients with a mechanical mitral valve.[128] The echocardiographic signal was described as bright and of high velocity; it appeared during systole and was regarded at first as an artifact. Later, improvement of ultrasound technology led researchers to recognize that the echocardiographic signal represented microbubbles formed due to local high-pressure gradients at the level of the valve leaflets, a process known as cavitation.[129] Kaps et al[130] succeeded in reducing echocardiographic signals in patients with mechanical heart valves by breathing 100% oxygen under hyperbaric conditions, proving that these microemboli were gaseous and not solid. Deklunder et al[13,131,132] used transcranial Doppler echocardiography in patients with prosthetic mechanical and biological heart valves with neurologic symptoms. They found that high-intensity transient signals were frequently found in the cerebral arteries of patients with mechanical heart valves. They attributed these signals to microbubbles formed by cavitation. Furthermore, they assumed that cognitive impairments may occur in these patients due to persistent microbubble generation by the valve, and confirmed this hypothesis by showing a significant decrease in working memory performance in patients with mechanical heart valves compared with biological valves and control subjects. Girod et al[133] suggested another explanation for microbubble formation by the mechanical valve. In their *in vitro* study,[133] they measured the dimensions of the bubbles and the time of their appearance. They concluded that microbubbles are the result of degassing of CO_2 in blood rather than the cavitation effect, since cavitation is a physical phenomenon of short duration whereas bubble formation by a mechanical heart

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valve is a much longer generation period, matching the degassing hypothesis. The finding of microbubble formation drives intensive engineering efforts to construct the optimal valve design that will be devoid of gas microembolization.[14,134]

Diving and DCS

The four main pathologies in diving medicine are barotraumas (cranial sinuses, otic and pulmonary), DCS, pulmonary edema, and toxic effect of increased partial pressure of gases.[135] The pathophysiology related to diving morbidity and mortality results from gas behavior during altering pressures. Similarly, aviation medicine and some of the extreme-sport types, such as air diving, contend with the same health problems due to intense changes in ambient pressure.

According to Boyle's law, in constant temperature the pressure (P) varies inversely as volume (V): $P_1V_1 = P_2V_2$. Thus, for every 10 m of depth diving, the pressure increases one atmosphere and air volume decreases 50%. The opposite happens on returning to the surface. Acute changes of pressure affect mainly organs and cavities that contain gas. As the pressure decreases, the gas volume expands and may rupture the surrounding membranes, causing barotrauma.

Another physical gas law is the Henry law, which states that the amount of a given gas dissolved in a liquid at a constant temperature is directly proportional to the partial pressure of that gas. Accordingly, when a diver breathes air in high pressure, air from the lungs is dissolved in body fluids and blood and is transported to peripheral organs. Oxygen is used for tissue metabolism, while nitrogen, which is physiologically inert, is not.[136] As the diver returns to surface level, the gas saturation in the fluid decreases and nitrogen bubbles are formed in all tissues causing DCS. This process depends on the rate of change in pressures and is termed DCS. The US Navy and the Royal Navy have decompression tables, instructing the use of stops in returning to the surface and enabling body adjustment to changes in pressure, thus reducing the risk of DCS. Nevertheless, severe DCS has been described within safe table limits.[137] Early studies[138,139] detected bubbles in the circulation of asymptomatic divers during decompression. These findings indicate that bubble formation may be clinically silent to some degree or amount of bubbles. DCS is an accurate example of humans exposed to microbubbles in the circulation, and thus can demonstrate the clinical presentation of that event. It is customary to classify DCS into two types based on the severity of symptoms.[136] Type 1 DCS is milder, expressed by joint pain, pruritus, and skin rash. More severe symptoms are seen in type 2 DCS. These are neurologic symptoms such as headache, blurred vision, parenthesis, paraparesis and, in serious cases, convulsions and death. The neurologic manifestations are attributed to bubble embolization in the CNS. Again, clinical studies[140,141] suggest that subclinical cerebral damage occurs in divers, raising the possibility that microbubble damage is underdiagnosed due to difficulties in detection and not because they are not present. The effect of recurrent diving was described by Skogstad et al,[142] who conducted a study of lung function in professional divers and found that exposure to diving contributed to changes in pulmonary function, mostly affecting small airway conductance. The authors interpreted these changes as thickening of bronchiole walls and loss of lung elasticity.

The effect of recurrent diving on brain function has been studied over the years, using various tests. EEG, CT, and MRI were used, as well as neuropsychologic tests. Although most researchers[143–146] found pathologic alterations comparing professional and recreational divers to control subjects, contradictory results have been published as well.[147] Most authors,[143,145,146] however, agree that the prevalence of changes in divers is inversely related to diving depth, cumulative diving time, participation in "unsafe diving," and DCS. The pathophysiology of the cumulative effect of recurrent diving is not yet fully understood and may be the basis for comprehension microbubble injury.

Detection and Prevention of Microbubble Exposure

Detection

Attempting to prevent the threat of air embolism during a cardiopulmonary bypass machine event, numerous devices were designed. In 1980, an air embolism detection device (Air-Bubble Detector System; Sarns; Ann Arbor, MI) was presented as a tool capable of detecting the presence of macroscopic air emboli (10^{-6} m^3 [1 mL] or larger) using an infrared light source and a photocell receptor.[148] When the detector was turned on, a control unit caused the cardiopulmonary bypass pump to shut off. A few false alarms triggered the pump shutoff, such as electrocauterization, defibrillation of the patient, high-pitched sounds, and low hematocrit, which made the detector difficult to operate.[148] The use of ultrasound technology for detecting air bubbles was studied first on an animal model.[149] Pulsed-Doppler ultrasound detected microbubbles within a fluid line[150] and *in vivo*.[151] The continuous progress of technology improved equipment and

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facilitated better detection capabilities.[152,153] Transcranial Doppler ultrasound made it possible to detect microbubbles in the cerebral circulation of patients during surgery, enabling the study of the effect of various types of oxygenators or atrial fibrillation on microbubble showering in real time.[154–157] The main disadvantage of transcranial Doppler ultrasound is the fact that bubbles are seen in the circulation postfactum, without the capability of preventing the event. Another recently presented technique to detect bubbles uses a tetrapolar electrical impedance measurement.[158] Tested *in vitro*, this noninvasive device detected 10^{-3} m (0.5 mm) diameter bubbles at a depth of $5.3 \cdot 10^{-3}$ m (5.3 mm). However, this device is not sensitive enough to deal with microbubbles. Therefore, in medical procedures prone to microbubble generation, the only current aid is still Doppler ultrasound.

Filters

Knowing the possible clinical consequences of microbubble exposure, it is agreed that prevention is the best policy, which means eliminating air from fluids before they enter the body. There are several filters used for microbubble elimination. The most common is a filter that is installed on the line and functions as a dense net for bubbles, as in cardiopulmonary bypass machines (see above). The filter traps bubbles that are larger than its pores. There are a few disadvantages to the use of these filters. The add-on to the tubing increases resistance to flow, as indicated by a pressure drop through the filter.[159,160] Moreover, when filtering blood, after a short time of function, it is filled with debris and fibrin and the resistance increases even further. In severe cases, the used filter may completely block the flow within the line. In addition, chemicals within the filter activate coagulation cascade, the complement, the immune response, and other biological reactions to foreign materials. A third disadvantage is the hazard of the chemical composing the filter, which may be toxic, as happened in 2001 in Europe.[161] In that case, the deaths of more than 50 hemodialysis patients have been linked to the dialysis membrane. Investigators found the deaths were connected to a solvent chemical used in the manufacturing process not completely removed from the filters. The last disadvantage of filters in use today is their inability to eliminate all microbubbles from the system, as demonstrated in open-heart surgery.[17,89] The conclusion of these disadvantages is that the future optimal device for microbubble elimination should use technologies other than mechanical obstructing filtering devices. For example, a multipurpose ultrasonic bubble detector and neutralizer capable of filtering small microbubbles from the blood, was recently developed (Thera-Sonics Ultrasound Technologies; Jordan Valley, Israel). It uses an ultrasound field to push microbubbles through an acoustic transparent module where they can be collected and removed. The possibility of affecting microbubbles in the blood by ultrasound was already shown by Schwarz et al.[162] Another type of filter was evaluated by Schonburg et al,[163] who tested a dynamic bubble trap in which the bubbles are directed to the center of the blood flow and collected in its distal end, where they are returned to the reservoir. Schonburg et al[163] found a significant reduction of microbubbles in the arterial line while using the DBT.

Management

The treatment of large air emboli is well established.[1,60,61] Little is written about the management of microbubble injury. Some of the known therapeutic modalities employed for massive air embolism may be applied in the case of microbubbles. In both scenarios, prevention is the best approach as "an ounce of prevention is worth a pound of cure." When the event of air embolism, macro as well as micro, has occurred, early detection is required to facilitate immediate action to interrupt the cause. While the detection of large air emboli is easy, usually manifested by acute cardiovascular collapse or sudden overt deterioration of the neurocognitive or motor functions, catastrophic in nature, the presentation of a microbubble event is more subtle and difficult to detect. We chose not to specify the treatment of large air emboli, which require cardiopulmonary resuscitation (Muth and Shank[1] and Petts and Presson[61]) and focused on small air emboli (Table 3).

Hyperbaric oxygen (HBO) is a treatment modality that is applied in DCS of divers[54,164] and in cases of large air emboli occurring during various medical procedures. Several clinical studies[165–167] have been published, demonstrating improvement in neurologic outcome following HBO therapy, although no

Table 3—*Management of Microbubble Event*

Prevention
Drip chambers; filters
HBO
Drugs
Heparin
Barbiturates
Corticosteroids
Lidocaine
Perfluorocarbons (?)
Surfactants (?)

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prospective randomized trials have been conducted. HBO should be employed as soon as possible after the insult, although delayed treatment is also helpful.[168] A few physiologic modes of action can explain the beneficial outcome of HBO therapy. HBO reduces the volume of intravascular bubbles by enhancing the ambient pressure (see Appendix: Epstein-Plesset equation); the increase in oxygen partial pressure favors denitrogenation. Furthermore, HBO increases the partial pressure of dissolved oxygen in the blood, allowing better oxygenation of ischemic tissues.[59,169] The physical properties of HBO therapy are applicable in a microbubble event and, although no study has been published to confirm this hypothesis, it is reasonable to believe that such therapy could be helpful in symptomatic microbubble cases as well.

The use of drugs in air embolism is empirical and controversial.[54,59] Most studies examined cases of cerebral air emboli and followed the neurologic outcome. Several drugs were tested in patients with air emboli, especially for managing complications and reducing their rate. Heparin inhibits thromboinflammatory processes, thus could decrease neurologic impairment after cerebral air embolism. It was tested in an animal model and found to be effective only when given prophylactically in massive air emboli.[53] Barbiturates reduce cerebral oxygen consumption, lower intracranial pressure, and inhibit release of endogenous catecholamines. Due to these beneficial effects, barbiturates are sometimes used for brain protection and may be helpful in cases of cerebral air emboli.[59] Two decades ago, steroids were used to reduce cerebral edema following air emboli,[170,171] but later studies showed that corticosteroids increase ischemic injury[172] and their use is no longer recommended. Experiments using animal models showed that lidocaine improves recovery following cerebral air emboli.[173,174] Lidocaine was found to be neuroprotective also in patients undergoing cardiac surgery;[175] nevertheless, it is not part of standard care in air emboli. While the abovementioned drugs failed to improve outcome following massive air emboli, they could have a potential place in microbubble injury.

There is encouraging experimental data on fluorocarbon compounds, which have high gas-dissolving capacity, may increase oxygen delivery and help shrink gas bubbles because of their high diffusion gradient.[176,177] Other studies[27,178] have presented surfactants as a possible compound that may change bubble adhesion by altering interfacial forces and reducing bubble absorption time. These future solutions deserve testing in humans after proved efficacy and safety in animal models.

Summary

We have presented published data concerning the microbubble phenomenon and its detrimental consequences. Indeed, the microbubble event and its significance have been proved in open-heart surgery and DCS. However, it awaits clinical confirmation in other conditions such as hemodialysis and rapid fluid infusion. To date, there is a limited knowledge about the management of the microbubble events. Nevertheless, acknowledgment of the problem is the first step in the path toward finding a solution. Contemporary technology offers us tools to cope with various difficulties. The best way to utilize highly developed technology is in cooperation between scientists and engineers in search of a resolution for a recognized problem. The problem of microbubbles awaits a breakthrough technological solution that will provide their detection and elimination, facilitating better care for the patient.

Appendix

The Epstein-Plesset equation

$$\frac{dr}{dt} = -DL\frac{\bar{p}^* + 2\sigma/r}{patm + 4\sigma/3r}\left\{\frac{1}{r} + \frac{1}{\sqrt{\pi Dt}}\right\}$$

where D is the diffusivity of gas in fluid; L is the partition coefficient of gas, Patm is the atmospheric pressure, P^* is the excess pressure, σ is the surface tension, r is the radius of the bubble, and t is time.

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Review Articles

Primary Care

GAS EMBOLISM

CLAUS M. MUTH, M.D., AND ERIK S. SHANK, M.D.

GAS embolism, the entry of gas into vascular structures, is a largely iatrogenic clinical problem that can result in serious morbidity and even death.[1] Since gas embolism can result from procedures performed in almost all clinical specialties (Table 1), it is important for all clinicians to be aware of this problem. In most cases, gas embolism is air embolism, although the medical use of other gases, such as carbon dioxide, nitrous oxide, and nitrogen, can also result in the condition. There are two broad categories of gas embolism, venous and arterial, which are distinguished by the mechanism of gas entry and the site where the emboli ultimately lodge.

VENOUS GAS EMBOLISM

Venous gas embolism occurs when gas enters the systemic venous system.[2] The gas is transported to the lungs through the pulmonary arteries, causing interference with gas exchange, cardiac arrhythmias, pulmonary hypertension, right ventricular strain, and eventually cardiac failure. Physical preconditions for the entry of gas into the venous system are the incising of noncollapsed veins and the presence of subatmospheric pressure in these vessels. Noncollapsing veins include the epiploic veins, the emissary veins, and the dural venous sinuses. Air may enter these veins during neurosurgical operations, especially those performed with the patient in the sitting position.[3] The veins of the throat, and in some cases the veins in the coagulated operative field,[4] may also be entryways for air. Air may also enter veins through central venous and hemodialysis catheters[5,6] and may enter the veins of the myometrium during pregnancy and after delivery.[7,8]

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Pathophysiology

The most frequent form of venous gas embolism is the insidious venous aeroembolism, in which a series of gas bubbles resembling a string of pearls enters the venous system. Rapid entry or large volumes of gas put a strain on the right ventricle because of the migration of the emboli to the pulmonary circulation. The pulmonary arterial pressure increases, and the increased resistance to right ventricular outflow causes diminished pulmonary venous return. Because of the diminished pulmonary venous return, there is decreased left ventricular preload, resulting in diminished cardiac output and, ultimately, systemic cardiovascular collapse.[9] Tachyarrhythmias often develop, but bradycardias are possible as well. When large quantities of gas (over 50 ml) are injected abruptly, acute cor pulmonale, asystole, or both are likely to occur.[2] The alteration in the resistance of the lung vessels and the mismatch between ventilation and perfusion cause intrapulmonary right-to-left shunting and increased alveolar dead space, leading to arterial hypoxia and hypercapnia.

Diagnosis

To diagnose venous gas embolism, the physician should assess the clinical findings. The so-called millwheel murmur, a splashing auscultatory sound due to the presence of gas in the cardiac chambers and great vessels, is often present and can be auscultated by a precordial or esophageal stethoscope. A decrease in the end-tidal carbon dioxide levels, as determined by capnometry, suggests a change in the relation between ventilation and perfusion due to the obstruction of the pulmonary arteries.[10] Doppler ultrasonography is a sensitive and practical means of detecting intracardiac air, and it is often used during neurosurgical procedures,[8,11] procedures with the patient in the sitting position, and other procedures that entail a high risk of gas embolism. An even more sensitive and definitive method for detecting intracardiac gas is transesophageal echocardiography, although it requires training in performance and interpretation (Fig. 1).[2,3,12]

Treatment

When venous gas embolism is suspected, further entry of gas must be prevented. In certain cases, therapy with catecholamines is required, and, if necessary, aggressive cardiopulmonary resuscitation is performed. Adequate oxygenation is often possible only with an increase in the oxygen concentration of the inspired gas (up to 100 percent oxygen). Supplemental oxygen also reduces the size of the gas embolus

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TABLE 1. MEDICAL SPECIALTIES WITH DOCUMENTED CASES OF GAS EMBOLISM.

SPECIALTY	MECHANISM OF GAS EMBOLISM
All medical specialties	Inadvertent entry of air through peripheral intravenous circuit
All surgical specialties	Intraoperative use of hydrogen peroxide, causing formation of arterial and venous oxygen emboli
Anesthesiology	Entry of air through disconnected intravascular catheter, inadvertent infusion of air through intravascular catheter
Cardiac surgery	Entry of air into extracorporeal-bypass pump circuit, incomplete removal of air from heart after cardioplegic arrest, carbon dioxide–assisted harvesting of peripheral veins
Cardiology	Entry of air through intravascular catheter during angiographic study or procedure
Critical care and pulmonology	Entry of air through disconnected intravascular catheter, pulmonary barotrauma, rupture of intraaortic balloon, entry of air into extracorporeal-membrane-oxygenator circuit
Diving and hyperbaric medicine	Pulmonary barotrauma, paradoxical embolism after decompression injury, entry of gas through disconnected intravascular catheter
Endoscopic and laparoscopic surgery	Entry of gas into veins or arteries during insufflation of body cavities
Gastroenterology	Entry of gas into veins during upper or lower endoscopy or endoscopic retrograde pancreatography
Neonatology and pediatrics	Pulmonary barotrauma in treatment of premature infants
Nephrology	Inadvertent entry of air through hemodialysis catheter and circuit on hemodialysis machine
Neurosurgery	Entry of air through incised veins and calvarial bone, especially during craniotomy with the patient in a sitting position
Obstetrics and gynecology	Cesarean section, gas insufflation into veins during endoscopic surgery, intravaginal and intrauterine gas insufflation during pregnancy
Otolaryngology	Nd:YAG laser surgery on the larynx, trachea, or bronchi*
Orthopedics	Gas insufflation into veins during arthroscopy, total hip arthroplasty, or spine surgery with the patient in a prone position
Radiology	Injection of air or gas as a contrast agent, inadvertent injection of air during angiography
Thoracic surgery	Entry of air into pulmonary vasculature during lung biopsy or video-assisted thoracoscopy, chest trauma (penetrating or blunt), lung transplantation
Urology	Entry of air during transurethral prostatectomy or radical prostatectomy
Vascular surgery	Entry of air during carotid endarterectomy

*Nd:YAG denotes neodymium:yttrium–aluminum–garnet.

by increasing the gradient for the egress of nitrogen from the bubble.[13] Rapid resuscitation with volume expansion is recommended to elevate venous pressure, thus preventing the continued entry of gas into the venous circulation.

Some authors recommend attempting to evacuate air from the right ventricle with the use of a central venous catheter (a multiorifice catheter may be more effective than one with a single lumen) or a pulmonary arterial catheter.[2,14,15] It may be possible to aspirate about 50 percent of the entrained air from an appropriately placed right atrial catheter,[2,14] but depending on the placement of the catheter and the position of the patient, a smaller effect is more likely.[2,15] Hyperbaric oxygen therapy is not a first-line treatment but may be a useful adjunct in severe cases. It should certainly be considered if there is evidence of neurologic changes. In this case, it should be assumed that a paradoxical embolism is present.

Paradoxical Embolism

A paradoxical embolism occurs when air or gas that has entered the venous circulation manages to enter the systemic arterial circulation and causes symptoms of end-artery obstruction. There are a number of mechanisms by which this can occur. One is the passage of gas across a patent foramen ovale into the systemic circulation. A patent foramen ovale, which is detectable in about 30 percent of the general population, makes possible right-to-left shunting of gas bubbles.[16] If there is a patent foramen ovale and if the pressure in the right atrium exceeds the pressure in the left atrium, right-to-left flow through the foramen ovale may occur.[17] Elevated pulmonary arterial pressure due to venous gas embolism may result in elevated right atrial pressure, making it possible for a bubble to be transported through a patent foramen. Furthermore, the decrease in left atrial pressure caused by controlled ventilation and the use of positive end-expiratory pressure may create a pressure gradient across the patent foramen ovale, favoring the passage of gas into the systemic circulation.[2,3]

In other situations, venous gas may enter the arterial circulation by overwhelming the mechanisms that normally prevent arterial gas embolism. Studies in animals suggest that either a large bolus of gas (20 ml or more) or small continuous amounts (11 ml per minute) introduced into the venous system may

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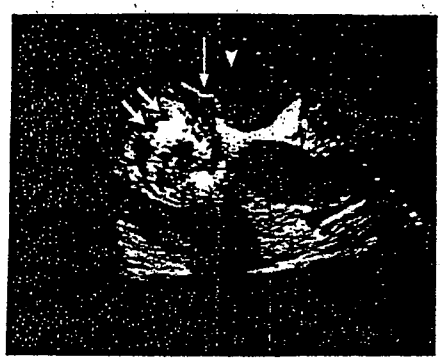

Figure 1. Transesophageal Echocardiogram from a Patient Evaluated for the Presence of a Patent Foramen Ovale.

Saline was agitated and injected rapidly into a central venous catheter. The bubbles appear as echodense areas in the right atrium (double arrows). If this patient had a patent foramen ovale, bubbles would be seen crossing the interatrial septum (thin arrow) and entering the left atrium (arrowhead). (Echocardiogram provided courtesy of S. Streckenbach.)

generate intraarterial bubbles.[18-20] There have been reports of fatal cerebral arterial gas embolism caused by a large venous gas embolus, although no intracardiac defects or shunt mechanisms could be demonstrated.[21] Various anesthetic agents diminish the ability of the pulmonary circulation to filter out gas emboli.[22] Studies in animals have shown that volatile anesthetics, specifically, may raise the threshold for a spillover of venous bubbles into systemic arteries. This finding may have relevance to surgical procedures that carry a substantial risk of venous gas embolism.

The treatment of paradoxical embolism is identical to that of primary arterial gas embolism (discussed below). Every venous gas embolism has the potential to evolve into an arterial gas embolism.

ARTERIAL GAS EMBOLISM

Arterial gas embolism is caused by the entry of gas into the pulmonary veins or directly into the arteries of the systemic circulation. Gas may enter the arteries as a result of overexpansion of the lung by decompression barotrauma or as a result of paradoxical embolism. Any cardiac surgical operation that uses extracorporeal bypass may also cause arterial gas embolism.[23] Even if only small amounts of gas enter the arterial system, the flow of gas bubbles into functional end arteries occludes these vessels. Although obstruction is possible in any artery, obstruction of either the coronary arteries or the nutritive arteries of the brain (cerebral arterial gas embolism) is especially serious and may be fatal because of the vulnerability of the heart and brain to short periods of hypoxia.[24]

Pathophysiology

The entry of gas into the aorta causes the distribution of gas bubbles into nearly all organs. Small emboli in the vessels of the skeletal muscles or viscera are well tolerated, but embolization to the cerebral or coronary circulation may result in severe morbidity or death.

Embolization into the coronary arteries induces electrocardiographic changes typical of ischemia and infarction; dysrhythmias, myocardial suppression, cardiac failure, and cardiac arrest are all possible, depending on the amount of gas embolized.[25] Circulatory responses may also be seen with embolization to the cerebral vessels.[26]

Cerebral arterial gas embolization typically involves the migration of gas to small arteries (average diameter, 30 to 60 μm).[25] The emboli cause pathologic changes by two mechanisms: a reduction in perfusion distal to the obstruction and an inflammatory response to the bubble (Fig. 2).[24]

Symptoms

The symptoms of cerebral arterial gas embolism develop suddenly. The clinical presentation, however, is determined by the absolute quantity of gas and the areas of the brain that are affected. Thus, there may be minor motor weakness and headache or moderate confusion; conversely, complete disorientation, hemiparesis, convulsions, loss of consciousness, and coma may occur.[27] Asymmetry of the pupils, hemianopia, and impairment of the respiratory and circulatory centers (manifested as bradypnea, Cheyne–Stokes breathing, cardiac arrhythmias, and circulatory failure)[25,26] are other well-known complications. In patients who have undergone surgical procedures that carry a risk of gas embolism, a delayed recovery from general anesthesia or a transitional stage of impaired consciousness may be a clue to the occurrence of cerebral arterial gas embolism. The diagnosis is not easy to establish in such patients, because complications of anesthesia, such as the central anticholinergic syndrome or the presence of residual anesthetic or muscle relaxant, can mimic mild cerebral arterial gas embolism.

Diagnosis

The most important diagnostic criterion is the patient's history, because the clinical suspicion of embolism is based on the initial neurologic symptoms and the direct temporal relation between these symptoms and the performance of an invasive procedure. The procedures that carry the greatest risk of venous or arterial gas embolism are craniotomy performed with the patient in the sitting position, cesarean section, hip replacement, and cardiac surgery with cardiopulmonary bypass. All these procedures have in common an incised vascular bed and a hydrostatic gradient favoring the intravascular entry of gas.

Cerebral arterial gas embolism can sometimes be

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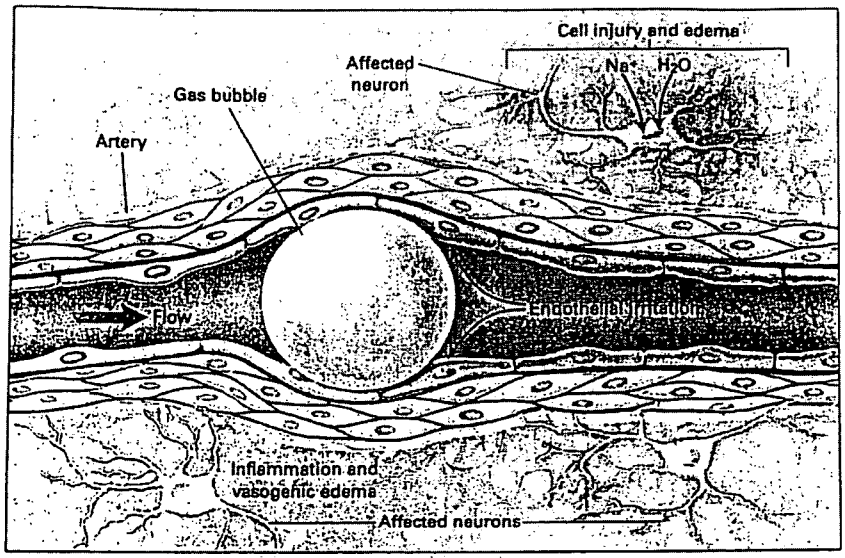

Figure 2. Bubble Obstructing End-Arterial Flow in a Cerebral Vessel with a Diameter of 30 to 60 μm, Causing Distal Ischemia.
The obstruction causes the metabolic processes of neurons to fail. Sodium and water enter the vessel, and cytotoxic edema develops. The surface of the bubble generates a foreign-body response through cellular and humoral immune mechanisms. The bubble also mechanically irritates the arterial endothelium. Both processes result in vasogenic edema and greater impairment of perfusion. The neuronal injury extends beyond the area of obstruction.

distinguished from a cerebral infarct or intracerebral bleeding on a computed tomographic (CT) scan.[28] However, pathologic changes are sometimes very subtle and not well visualized on CT, and the diagnosis of cerebral arterial gas embolism must be considered early. Magnetic resonance imaging of the cerebrum can sometimes show an increased volume of water concentrated in the injured tissue. But this method is also not reliable and may fail to detect an embolism if the symptoms are mild.[24]

Gas bubbles in the vessels of the retina can occasionally be identified, but their absence does not rule out gas embolism.[24] Another finding that is nonspecific but that has been described in a number of cases is hemoconcentration with an increase in the hematocrit, possibly as a direct consequence of the extravascular shift of fluid into the injured tissues.[29]

Treatment

The primary goal of treatment is the protection and maintenance of vital functions. If necessary, cardiopulmonary resuscitation should be performed, since not only venous but also primary arterial gas embolism may lead to serious impairment of the cardiovascular system. Endotracheal intubation should be performed in a somnolent or comatose patient in order to maintain adequate oxygenation and ventilation. Oxygen should also be administered, at as high a concentration as possible.[30] Administration of oxygen is important not only to treat hypoxia and hypoxemia but also to eliminate the gas in the bubbles by establishing a diffusion gradient that favors the egress of gas from the bubbles.[13,24]

It is currently recommended that patients with arterial gas embolism be placed in the flat supine position.[31] The buoyancy of gas bubbles is not sufficient to counteract blood flow propelling such bubbles toward the head, even when the patient is placed in a head-down position. In addition, the head-down position may aggravate the cerebral edema that develops in these patients.[32]

Treatment of Generalized Seizures

Cerebral gas embolism often causes generalized seizures,[27] which may not respond to benzodiazepines. In these cases, it is recommended that the seizures be suppressed with barbiturates.[27,33] Although there is no proof that barbiturates provide cerebral

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protection after cerebral ischemia, the use of barbiturates for ischemic brain lesions has certain advantages. They reduce cerebral oxygen consumption, intracranial pressure, the production of free radicals, and the release of endogenous catecholamines.[34,35] High doses of barbiturates depress respiration; ventilatory support must therefore be available when a patient is given barbiturates.

Hyperbaric-Oxygen Therapy

With hyperbaric-oxygen therapy, the patient breathes 100 percent oxygen at a pressure above that of the atmosphere at sea level. This therapy decreases the size of the gas bubble both by raising the ambient pressure (Fig. 3) and by causing systemic hyperoxia. An arterial partial pressure of oxygen greater than 2000 mm Hg is frequently achieved. The hyperoxia produces enormous diffusion gradients for oxygen into the bubble and for nitrogen out of the bubble.[31,32] The hyperoxia also allows much larger quantities of oxygen to be dissolved in the plasma and increases the extent of oxygen diffusion in tissues.[27] The improvements in the oxygen-carrying capacity of plasma and in the delivery of oxygen to tissues offset the embolic insult to the microvasculature.

Other benefits of hyperbaric oxygen have been proposed. It may help prevent cerebral edema by reducing the permeability of blood vessels while supporting the integrity of the blood–brain barrier.[36,37] Furthermore, experiments have suggested that hyperbaric oxygen diminishes the adherence of leukocytes to damaged endothelium.[38]

These benefits suggest that all patients with clinical symptoms of arterial gas embolism should receive recompression treatment with hyperbaric oxygen. Although immediate recompression produces the best response,[23] delayed treatment in a hyperbaric chamber may still be indicated to ameliorate the patient's condition.[39] Hyperbaric oxygen is the first-line treatment of choice for arterial gas embolism.[22,25,31,40] Thus, as soon as cardiopulmonary stabilization has been achieved, the patient should be transferred to a hyperbaric chamber.

Infusion Therapy

There is some evidence that gas embolism may cause hemoconcentration, which increases blood viscosity and impairs the already compromised microcirculation.[29] Therefore, normovolemia should be achieved to optimize the microcirculation. Hypovolemia is always tolerated less well than relative anemia. It is therefore acceptable to decrease the hematocrit, within certain limits. In animals, moderate hemodilution to a hematocrit of 30 percent reduces neurologic damage.[41] Colloid solutions are preferable to crystalloid solutions for hemodilution, because the latter may promote cerebral edema. Hypertonic solutions (e.g., 7.5 percent sodium chloride solution) may become the first choice for volume replacement, but their use is still controversial and therefore cannot yet be recommended.

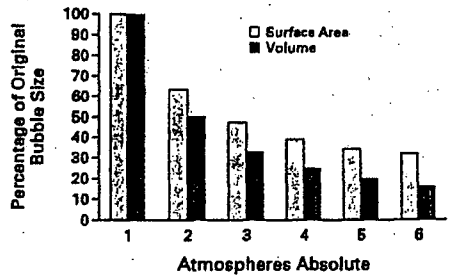

Figure 3. Relation between the Size of the Bubble and Pressure.
The surface area and volume of the gas bubble are inversely proportional to pressure at a constant temperature (Boyle's law). Thus, as the patient is exposed to increasing ambient pressure, the gas bubbles shrink.

The goal of infusion therapy is normovolemia. Placement of a central venous catheter is strongly recommended to assess central venous pressure, which should be maintained at approximately 12 mm Hg. As a further method of ensuring adequate volume status, the urinary output should be monitored with a Foley catheter and maintained above 1 to 2 ml per kilogram of body weight per hour.

Anticoagulant Therapy

There is evidence that heparin may be beneficial in the treatment of gas embolism.[42] Studies have shown that the clinical course of arterial gas embolism is less severe if the patient has been treated with heparin before the embolic event occurs. An argument against heparin therapy is the risk it entails of hemorrhage into the infarcted tissue. At present, the use of heparin for the short-term treatment of cerebral arterial gas embolism is not generally recommended.

Corticosteroid Therapy

The use of corticosteroids in patients with arterial gas embolism remains controversial. Some authors recommend treatment with corticosteroids to combat the brain edema[43] that results from gas embolization in the cerebral arteries. Cerebral gas embolism initially induces the rapid development of cytotoxic brain edema, with diminished extracellular space and enlarged intracellular areas. This form of edema does not usually respond to corticosteroids.[44] Some authors report that corticosteroids aggravate ischemic injury after occlusion of the vessels.[45,46] Thus, since corticosteroids appear to offer no benefit in patients with cytotoxic edema and since these drugs may aggravate neuronal ischemic injury, we do not recommend them.

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TABLE 2. TREATMENT OF GAS EMBOLISM.

TYPE OF TREATMENT	VENOUS GAS EMBOLISM	ARTERIAL GAS EMBOLISM
Prevention of further entry of gas	Measures to increase venous pressure (e.g., Valsalva maneuver or intravenous administration of fluids) Identification and shutting down of entryway for gas	Identification and shutting down of entryway for gas
Primary therapy	Supportive	Hyperbaric oxygen therapy as soon as patient's condition is stable enough for transfer to hyperbaric chamber
Supportive therapy	Oxygen, intravascular volume expansion, catecholamines	Oxygen, intravascular volume expansion, catecholamines
Positioning of patient	Supine, flat	Supine, flat
Evacuation of embolized gas	Aspiration with multiluminal central venous catheter (with patient in left lateral decubitus position)	Hyperbaric oxygen
Adjunctive therapy	Hyperbaric oxygen	Lidocaine, antiepileptic agents, physical therapy

Lidocaine Therapy

Although the results of clinical studies of lidocaine for the treatment of arterial gas embolism are not yet available, studies in animals suggest that lidocaine may be beneficial.[47-51] In animals given prophylactic doses of lidocaine, the depressant effects of gas embolism on somatosensory evoked potentials and the elevations in intracranial pressure caused by gas embolism were both reduced. In a clinical trial, lidocaine provided cerebral protection during cardiac surgery.[51] Therefore, a strong argument can be made for administering lidocaine in a bolus dose of 1.5 mg per kilogram and maintaining a therapeutic concentration, with continuous intravenous administration in patients with severe arterial gas embolism. However, an overdose of lidocaine may cause central nervous system depression, cerebral convulsions, and bradyarrhythmias.

CONCLUSIONS

The entry of gas into the venous or arterial system is a risk in virtually all areas of clinical care. Venous emboli may lead to cardiovascular collapse or to paradoxical arterial emboli. Arterial emboli may occlude end arteries throughout the body and may cause serious morbidity or death if they occlude cardiac or cerebral vessels.

Regardless of the mechanism responsible for the embolism, rapid and aggressive treatment is essential to preserve life and function (Table 2). For venous gas embolism, the mainstays of treatment are the prevention of further entry of gas, volume expansion, the administration of 100 percent oxygen, often with ventilatory support; positive inotropic support; and cardiopulmonary resuscitation, if necessary. For arterial gas embolism, hyperbaric oxygen is the treatment of choice, as soon as cardiopulmonary stabilization has been achieved.

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Venous Air Embolism

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Author and Editor Disclosure

Synonyms and related keywords: VAE, right ventricular dysfunction, pulmonary endothelial injury, pulmonary vascular injury, venous air embolism, AGE, arterial gas embolism

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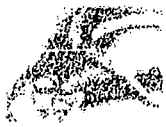

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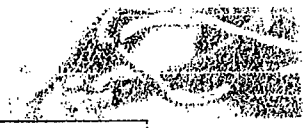

Background

Venous air embolism (VAE), the entry of gas into the peripheral or central vasculature, can occur secondary to iatrogenic complications, trauma, and even certain recreational activities. Although many occurrences of VAE are believed to go unreported because they are asymptomatic, entrapment of large quantities of intravascular gas can lead to severe neurologic injury, cardiovascular collapse, and even death. The factors that determine the subsequent morbidity and mortality in VAE include the rate of air entrainment, the volume of air introduced, and the position of the patient at the time of the embolism.

Gas emboli are usually composed of air, but they can also occur with medically used gases such as carbon dioxide, nitrous oxide, and nitrogen. Although very small volumes of air can lead to severe sequelae, it is generally accepted that more than 50 mL of air can cause hypotension and dysrhythmias and more than 300 mL of air can be lethal.

Arterial gas embolism (AGE) is a separate but related entity that is not discussed in any detail in this article. AGE can occur through a patent foramen ovale (present in approximately 27% of the general population) or can form by gas movement across the alveolar-capillary membranes into the pulmonary venous circulation.

Pathophysiology

VAE results when a pressure gradient develops that favors the ingress of air into the venous system. Upon entry into the venous system, air is transported to the right atrium and ventricle. From there, it has the potential to continue on to the pulmonary arteries where it may cause interference with gas exchange, cardiac arrhythmias, pulmonary hypertension, and even cardiac failure and arrest. A large bolus of air entering the venous system can cause an air lock in the right atrium and ventricle, leading to outflow obstruction, decreased pulmonary venous return, and subsequent decreased left ventricular preload and cardiac output.

Intermediate amounts of air collect in the pulmonary circulation and produce a pulmonary vascular injury manifested by precapillary and postcapillary pulmonary vasoconstriction, pulmonary hypertension, endothelial injury, and permeability pulmonary edema. Subsequent ventilation-perfusion mismatch can cause right to left shunting and increased arterial hypoxia and hypercapnia.

Small amounts of air do not produce symptoms because the air is broken up and absorbed from the circulation. Although classical teaching states that more than 5 mL/kg of air (IV) is required for significant injury (including shock and cardiac arrest), patient complications secondary to as little as 20 mL of air (the length of an unprimed IV infusion set) have been reported. Further, as little as 0.5 mL of air in the left anterior descending coronary artery has been shown to lead to ventricular fibrillation.

The pathogenesis of pulmonary endothelial injury may have components of platelet-fibrin thrombi from the right ventricle, cytokine release, neutrophil, platelet, and complement activation at the microvascular air-blood interface, and injury mediated by lipid peroxidation and oxygen radicals.

Frequency

United States

The true incidence of VAE is unknown. Subclinical air embolism in hospitalized patients may be quite common. Frequency of clinically recognized VAE following central venous (CV) cannulation is less than 2%. Case report series (as mentioned above) have estimated VAE from central venous catheterization at 1 in 47 to 1 in 3000, and neurosurgical complications of VAE range from 10-80%.

Mortality/Morbidity

VAE is associated with significant morbidity and mortality. Morbidity can include lung injury, neurologic injury, cardiovascular ischemic injury, and ultimately cardiopulmonary collapse and arrest. Symptomatic VAE following CV catheterization has a mortality rate as high as 30%.

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History

Signs and symptoms of VAE usually develop immediately following embolization. Severity of signs and symptoms are related to the degree of air entry into the body. The diagnosis can be a difficult one to make because of its similarity in presentation to pulmonary embolism (thromboembolic) and/or hypovolemic shock. Subsequently, physicians must maintain a high index of suspicion for this disease given the appropriate clinical scenario. The following historical events should be considered in taking a patient's history for suspected VAE:

- Recent surgery, especially neurosurgical, cardiovascular, or orthopedic procedures
- Blunt and penetrating trauma to the face, neck, chest, and/or abdomen
- Recent invasive procedures such as central venous catheterization or pressurized infusion of fluids, blood, or contrast
- Patients with indwelling central venous catheters
- Decompression injuries/sickness
- Orogenital sex during pregnancy or hydrogen peroxide ingestion (rare)
- Symptoms may include the following:
  - Dyspnea
  - Chest pain
  - Agitation or disorientation

Physical

Physical examination may reveal the following signs:

- Tachycardia
- Tachypnea
- Cyanosis
- Altered level of consciousness
- Hypotension
- Cardiac "mill wheel" murmur - A loud, churning, machinerylike murmur heard over the precordium (a late sign)
- Sudden loss of consciousness followed by convulsion in an intubated patient on positive-pressure ventilation
- Circulatory shock or sudden death (patients with severe VAE)

Causes

The primary cause of VAE is surgical procedures, especially neurosurgical procedures performed in the upright, sitting position. Anytime the operative site is more than 5 cm above the right atrium, VAE is a risk. Other surgical procedures that can lead to the infusion of air include obstetric/gynecologic procedures (cesarean section), craniofacial surgery, dental implant surgery, vascular procedures, liver transplantation, and orthopedic procedures (eg, hip replacement, arthroscopy). The frequency of reported VAE in surgical procedures ranges from 10% in cervical laminectomy up to 80% in posterior fossa surgery.

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A second cause of VAE is iatrogenic creation of a pressure gradient for air entry. Examples include spinal needles in lumbar punctures (case report), peripheral intravenous lines, central venous catheters, pulmonary artery catheters, hemodialysis catheters, and long-term (Hickman) catheters. Most cases occur during catheter manipulation, disconnection, or removal. A pressure difference of 5 cm of H_2O across a 14-gauge needle allows 100 mL of air per second to enter the venous system. The frequency of reported VAE with central catheter use ranges from 1 in 47 to 1 in 3000.

A third cause of VAE is mechanical insufflation or infusion. Insufflation has been documented to occur during arthroscopic procedures, CO_2 hysteroscopy, laparoscopy, urethral insufflation, and orogenital sexual activity during pregnancy. Infusion air entry can occur during the injection of contrast agents for CT scans, angiography, and cardiac catheterization, and during cardiac ablation procedures.

A fourth cause of VAE is positive-pressure ventilation, which can occur during mechanical ventilation and SCUBA diving.

Finally, blunt and penetrating trauma to the chest, abdomen, neck, and face can lead to the entry of air and ultimately to VAE.

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Acute Coronary Syndrome
Anemia, Acute
Anemia, Chronic
Angina Pectoris
Aortic Stenosis
Atrial Fibrillation
Atrial Flutter
Chronic Obstructive Pulmonary Disease and Emphysema
Decompression Sickness
Dissection, Aortic
Dysbarism
Pneumonia, Bacterial
Pneumothorax, Iatrogenic, Spontaneous and Pneumomediastinum
Pneumothorax, Tension and Traumatic
Pulmonary Embolism
Shock, Cardiogenic

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Lab Studies

- Arterial blood gases are indicated and usually demonstrate hypoxemia, hypercapnia, and metabolic acidosis. Mild cases may demonstrate mild hypoxemia and hypocapnia.
- Other laboratory studies are nonspecific and are obtained as indicated by associated conditions.

Imaging Studies

- Transesophageal echocardiography is the most sensitive monitoring modality for VAE and can detect as little as 0.02 mL/kg of air. Precordial Doppler ultrasonography is also an effective monitoring technique and can detect as little as 0.25 mL of air. Transcranial Doppler is commonly used to help identify cerebral microemboli during neurosurgical and endovascular procedures.
- Chest radiography may be normal or may show one of the following signs:
  - Air in the pulmonary arterial system
  - Pulmonary arterial dilatation

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- Focal oligemia (Westermark sign)
- Pulmonary edema

Other Tests

- Electrocardiographic (ECG) findings, if present, are the same as those found in venous thromboembolism.
  - Tachycardia
  - Right ventricular strain pattern
  - ST depression
- Increased dead space may be present and can be identified as an increased end-tidal to arterial blood carbon dioxide gradient (normal value is <5).
- If a central venous (CV) catheter is in place, aspiration of air may help establish the diagnosis. CV catheters can also be used to measure central venous pressure, which may be elevated in the case of VAE.
- Pulmonary artery (PA) catheters can detect increased PA pressure that may be caused by mechanical obstruction/vasoconstriction from the hypoxemia induced by VAE. However, this modality is not specific for VAE.
- Mass spectrometry for end-tidal nitrogen is also highly specific for air but is very limited in availability and practical use.

Procedures

- Once VAE is suspected, any central line procedure in progress should be terminated immediately, and the line should be clamped (or removed if it cannot be clamped). One attempt at aspirating air back from the line may be useful.
- If aspiration from a central catheter is going to be attempted, optimal placement of the tip is 2 cm below the junction of the superior vena cava and the right atrium. Catheters may have to be advanced for this to be successful. Some authors recommend placing a central venous catheter or PA catheter to attempt evacuation of air if one is not already in place.
- In circulatory collapse, CPR should be started to maintain cardiac output as well as to potentially break large air bubbles into smaller ones and force air out of the right ventricle into the pulmonary vessels. In arrest that is refractory to CPR, emergency thoracotomy may be indicated. Hilar injury and bronchovenous fistulae should be ruled out by the absence of bloody froth during positive-pressure ventilation, and then needle aspiration of intracardiac air from the ventricles should be performed. Consider cross-clamping the aorta in hypotensive patients.

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Emergency Department Care

Once VAE is suspected, any central line procedure in progress should be terminated immediately.

- Administer 100% oxygen and intubate for significant respiratory distress or refractory hypoxemia. Oxygen may reduce bubble size by increasing the gradient for nitrogen to move out.
- Promptly place patient in Trendelenburg (head down) position and rotate toward the left lateral decubitus position. This maneuver helps trap air in the apex of the ventricle, prevents its ejection into the pulmonary arterial system, and maintains right ventricular output.
- Maintain systemic arterial pressure with fluid resuscitation and vasopressors/beta-adrenergic agents if necessary.

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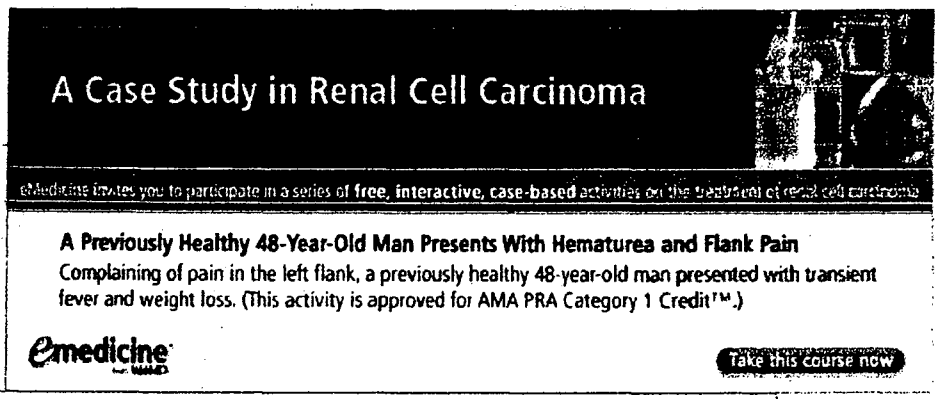
- Consider transfer to a hyperbaric chamber. Potential benefits of this therapy include (1) compression of existing air bubbles, (2) establishment of a high diffusion gradient to speed dissolution of existing bubbles, and (3) improved oxygenation of ischemic tissues and lowered intracranial pressure.
- Circulatory collapse should be addressed with CPR and consideration of more invasive procedures as described above.

Consultations

Hyperbaric medicine for symptomatic venous air embolism syndrome.



Further Inpatient Care

- Admit patients to the intensive care unit (ICU); pulmonary insufficiency may develop following VAE

Deterrence/Prevention

- In general, prevention of VAE stems from decreasing the pressure gradient between the site of potential entry and the right atrium.
- With regard to central venous catheterization and manipulation of catheters, several general principles apply to preventing VAE:
  - Whenever possible, place patients in Trendelenburg position.
  - Keep patient agitation to a minimum.
  - Use closed catheterization systems when possible.
  - Constantly maintain vigilance to avoid opening the catheters during subsequent manipulation.
  - VAE also can occur following catheter removal and may be delayed for 30 minutes or more; initial dressing after removal should be occlusive.
  - Take particular care in patients with known right-to-left shunts, since paradoxical embolism to the arterial system can occur.

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Medical/Legal Pitfalls

- Failure to take precautions to prevent VAE during CV catheterization
- Failure to recognize early signs of VAE following CV procedures.
- Failure to consider paradoxical embolism, which can lead to arterial gas embolism. Presentation may differ from the signs and symptoms of VAE and may present more similarly to cerebrovascular accident or acute coronary syndrome.

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Venous Air Embolism excerpt

Article Last Updated: May 2, 2006

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CARDIOPULMONARY SUPPORT AND PHYSIOLOGY

NEUROPSYCHOLOGIC IMPAIRMENT AFTER CORONARY BYPASS SURGERY: EFFECT OF GASEOUS MICROEMBOLI DURING PERFUSIONIST INTERVENTIONS

Michael A. Borger, MD
Charles M. Peniston, MD
Richard D. Weisel, MD
Marie Vasiliou, MSc
Robin E. A. Green, PhD
Christopher M. Feindel, MD

Objective: Neuropsychologic impairment is a common complication of coronary bypass surgery. Cerebral microemboli during cardiopulmonary bypass are the principal cause of cognitive deficits after coronary bypass grafting. We have previously demonstrated that the majority of cerebral emboli occur during perfusionist interventions (ie, during the injection of air into the venous side of the cardiopulmonary bypass circuit). The purpose of this study was to determine whether an increase in perfusionist interventions is associated with an increased risk of postoperative cognitive impairment.

Methods: Patients undergoing elective coronary artery bypass grafting (n = 83) underwent a battery of neuropsychologic tests preoperatively and 3 months postoperatively. Patients were divided into 2 groups according to the median value of perfusionist interventions during cardiopulmonary bypass. Group 1 patients (n = 42) had fewer than 10 perfusionist interventions, and group 2 patients (n = 41) had 10 or more interventions.

Results: The 2 groups of patients were similar for all preoperative, intraoperative, and postoperative variables, with the exception of longer cardiopulmonary bypass times in group 2 patients ($P < .001$). Group 2 patients had lower mean scores on 9 of 10 neuropsychologic tests, with 3 (Rey Auditory Verbal Learning, Digit Span, and Visual Span) being statistically significant. Group 2 patients had worse cognitive test scores, even when controlling for increased bypass times. Group 2 patients had a nonsignificant trend toward an increased prevalence of neuropsychologic impairment 3 months postoperatively.

Conclusions: Introduction of air into the cardiopulmonary bypass circuit by perfusionists, resulting in cerebral microembolization, may contribute to postoperative cognitive impairment. (J Thorac Cardiovasc Surg 2001; 121:743-9)

Neurologic complications are an important cause of morbidity and mortality during cardiac operations.[1,2] Neuropsychologic impairment is a well-documented and very common complication, occurring in the majority of patients in the early postoperative period and in approximately one third of patients several months after the operation.[3-6] The principal cause of cognitive impairment is cerebral microemboli during cardiopulmonary bypass (CPB).[7-10]

We have previously demonstrated that the majority of cerebral microemboli during coronary artery bypass grafting (CABG) are caused by the injection of air into the venous side of the CPB circuit, events we have termed *perfusionist interventions*.[11,12] The purpose of this study was to determine whether an increase in perfusionist interventions is associated with an increased risk of postoperative cognitive impairment.

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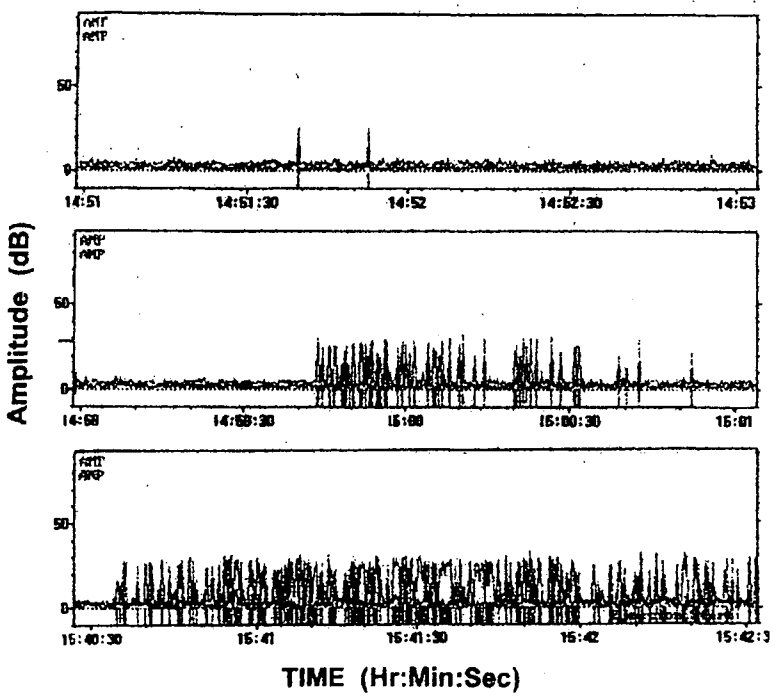

Fig 1. Representative transcranial Doppler tracings of a single patient undergoing CPB during baseline *(top panel)*, during a perfusionist intervention *(middle panel)*, and during venous air entrapment by the atrial cannula *(bottom panel)*. High-amplitude deflections represent cerebral emboli.

Methods

Patients were part of an ongoing, prospective, clinical trial assessing cognitive outcomes after CABG. Patients undergoing elective CABG were divided into 2 groups according to the median number of perfusionist interventions during CPB. Group 1 patients (n = 42) had fewer than 10 perfusionist interventions, and group 2 patients (n = 41) had 10 or more interventions. Perfusionist interventions were defined as the administration of drugs or the injection of blood into the venous reservoir during CPB, events we have previously demonstrated to be associated with cerebral microembolization.[11,12]

Patients were excluded if they had a history of carotid disease, stroke, or other neurologic disease; if they were undergoing reoperative or concomitant surgical procedures; or if they had a poor understanding of English. The study protocol was approved by our institutional ethics review board, and participating patients gave signed informed consent.

Anesthesia and surgical management. Our standardized anesthetic and surgical protocols for CABG operations have been previously described.[13,14] In brief, patients received an anesthetic consisting of induction with midazolam hydrochloride, fentanyl, and sodium thiopental, followed by maintenance with isoflurane and propofol. A pulmonary artery catheter was inserted through the right internal jugular vein. Antegrade cold blood cardioplegia was used in the majority of patients, with some patients receiving retrograde cardioplegia. The left internal thoracic artery was anastomosed to the left anterior descending coronary artery in all patients, and supplemental saphenous vein grafts were added as necessary. All proximal anastomoses were performed under a single aortic crossclamp application.

CPB. CPB was established with arterial inflow through the ascending aorta and venous drainage through a single, 2-stage, right atrial cannula. The hematocrit level was main-

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Table I. *Preoperative characteristics for patients with fewer than 10 perfusionist interventions (group I) and for patients with 10 or more perfusionist interventions (group II)*

Variable	Group I (n = 42)	Group 2 (n = 41)	P value
Male sex	35 (83)	32 (78)	.5
Age (y)	58.8 ± 9.8	61.8 ± 8.9	.15
CCS class 3 or 4	8 (19)	8 (20)	.9
LVEF <40%	8 (19)	6 (15)	.6
Left main disease	8 (19)	6 (15)	.6
Triple-vessel disease	23 (55)	29 (71)	.2
Hypertension	15 (36)	22 (54)	.10
Hypercholesterolemia	29 (69)	34 (83)	.14
Peripheral vascular disease	3 (7)	5 (12)	.4
Congestive heart failure	3 (7)	5 (12)	.4
COPD	3 (7)	0 (0)	.12
Renal failure	0 (0)	0 (0)	1.0

Values are given as numbers of patients (percentages) or mean ± SD as shown. *CCS*, Canadian Cardiovascular Society angina classification; *LVEF*, left ventricular ejection fraction; *COPD*, chronic obstructive pulmonary disease.

tained between 20% and 25% during CPB, pump flow rates between 2.0 and 2.5 $L \cdot min^{-1} \cdot m^{-2}$, and mean arterial pressure between 60 and 80 mm Hg by use of phenylephrine or nitroprusside as required. Systemic body temperature was allowed to drift to a minimum of 34°C, with active rewarming to 37.5°C at the end of CPB.

Our CPB circuit consisted of a collapsible soft-shell venous reservoir (Baxter BMR 1900, Uden, Holland), a hollow-fiber membrane oxygenator (Medtronic Maxima Plus, Mississauga, Canada), and nonpulsatile roller pumps (Cobe, Arvada, Colo). A 32-μm filter (Avecor Affinity, Minneapolis, Minn) was used in the arterial perfusion line. Perfusionists administered drugs into the bypass circuit by using a manifold directly connected to the bottom of the venous reservoir.

Neuropsychologic testing. Patients underwent a battery of neuropsychologic tests preoperatively and 3 months postoperatively. All tests were administered by a trained psychometrist in a quiet, isolated room. The test battery included those tests suggested by an international consensus conference[15] and was designed to assess the following cognitive domains (with corresponding tests in parentheses): (1) learning and memory (Rey Auditory Verbal Learning Test and Rey Visual Design Learning Test); (2) psychomotor skills (Halstead-Reitan Trail Making Tests Parts A and B and Grooved Pegboard Test); (3) attention and concentration (Wechsler Memory Scale [WMS] Mental Control, WMS-R Digit Span, and WMS-R Visual Span); and (4) language and higher intellectual functioning (Verbal Fluency Test and American National Adult Reading Test).

Neuropsychologic impairment was analyzed by severity, defined as group mean scores on individual tests, and by prevalence, defined as a 20% decrease from preoperative scores on 20% or more of the tests.[16]

Statistical analysis. All statistical analyses were performed with the SAS system (SAS Institute, Cary, NC). Categoric data were evaluated with the χ^2 square or Fisher exact tests. Continuous variables were evaluated by using the Student t test. Associations between neuropsychologic test scores and number of perfusionist interventions were examined with the Spearman rank correlation coefficient. Increased CPB time was tested as a possible confounding variable by using analysis of covariance. All categoric variables are expressed as percentages, and continuous variables are expressed as means ± SD. So that neuropsychologic test scores could be compared easily, all test data were transformed such that higher scores indicated better neuropsychologic test performance.

Results

Perfusionist interventions. Group 1 patients had 6.0 ± 3.2 perfusionist interventions during CPB compared with 13.4 ± 3.3 in group 2 patients ($P < .001$). Fig 1 displays transcranial Doppler tracings of the middle cerebral artery in a single patient undergoing CPB. The high-amplitude deflections represent cerebral emboli. These representative tracings illustrate the increased number of cerebral emboli during perfusionist interventions compared with those at baseline, as well as the tremendous amount of embolization that occurs during air entrapment by the atrial cannula.

Group characteristics. Table I displays the preoperative characteristics for the 2 groups of patients. The 2 groups had similar preoperative profiles. Intraoperative variables are displayed in Table II. Group 2 patients had significantly longer CPB and aortic crossclamp times (both $P < .001$). Postoperative characteristics for the 2 groups of patients are revealed in Table III. There were no significant differences between the 2 groups for any postoperative variable.

Neuropsychologic test results. Fig 2 reveals the change in neuropsychologic test scores for the 2 groups of patients. The percentage change in test score was calculated as the 3-month postoperative test score

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Table II. *Intraoperative characteristics for the 2 groups of patients*

Variable	*Group 1 (n = 42)*	*Group 2 (n = 41)*	*P value*
Atherosclerotic ascending aorta	5 (12)	4 (9)	.7
Retrograde cardioplegia	3 (7)	2 (5)	.8
Right internal thoracic artery	1 (2)	1 (2)	.9
No. of bypasses	3.6 ± 0.9	4.0 ± 0.8	.08
Crossclamp time (min)	57 ± 17	73 ± 20	<.001
CPB time (min)	75 ± 21	101 ± 34	<.001
Time to rewarm (min)	23 ± 11	23 ± 10	.8

Values are given as numbers of patients (percentages) or mean ± SD as shown.

Table III. *Postoperative characteristics for the 2 groups of patients*

Variable	*Group 1 (n = 42)*	*Group 2 (n = 41)*	*P value*
Use of inotropic agents	8 (19)	4 (10)	.2
Low-output syndrome	0 (0)	1 (2)	.5
Intra-aortic balloon pump	0 (0)	1 (2)	.5
Myocardial infarction	0 (0)	1 (2)	.5
Renal failure	0 (0)	0 (0)	1.0
Stroke/TIA	0 (0)	0 (0)	1.0
Ventilation time (h)	6.3 ± 3.0	6.8 ± 3.8	.2
ICU time (h)	23 ± 9	25 ± 12	.14
Hospital length of stay (d)	5.8 ± 2.3	6.4 ± 2.3	.18

Values are given as numbers of patients (percentages) or mean ± SD as shown. *TIA*, Transient ischemic attack; *ICU*, intensive care unit.

minus the preoperative (baseline) score divided by the preoperative score. Patients with increased perfusionist interventions (group 2) had lower mean scores 3 months postoperatively on 9 of the 10 neuropsychologic tests. In 3 tests, Rey Auditory Verbal Learning, Digit Span, and Visual Span, these differences were statistically significant ($P < .05$).

We also examined the association between the number of perfusionist interventions, expressed as a continuous variable, and neuropsychologic test percentage change in scores. There was a significant negative correlation between perfusionist interventions and Digit Span ($r = -0.34$, $P = .004$) and Visual Span ($r = -0.31$, $P = .009$) test scores. There was a moderate negative correlation between perfusionist interventions and Rey Auditory Verbal Learning test scores ($r = -0.24$, $P = .10$).

Although group 2 patients had longer CPB times than group 1 patients, analysis of covariance did not reveal CPB time as a confounding variable for the Rey Auditory Verbal Learning Test, Digit Span, or Visual Span scores. That is, an increased number of perfusionist interventions was associated with worse neuropsychologic test scores, even when controlling for increased CPB times.

Prevalence of neuropsychologic impairment, as defined by a 20% decline on 20% or more of the neuropsychologic test scores, was also compared between groups. Group 2 patients had a nonsignificant trend toward a higher prevalence of neuropsychologic impairment 3 months after CABG (50% vs 34%, $P = .18$).

Discussion

Neuropsychologic impairment is a very common complication of coronary bypass operations.[3-6] Cerebral microemboli during CPB, events that occur in virtually all patients undergoing CPB, are thought to be the principal cause of postoperative cognitive deficits.[10] Several investigators have demonstrated that patients who have less cerebral microemboli during CPB have a lower incidence of postoperative neuropsychologic impairment.[8,9,17,18]

The precise composition of cerebral microemboli during CPB is not known. However, we have previously reported evidence that the majority of emboli probably consist of air.[11,12] We used transcranial Doppler scanning to continuously monitor patients undergoing isolated CABG, carefully noting the timing of cerebral embolism occurrence. We defined perfusionist interventions as those time periods immediately after the injection of drugs, along with small amounts of air, into the venous side of the CPB circuit. Perfusionist interventions resulted in a 7-fold increase in cerebral

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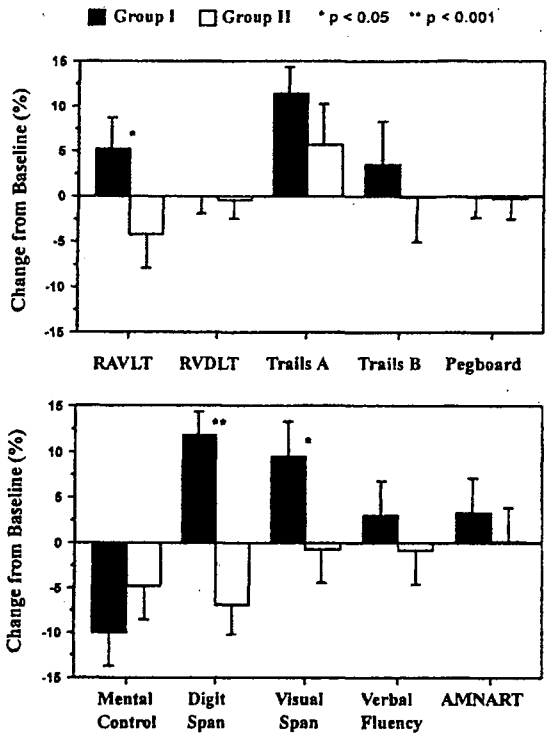

Fig 2. Change in neuropsychologic test scores for patients with fewer than 10 perfusionist interventions (group 1) and for patients with 10 or more perfusionist interventions (group 2). Values shown are mean ± SD percentage change in scores (see text for definition), with more positive values representing better cognitive performance. *RAVLT,* Rey Auditory Verbal Learning Test; *RVDLT,* Rey Visual Design Learning Test; *AMNART,* American National Adult Reading Test.

embolic rate when compared with any other time period (Fig 1).[11] We also noted that if perfusionists carefully removed air from the syringe before injecting drugs into the CPB circuit, much fewer cerebral emboli occurred. Administration of drugs by a continuous infusion, rather than by syringe injection, did not result in any emboli production. In addition, we noted that a tremendous number of cerebral emboli occurred during accidental venous air entrapment (Fig 1). We concluded from our studies that the majority of emboli during CPB consist of gaseous microbubbles and that simple techniques can be used to minimize embolization.

It should be emphasized that all drugs were administered into the venous side of the CPB circuit during the aforementioned studies, with resultant microbubbles traversing the membrane oxygenator and arterial line filter before being detected in the middle cerebral arteries of the patients. The ability of venous air to result in arterial line emboli has been noted by other investigators.[19,20] It should also be noted that different CPB circuits may have varying capabilities to remove gaseous emboli.[20,21] Therefore, the association between perfusionist interventions and cerebral emboli may not be as strong in CPB circuits, which differ from ours, particularly in those with hard-shell venous reservoirs.

The current study was intended to determine whether perfusionist interventions, and therefore gaseous microemboli, are associated with post-CABG cognitive

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impairment. We focused on 83 patients undergoing CABG who also underwent detailed neuropsychologic testing as part of an ongoing trial of neurologic outcomes. (The patients in the current study did not receive intraoperative transcranial Doppler monitoring.) Patients were divided into 2 groups according to the median number of perfusionist interventions. We found that patients with increased perfusionist interventions had worse mean scores on the majority of tests 3 months postoperatively (Fig 2). In particular, patients with more gaseous microemboli had significantly worse scores on the Rey Auditory Verbal Learning Test, the Digit Span test, and the Visual Span test. We also found negative correlations between the number of perfusionist interventions and postoperative test scores. Although the group with increased perfusionist interventions had longer CPB times, our results remained unchanged when we controlled for CPB times. We failed to demonstrate a significant difference in the prevalence of neuropsychologic impairment (as defined by a 20% decrease on 20% or more of test scores),[16] probably because of our small sample size.

Patients with increased perfusionist interventions had significantly worse cognitive performance on tests of learning and memory (Rey Auditory Verbal Learning Test) and attention and concentration (Digit Span and Visual Span). The cognitive domains of learning, memory, and attention and concentration are particularly sensitive to the deleterious effects of CPB.[3,22] It should be noted that improvement occurred on several of the neuropsychologic tests 3 months postoperatively (Fig 2). Improved performance is expected on repeated administrations of neuropsychologic tests because of their intrinsic practice effects.[23]

The deleterious neurologic effects of massive arterial air embolism (>20 mL) have long been recognized.[24] Massive air embolism is an infrequent but well-documented risk of CPB.[25,26] To the best of our knowledge, this is the first report of an association between air microemboli and cerebral dysfunction. There are 2 methods by which air microemboli can cause cerebral injury. First, microbubbles may occlude small arterioles and cause distal ischemia. Bubbles with a diameter of 200 μm that are composed of 100% oxygen will take approximately 16 minutes to absorb.[27] Second, bubbles can activate platelets, leukocytes, and complement.[28-30] Activation of the inflammatory cascade can in turn lead to local injury and exacerbation of the ischemic insult.[24]

Conclusions

We found that patients with increased perfusionist interventions, and therefore increased gaseous microemboli, had significantly worse performances on tests of learning, memory, and attention and concentration. We therefore conclude that introduction of air into the venous aspect of the CPB circuit should be minimized to decrease the risk of postoperative cognitive impairment.

We thank our study coordinators, Barb Weller and Pat Peterson, for their important contributions, as well as our psychometrist, Ellen Harrington. We also thank the cardiovascular surgeons, cardiac anesthetists, and perfusionists at our institution for their continued support.

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Assessment of neurocognitive impairment after off-pump and on-pump techniques for coronary artery bypass graft surgery: prospective randomised controlled trial

Vipin Zamvar, David Williams, Judith Hall, Nicola Payne, Clare Cann, Karen Young, S Karthikeyan, John Dunne

Abstract

Objective To assess neurocognitive impairment after the off-pump and on-pump techniques for coronary artery bypass graft surgery in patients with triple vessel disease.

Design Randomised controlled trial.

Setting University Hospital of Wales, Cardiff.

Participants 60 patients undergoing coronary artery bypass graft surgery for triple vessel disease prospectively randomised to the off-pump or on-pump technique.

Main outcome measures Change in scores in nine standard neuropsychometric tests administered preoperatively and at 1 and 10 weeks postoperatively.

Results The on-pump group showed a significantly greater deterioration in scores for two and three tests at 1 week and 10 weeks postoperatively, respectively, than the off-pump group. The on-pump group also showed a significantly higher incidence of major deterioration in one of the tests both 1 week and 10 weeks postoperatively. The incidence of neurocognitive impairment at 1 week postoperatively was 27% (8 out of 30) in the off-pump group and 63% (19 out of 30) in the on-pump group (P=0.004); and at 10 weeks postoperatively was 10% (3 out of 30) in the off-pump group and 40% (12 out of 30) in the on-pump group (P=0.017).

Conclusion Off-pump coronary artery bypass graft surgery results in less neurocognitive impairment than the on-pump technique.

Introduction

Coronary artery bypass graft surgery is one of the most commonly performed procedures. Advances in surgical techniques, anaesthetic management, and postoperative care resulted in a steady decline in mortality from the procedure during the 1980s and '90s, despite a gradual increase in the risk profile of patients.[1] Neurological injury is an important complication after coronary artery bypass graft surgery. It comprises two types.[2] Type 1 injury includes stroke, transient ischaemic attack, and coma (incidence 3 to 6%). Type 2 injury is more subtle and includes impairment of cognitive function. These are defects associated with attention, concentration, short term memory, fine motor function, and speed of mental and motor responses. The incidence of neurocognitive impairment after cardiac surgery varies from 20% to 80%.[3-6] These defects are not always transient, and longitudinal assessment studies have shown a major impairment at 5 years[7 8]; impairment immediately after surgery has been shown to correlate with long term impairment.[9] Recent work has focused on the role of cardiopulmonary bypass in neurocognitive impairment, but the literature is inconclusive.[8 9-11] In recent years coronary artery bypass graft surgery without using cardiopulmonary bypass (off-pump technique) has been shown to be a reliable and reproducible technique, and both short and medium term results have been favourable.[12 13]

Patients with single and double vessel disease are increasingly being managed by percutaneous coronary interventions. Most patients undergoing coronary artery bypass graft surgery have triple vessel disease. We aimed to assess the impact of the on-pump and off-pump techniques on neurocognitive impairment in patients undergoing coronary artery bypass graft surgery for triple vessel disease.

Methods

Patient selection

We enrolled 60 patients undergoing urgent or elective coronary artery bypass graft surgery for triple vessel disease between May and October 2001. All patients gave written informed consent. We excluded patients with a greater than 50% carotid artery stenosis, recent myocardial infarction (within one month), previous transient ischaemic attack or cerebrovascular attack, previous psychiatric illness, renal failure, or those who needed emergency operation, reoperation, or combined valvular surgery. We screened 76 patients; 10 had one or more of the exclusion criteria leaving 66 eligible for randomisation (figure). Two patients refused to take part and four were not invited because they were last minute additions to the operating list and therefore precluded performance of the neuropsychometric tests. We randomised the patients into two groups using sequentially numbered, sealed, opaque envelopes containing computer generated random allocations. We randomised 30 patients to receive conven-

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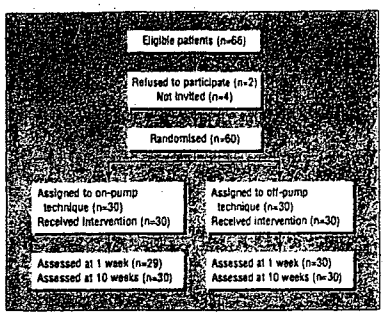
Table 1 Preoperative clinical data. Values are numbers of patients unless stated otherwise

Variable	On-pump (n=30)	Off-pump (n=30)
Mean (SD) age (years)	61.6 (10)	63.5 (9.1)
Male	27	25
Angina class:		
Grade 1	0	0
Grade 2	8	5
Grade 3	19	22
Grade 4	3	3
Three vessel disease	30	30
Left main stem lesion (>50%)	2	4
Left ventricular function (ejection fraction):		
Good (>50%)	23	23
Fair (30-50%)	5	6
Poor (<30%)	2	1



Flow of participants through trial

tional on-pump coronary artery bypass graft surgery (group A) and 30 to receive the off-pump technique (group B). The operations were performed by one surgeon (VZ) at the University Hospital of Wales, Cardiff. We obtained ethical approval for our study from the Bro Taf local research ethics committee.

The anaesthetic technique was standardised and all patients received the same medication. The surgical technique was standardised, the left internal mammary artery being attached to the left anterior descending artery, and vein grafts to the other coronary arteries as appropriate in all patients. In both groups the top end anastomoses were constructed with the help of a side biting clamp. The only difference between the two groups was the use of cardiopulmonary bypass. Cardiotomy suction was not used in the on-pump group. In both groups the cell saver was used.

Neuropsychometric assessment

We carried out nine neuropsychometric tests to assess the patients both preoperatively and at 1 week and 10 weeks postoperatively. A qualified examiner (CC), blinded to treatment allocation, carried out the tests in a standardised fashion, in the same order. The battery of tests included the core tests according to the recommendations of the statement of consensus on assessment of neurobehavioural outcomes after cardiac surgery.[14] The tests comprised the Rey auditory verbal learning test, part A and part B of the trail making test, the digit symbol substitution test, the digit span forward and the digit span backward test, the grooved pegboard test using the dominant hand and the non-dominant hand, and the controlled oral word association test. We estimated the premorbid full scale IQ by using the national adult reading test.[15]

Table 2 Operative details and postoperative details. Values are numbers of patients unless stated otherwise

Variable	On-pump (n=30)	Off-pump (n=30)	P value
Mean (SD) No of grafts; range	2.93 (0.45); 2-4	2.93 (0.37); 2-4	1
No of grafts:			
2 grafts	4	2	
3 grafts	24	26	
4 grafts	2	1	
Mean (SD) cross clamp time (min); range	29.9 (8.9); 20-62		
Mean (SD) cardiopulmonary bypass time (min); range	54.7 (14.8); 36-104		
Low cardiac output:			0.34
Ionotropes	7	4	
Intra-aortic balloon pump	0	0	
Postoperative atrial fibrillation	10	4	0.18
Transfused patients	23	10	0.01
Mean (SD) ventilation (h)	10.7 (7.8)	7.9 (9.4)	0.23
Mean (SD) discharge (days)	9 (5.5)	7.8 (2.7)	0.23

Statistical analysis

We expressed continuous data as means (standard deviations) and compared them by using the independent sample *t* test or Mann-Whitney U test as appropriate. We compared proportions with χ^2 tests with continuity correction or Fisher's exact test as appropriate.

The primary outcome variable was the change in scores at 10 weeks from preoperative levels, assessed by repeated measures analysis of variance with post hoc comparison and Bonferroni correction. We considered a patient to have major deterioration in a particular test if the score deteriorated by 1 SD of the baseline score of all patients.[16] We considered a patient to have neurocognitive impairment if there was a major deterioration in two or more tests.[16] We used the χ^2 test to compare the proportion of patients with neurocognitive deterioration in the two groups.

Our sample size was based on data obtained from a previous non-randomised study performed in our department (unpublished data). The standardised difference was 1. To achieve a power of 87% we needed 40 patients (20 per group), with an α error set at 0.05 (two sided). Overall, we recruited 60 patients (30 in each group) to allow for loss to follow up and conversions to the other technique during surgery.

We performed all analyses with the SPSS10 software package. We present 95% confidence intervals for the main results. We considered a P value of < 0.05 as significant.

Results

Table 1 shows the patient characteristics in both groups. Both groups were similar for age, sex, angina class, left ventricle function, and extent of coronary artery disease, and they had a similar number of grafts (table 2). Neither group had any deaths, major neurological complications, or perioperative myocardial infarctions (based on electrocardiographic evidence only). Intubation time and length of hospital stay were shorter in the off-pump group than in the

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Table 3 Mean (SD) preoperative scores for all tests, and full scale IQ and mean differences for all tests*

Test	Mean (SD) preoperative scores		Mean difference 7 days postoperatively			Mean difference 10 weeks postoperatively		
	Off-pump (n=30)	On-pump (n=30)	Off-pump (n=30)	On-pump (n=29)	P value	Off-pump (n=30)	On-pump (n=30)	P value
Rey auditory verbal learning test	36 (8.83)	35.2 (8.99)	−1.20 (4.1)	−2.58 (10.0)	0.98	2.60 (9.2)	1.33 (8.0)	0.99
Part A of trail making test	43.57 (15.41)	40.37 (14.22)	−6.20 (17.8)	−13.55 (15.5)	0.20	3.00 (8.6)	1.53 (13.0)	0.99
Part B of trail making test	98.30 (36.09)	94.93 (34.99)	−17.96 (53.1)	−33.41 (34.4)	0.38	−0.26 (19.9)	−27.24 (31.0)	<0.002
Grooved pegboard test using dominant hand	99.93 (48.52)	91.20 (38.05)	−5.33 (32.5)	−13.44 (37.2)	0.76	4.20 (14.1)	−20.70 (22.9)	<0.002
Grooved pegboard test using non-dominant hand	109.37 (37.99)	106.57 (42.45)	−4.53 (26.0)	−32.27 (35.2)	0.002	3.63 (15.2)	0.80 (36.2)	0.99
Digit symbol substitution test	42.47 (10.23)	42.80 (18.19)	−1.50 (8.1)	−7.34 (9.6)	0.028	2.83 (6.7)	−4.06 (8.1)	0.002
Digit span forward test	9.00 (2.48)	8.97 (2.37)	−0.26 (1.9)	−0.75 (2.5)	0.78	0.36 (1.4)	−0.16 (2.0)	0.54
Digit span backward test	6.43 (2.27)	6.57 (2.47)	−0.02 (1.8)	−1.14 (2.9)	0.14	0.67 (1.3)	0.97 (0.9)	0.84
Controlled oral word association test	40.97 (10.49)	40.93 (16.01)	0.23 (7.8)	−0.79 (16.8)	0.99	2.23 (7.9)	1.66 (10.4)	0.99
Full scale IQ	114.9 (8.81)	114.16 (8.24)						

P values adjusted for multiple comparisons.
*Positive difference is improvement and negative difference is deterioration

on-pump group but did not reach significance. Significantly fewer patients in the off-pump group required blood transfusion. Both groups had similar baseline scores for the neuropsychometric tests and full scale IQ (table 3).

Change in scores

One patient in the on-pump group was not tested 1 week postoperatively because of tiredness and loss of motivation. All patients were tested 10 weeks postoperatively. At 1 week postoperatively the on-pump group showed a significantly greater deterioration in scores in the grooved pegboard test using the non-dominant hand and the digit symbol substitution test than the off-pump group. At 10 weeks postoperatively the on-pump group showed a significantly greater deterioration in part B of the trail making test, the grooved pegboard test using the dominant hand, and the digit symbol substitution test (table 3).

Patients with 1 SD or more deterioration in individual tests

One week postoperatively two patients (7%) in the off-pump group and 14 patients (48%) in the on-pump group showed a deterioration of 1 SD or more in the grooved pegboard test using the non-dominant hand (P=0.001; table 4). Ten weeks postoperatively no patient in the off-pump group and six patients (20%) in the on-pump group showed a deterioration of 1 SD or more in the grooved pegboard test using the dominant hand (P=0.03). In the other tests the difference in the proportion of patients in each group did not reach significance.

Patients with neurocognitive impairment

Patients were considered to have neurocognitive impairment if they showed a deterioration of 1 SD or more in two or more tests. One week postoperatively eight patients (27%) in the off-pump group and 19 (66%) in the on-pump group (P=0.004) had neurocognitive impairment. Ten weeks postoperatively three patients (10%) in the off-pump group and 12 (40%) in the on-pump group (P=0.017) had neurocognitive impairment.

Discussion

The incidence of neurocognitive impairment after coronary artery bypass graft surgery varies noticeably between studies.[3–5 10] This is because of variations in the tests used, the time points of assessment, the definition of impairment, and the statistical methods used for comparing groups.[16]

We found significantly less neurocognitive impairment 1 week and 10 weeks after off-pump coronary artery bypass graft surgery for patients with triple vessel disease. Previous studies have shown equivocal results. One prospective randomised study found increased concentrations of S100 protein, a marker of neurological injury, in the on-pump group, but no difference in neurocognitive impairment.[11] The definition of neurocognitive impairment was, however, unclear. More than 60% of patients recruited in that study had single or double vessel disease. Another study found a higher concentration of serum S100 protein, a higher number of high intensive transient signals picked up

Table 4 Percentage of patients in each group who had deterioration ≥1 standard deviation in individual tests at 1 week and 10 weeks postoperatively

Test	1 week postoperatively				10 weeks postoperatively			
	Off-pump (n=30)	On-pump (n=29)	Difference		Off-pump (n=30)	On-pump (n=30)	Difference	
			%	95% CI			%	95% CI
Rey auditory verbal learning test	13.3	34.5	21.2	(−0.7 to 41.0)	10.0	23.3	13.3	(−6.1 to 32.1)
Part A of trail making test	26.7	44.8	18.2	(−6.0 to 39.8)	6.7	16.7	10.0	(−7.4 to 27.6)
Part B of trail making test	23.3	44.8	21.5	(−2.6 to 42.6)	10.0	30.0	20.0	(−0.5 to 39.0)
Grooved pegboard test using dominant hand	13.3	31.0	17.7	(−3.7 to 37.6)	0	20.0	20.0	(4.5 to 37.3)*
Grooved pegboard test using non-dominant hand	6.7	48.3	41.6	(19.3 to 59.6)*	3.3	16.7	13.3	(−2.9 to 30.5)
Digit symbol substitution test	6.7	24.1	17.5	(−1.4 to 36.1)	3.3	13.3	10.0	(−5.6 to 26.6)
Digit span forward test	10.0	27.6	17.6	(−2.7 to 36.9)	0	10.0	10.0	(−3.1 to 25.6)
Digit span backward test	6.7	20.7	14.0	(−4.2 to 32.4)	0	0	0	(−11.4 to 11.4)
Controlled oral word association test	6.7	27.6	20.9	(1.4 to 39.7)*	3.3	10.0	6.7	(−8.2 to 22.5)

*Excludes 0.

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by transcranial Doppler, and an increased incidence of neurocognitive impairment in the on-pump than off-pump group.[8] This was a randomised study including 40 patients. The neuropsychological assessment was limited to the preoperative period and 1 week postoperatively, and the tests used did not conform to the consensus statement.[14] In one randomised controlled trial, neurocognitive outcome was assessed in 281 patients, using 10 neuropsychometric tests.[8] Improved cognitive outcomes were found in the off-pump group at 3 months, but the effects were limited and became negligible at 12 months. A significant proportion of the patients in this study had single and double vessel disease (76%); only 24% had triple vessel disease. Anaesthetic management differed between the groups: 99% of patients in the on-pump group received total intravenous anaesthesia including high dose opioids, and 54% of patients in the off-pump group received thoracic epidural anaesthesia.

Strengths of study

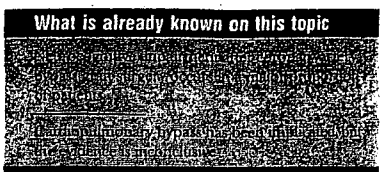
Overall, we included 91% of eligible patients in our trial. The operations were performed by a single surgeon (VZ). We standardised anaesthetic and surgical factors that might lead to cerebral injury. Both groups underwent the same surgical procedure, including the use of the same conduits and the same technique for proximal grafting. We included only patients with triple vessel disease. Previous studies have included a significant proportion of patients with single or double vessel disease.[8 9-11] No cross over occurred. None of the patients in the off-pump group required conversion to on-pump surgery. Follow up was 100% at 10 weeks. Our prospective randomised trial produced two similar groups (table 1). We are thus confident that cardiopulmonary bypass was the only major difference between our study groups.

Limitations of study

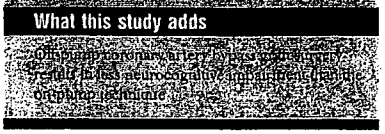
One limitation of our study is that a single surgeon operating in a single hospital, with standardisation of the anaesthetic and surgical techniques allows reproducibility of findings, but generalisability is affected. Our findings need to be tested in a multicentric study with different surgeons and hospitals. Aortic atherosclerosis is an important factor in neurological and neurocognitive outcomes. We did not use epiaortic scanning or transoesophageal echocardiography to detect aortic atherosclerosis. Our patients were assessed only at 1 week and 10 weeks postoperatively. Although outcomes at 10 weeks may reflect more important longer term outcomes, they may not necessarily reflect any permanent sequelae. The incidence of neurocognitive outcome decreased from 1 to 10 weeks; future studies need to incorporate longer term follow up.

Cardiopulmonary bypass has been implicated in the pathogenesis of neurocognitive impairment. Various mechanisms are responsible, including hypoperfusion during cardiopulmonary bypass, venous hypertension due to manipulation of the heart during surgery, emboli originating from the cardiopulmonary bypass circuit and the ascending aorta, and systemic inflammatory response syndrome leading to cerebral swelling and an increase in the permeability of the blood-brain barrier.[12-15]

What is already known on this topic



What this study adds



Neuropsychometric testing and the measurement of serum levels of biochemical markers (S100β and neurone specific enolase) are two ways of measuring neurological injury. Neuropsychometric tests assess specific domains of the brain, whereas the serum markers assess global injury. Two studies showed an association between neurocognitive impairment and S100β and neurone specific enolase levels.[16 17] Others have found no such association.[11 18] Administering a comprehensive battery of neuropsychometric tests is time consuming. Development of a serum marker or a computerised objective test that could be administered in less time and that correlated well with the severity of neuropsychometric impairment would improve the work of future researchers. At present, comprehensive neuropsychometric tests need to be administered to assess neurocognitive impairment.

We found one notable difference between our patient population and those in other studies. The average IQ of our patients was 115, higher (107 and 108) than in other studies.[19 20] It is possible that the slightly higher incidence of neurocognitive impairment in our patients could be related to a higher premorbid IQ. One study found a higher composite neurocognitive score at baseline to be a significant predictor of change in the composite cognitive index.[7]

We thank Gwen Phillips (Department of Neuropsychology, University Hospital of Wales) for advice on the neuropsychometric tests.

Contributors: JH and VZ had the original idea for the study and secured the funding. DW, VZ, and SK wrote the original protocol. JH coordinated the study. DW generated the allocation sequence and assigned participants to their allocation groups. VZ performed the operations. JD anaesthetised most of the patients and coordinated the collection of intraoperative data and blood samples. CC performed the neuropsychometric tests and collated the data. DW and SK coordinated the collection of follow up data. DW, SK, and JD recruited the patients. NP and VZ performed the statistical analyses and contributed to the interpretation of results. VZ wrote the original manuscript. All authors contributed to revisions of the manuscript. JH will act as guarantor for the paper.

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were recorded in 50 CABG patients (46 men and 4 women; mean age ± SD, 59.9 ± 7.5 years). The sex ratio of this sample reflects the usual gender distribution in the population undergoing cardiac surgery. Patients were classified into two subgroups: all patients undergoing on-pump surgery (n = 32) were compared to patients undergoing off-pump CABG (n = 18) 6 days after surgery. A Dutch version of the National Adult Reading Test (Nederlandse Leestest voor Volwassenen [NLV])[8] was used to obtain an estimated the intelligence quotient (IQ). State anxiety was measured by the Dutch version of the Spielberger state anxiety questionnaire.[9] For further details about this patient group, we refer to Table 1. Six months after surgery, the on-pump group consisted of 22 patients and the off-pump group consisted of 11 patients. Some of the reasons for not coming back were difficulties in transport to revisit the hospital, and lack of interest/motivation. Interestingly, a statistical analysis with belonging or not belonging to the dropout group as a between-subjects factor was performed. We found no statistical differences for demographic, intraoperative, or postoperative variables.

Patients underwent preoperative identification of both MCAs. Two 2-MHz transducers fitted on an elastic headband (DWL 40389; DWL Elektronische Systeme GmbH) were placed on each of the left and right temporal skull windows transmitted the ultrasonic signal and received the echoes. Details of the insonation technique and the correct insonation of the MCA have been described elsewhere.[10] Starting from insonation depths of 50 mm and 55 mm, depth and angles of insonation were adjusted to obtain the highest signal intensity of the M1 segment of the MCA. HITS were continuously and bilaterally recorded by a sonographer from the moment of induction of heparin until 5 min after aortic decannulation (on-pump) or 5 min after the last distal anastomosis (off-pump). HITS were defined as having high amplitudes (greater than flow velocity), unidirectional, transient signals lasting < 0.1 s, greater than nine decibels, and associated with a characteristic chirping sound. The sonographer was informed of major procedural events, and HITS distribution was recorded accordingly. For on-pump CABG, eight categories of surgery manipulation were noted, and if a HITS signal was detected in the immediate 1-min period after one of these categories, it was considered to be associated with that event. The categories were aortic cannulation, aortic decannulation, cross-clamp on, cross-clamp off, ECC on, ECC off, partial clamp on, and partial clamp off.

Neuropsychological Testing

One examiner (N.S.) administered a battery of seven standardized neuropsychological tests 1 day before, 6 days after, and 6

Table 1—*Patient Characteristics

Characteristics	On-Pump Group (n = 32)	Off-Pump Group (n = 18)	F Test	p Value
Demographics				
Mean age, yr	59.1 ± 7.7	61.3 ± 7.1	0.98	0.327
Male gender	90.6	94.4	0.47	0.641
IQ estimate (NLV)	94.9 ± 9.6	84.4 ± 10.2	13.05	0.001†
State	42.3 ± 14.6	44.5 ± 16.7	0.20	0.656
Preoperative risk factors				
Hypertension	43.8	61.1	1.17	0.247
Hyperlipidemia	56.3	50	0.42	0.678
Hyperurecemia	12.5	16.7	0.4	0.691
Diabetes	31.3	33.3	0.15	0.863
Tobacco use	71.9	94.4	2.3	0.026‡
Recent myocardial infarction	21.9	33.3	0.88	0.386
Ejection fraction	67.3 ± 14.9	71.7 ± 12.5	1.08	0.304
COPD	6.3	5.6	0.10	0.923
No. of diseased vessels			2.06	0.049‡
1	3.1	16.7		
2	18.8	33.3		
3	78.1	50		
Body mass index	26.9 ± 4.8	28.3 ± 3.9	1.16	0.287
Perioperative and postoperative factors				
No. of grafts			3.85	0.001†
1		5.6		
2	3.1	16.7		
3	28.1	50.0		
4	40.6	27.8		
5	21.9			
6	6.3			
Operation time, min	188.8 ± 42.5	169.6 ± 28.7	2.91	0.095
Anesthesia time, min	248.5 ± 46.9	230.0 ± 38.0	2.04	0.16
Ventilation time, h	11.3 ± 5.1	10.6 ± 4.4	0.29	0.596
Stay in ICU, h	44.1 ± 40.3	44.2 ± 32.0	0.00	0.989
Atrial fibrillation	18.8	16.7	− 0.20	0.846

*Data are given as mean ± SD or % unless otherwise indicated.
†Significant at 0.01 level.
‡Significant at 0.05 level.

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months after surgery in the 50 patients with emboli measurement. This group was part of the larger group of 66 patients. At the time of the first assessment, it was unknown whether an on-pump or off-pump strategy would be used. The tests were selected to sample a broad range of cognitive abilities and included measures of attention and concentration, verbal and nonverbal memory, language, visuospatial functions, executive functions, and motor and psychomotor speed. To reduce test-retest effects, we used alternate test versions when possible. The tests used in the study are listed in Appendix 1.

Definition of Cognitive Decline

Since direct comparisons of the group means of preoperative and postoperative neuropsychological measurements usually show improvement rather than cognitive decline,[11] researchers have focused on preoperative and postoperative differences in cognitive performance on an individual level.[12] This allows each patient to serve as his/her own control. If these differences exceed a certain threshold, a patient is considered to have a cognitive decline. Several thresholds have been proposed. We used the "20% definition" because it is believed to be the most sensitive method for identifying patients with signs of cognitive decline.[11] The 20% definition implies that a decrease in test scores by at least 20% from the preoperative baseline is said to constitute significant decline. Studies have also varied in the number of tests that a patient's score must have declined on, before a subject can said to be declined. For this study, we defined cognitive decline as having 20% on two or more tests.

To further refine our results, we described the severity of neuropsychological test decline by counting the number of impaired test performances for each individual (possible range, 0 to 7). This is called the cognitive impairment index (CII).

Measurement of BFV

Cerebral BFV changes in the MCAs were continuously and simultaneously recorded with the same TCD device as for emboli measurement. Following an initial rest phase, subjects were confronted with three verbal and two visual-spatial tasks, most of which were presented on a computer screen. Each activation and rest condition lasted 120 s and was delineated on the TCD record by a set of markers. The speed of the stimulus presentation was individualized to reduce frustration with stimulus pacing (either too slow or too fast) and to maximize the mental activity of the individual. As soon as the subject gave a response, the next item was shown. To obtain a stable measurement during activation, only the middle 60 s of each 120-s activation condition were used to determine the mean BFV for that task. During the rest periods, subjects were asked to look at an illuminated blank computer screen, to relax and breathe regularly without falling asleep, and to clear their thoughts. They were not allowed to move or speak, nor were they spoken to. The first 60 s of each rest period served as a recovery period in which posttask activation could subside. Only the last 60 s of the rest period served as the baseline measurement for the subsequent activation phase. We always used the immediately preceding rest period to determine the BFV change of the cognitive task under study. Because TCD cannot detect the differences between real asymmetries in BFV and differences caused by slightly different insonation angles, we calculated the relative increase from baseline to activation: ([BFV activation − BFV baseline/BFV baseline] × 100).

We selected cognitive tasks that had demonstrated potential for lateralized cognitive activity (and lateralized cerebral hemodynamics) in previous functional imaging or TCD research.[13] The cognitively induced cerebrovascular reactivity tasks are listed in Appendix 2.

Preoperative BFV measurements were obtained for 66 patients, early postoperative BFV measurements for 63 patients (on-pump CABG, n = 41; off-pump CABG, n = 22) and late postoperative measurements for 44 patients (on-pump CABG, n = 30; off-pump CABG, n = 14). The total patient group was divided into the on-pump and the off-pump groups.

Statistical Analysis

All continuous variables are expressed as mean ± SD. Categorical variables are expressed as a percentage of those exhibiting the trait out of all patients for whom data were available. Statistical analysis (SPSS/PC+; SPSS; Chicago, IL) was based on two independent groups of patients (on-pump vs off-pump groups). Baseline characteristics, outcome measures, and complications between the two groups were compared. Normally distributed data (ratio scale) were compared with independent *t* tests. If the data were not normally distributed, the nonparametric Mann-Whitney test was used. Nominal data were analyzed with χ^2 statistics if all expected cell frequencies were greater or equal to five. Otherwise, Fisher Exact Test was used.

Analyses of neuropsychological and BFV data between groups were analyzed with repeated-measures multivariate analysis of variance and corrected for between-groups differences with the proper covariates (multivariate analysis of covariance [MANCOVA]). Associations between the number of HITS and neuropsychological and BFV data were calculated by Spearman ρ and Pearson correlation coefficients. In the parametric tests, dependent variables were checked for normal distribution by Kolmogorov-Smirnov tests and transformed if necessary. Detailed information about each statistical procedure follows.

Results

HITS

In the on-pump group, the mean number of HITS was 335.1 ± 333.5 (range, 24 to 1,229), whereas in the off-pump group, the mean number of HITS was 144.7 ± 180.4 (range, 5 to 632). This difference was significant ($Z = -2.698$; $p < 0.01$).

Since all patients were monitored bilaterally, we could compare the HITS detection in the left and right MCAs. For the on-pump group, we counted 179 ± 227 HITS (53%) in the left MCA and 156 ± 151 HITS (47%) in the right MCA. This difference was not significant. In off-pump patients, HITS tended to be more numerous on the right MCA (106 ± 149; 73%) compared to the left MCA (39 ± 62; 27%), although this trend failed to reach significance ($p = 0.057$). After square-root transformation of the HITS count to obtain a normal distribution, a repeated-measures, multivariate analyses of variance with eight different surgical maneuvers of on-pump CABG as within-subjects factor was performed and revealed a main effect of surgical maneuver ($F = 8.128$, $p < 0.01$). When the different surgical maneuvers of on-pump CABG were assessed separately with paired *t* tests, significantly more HITS were detected immediately after aortic cannulation (Table 2). Significantly fewer HITS were

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Table 2—*Occurrence of HITS*

Variables	Average HITS Count (% of Total No. of HITS)
Aortic cannulation	9.24 (2.9)
ECC on	5.61 (1.8)
Cross-clamp on	0.67 (0.2)
Cross-clamp off	5.7 (1.8)
Partial clamp on	5.2 (1.6)
Partial clamp off	4.9 (1.6)
ECC off	6.6 (2.1)
Aortic decannulation	6.1 (1.9)

found after cross-clamping. When cumulating the percentage of HITS associated with the different stages of the operation, 13.9% of the total number of HITS was explained.

Effect of Surgical Technique on Cognition

The neuropsychological testing results for the preoperative, early, and late postoperative periods are presented in Table 3. Neuropsychological data were analyzed on a general level. Patients in the on-pump group showed a higher IQ ($p < 0.01$), less tobacco use ($p < 0.05$), a higher number of diseased vessels ($p < 0.05$), and a higher number of grafts ($p < 0.01$). For further analysis of cognitive measures in this group, these variables were included as covariates. MANCOVAs with time of neuropsychological assessment (preoperative vs early postoperative and preoperative vs late postoperative) as within-subjects factor, type of surgery as between-subjects factor, and differences between both groups as covariates revealed no main effect of time, no main effect of surgery, and no interaction effects.

According to the 20% definition, 60% from the total group had a cognitive decline 6 days after surgery, 59.4% in the on-pump group and 61.2% in the off-pump group. After 6 months, 24.2% still had a cognitive decline, 31.8% in the on-pump group and 9.1% in the off-pump group.

For the results according to the CII, we refer to Tables 4, 5. Early neurocognitive impairment was most frequently observed on the blocks tap test and the line bisection test. Six months after surgery, the CII was significantly different in the on-pump group vs the off-pump group ($Z = -2.24$, $p < 0.05$) with less neurocognitive tests that remained impaired in the off-pump group. Neurocognitive impairment was most frequently observed on the line bisection test (on-pump group), trail-making test, and blocks tap test (on-pump and off-pump groups) after 6 months.

BFV Before and After Surgery

Percentages change for the preoperative, early postoperative, and late postoperative period for the total group are presented in Table 6. MANCOVAs with time of BFV measurements (preoperative vs early postoperative and preoperative vs late postoperative on absolute rest values, absolute activation

Table 3—*Neuropsychological Test Results in On-Pump Group Compared to Off-Pump Group After 6 Days and 6 Months**

Tests/Groups	Preoperative	6 Days	6 Months
Auditory verbal learning test			
On-pump	44.8 ± 8.5	42.6 ± 9.2	48.5 ± 9.5
Off-pump	41.72 ± 10.7	43.2 ± 7.9	49.6 ± 9.2
Block taps test			
On-pump	37.7 ± 19.9	43.9 ± 22.2	35.8 ± 22.5
Off-pump	41.8 ± 16.0	53.2 ± 18.9	34.5 ± 19.7
Trail-making test part B			
On-pump	121.3 ± 67.1	134.4 ± 65.3	100.1 ± 38.7
Off-pump	154.8 ± 96.6	116.9 ± 36.1	123.2 ± 88.6
Grooved pegboard test			
On-pump	183.5 ± 50.2	209.9 ± 58.4	108.2 ± 53.7
Off-pump	197.3 ± 36.4	218.2 ± 52.4	123.2 ± 88.6
Judgment of line orientation			
On-pump	23.7 ± 3.8	23.5 ± 4.5	24 ± 4.6
Off-pump	23.7 ± 4.2	23.1 ± 4.4	25.2 ± 3.9
Line bisection test			
On-pump	68.2 ± 24.8	74.5 ± 28.5	65.9 ± 20.3
Off-pump	69.0 ± 27.7	71.9 ± 20.4	64 ± 34.4
Controlled oral word association test			
On-pump	29.1 ± 8.5	28.6 ± 7.7	33.3 ± 8.9
Off-pump	22.4 ± 6.1	24.9 ± 8.7	25.9 ± 6.4

*Data are presented as mean ± SD. For explanation of tests see Appendix 1.

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Table 4—*Results According to CII After 6 Days**

CII	Total Group	On-Pump Group	Off-Pump Group
0	18	15.6	22.2
1	22	25	16.7
2	34	37.5	27.8
3	18	12.5	27.8
4	6	6.3	5.6
5	2	3.1	0.0

*Data are presented as %.

values, and percentage change) as within-subjects factor, type of surgery as between-subjects factor and IQ, tobacco use, number of diseased vessels, and number of grafts as covariates revealed no main effect of time, no main effect of surgery, and no interaction effects.

Relation Between Number of HITS With Cognitive Performance and BFV

We tested whether patients showing significant cognitive decline (as defined by the 20% definition) received significant more HITS during operation than patients showing no significant decline. A t test with total number of HITS (log-transformed) as dependent variable and absence/presence of cognitive decline as independent variable showed no significant differences between both groups.

In addition, we tested if there was a significant association between HITS and CII. A Spearman ρ correlation was performed for total number of HITS and CII. No significant correlations were found.

With regard to the BFV variables, we investigated whether the number of HITS was related to changes in pre-cerebrovascular reactivity to post-cerebrovascular reactivity. We calculated Pearson correlations between the total number of HITS (log-transformed variable) and BFV values (preoperative BFV percentage change minus early postoperative BFV percentage change, and preoperative BFV percentage change minus late postoperative BFV percentage change). No significant correlations were found.

An explorative multivariate regression analysis with log-transformed number of HITS as the dependent variable and mean activation BFV value (sum of five BFV tasks left and right side divided by 10), left ventricle ejection fraction, age, hypertension, and number of diseased vessels as clinically relevant independent variables revealed that mean activation BFV value ($\beta = -0.387$, $t = -3.037$, $p < 0.01$), number of diseased vessels ($\beta = 0.319$, $t = 2.469$, $p < 0.05$), and left ventricle ejection fraction ($\beta = -0.27$, $t = -2.125$, $p < 0.05$) are significant predictors for number of HITS. The model explained 34.2% of the variance. We also found significant negative correlations between the number of HITS as well as between mean BFV activation value and left ventricle ejection fraction. This means that the lower the mean activation BFV value and left ventricle ejection fraction, the higher the embolic load.

Table 5—*Results According to CII After 6 Months**

CII	Total Group	On-Pump Group	Off-Pump Group
0	36.4	22.7	63.6
1	39.4	45.5	27.3
2	24.2	31.8	9.1

*Data are presented as %.

Discussion

Despite improvements in ECC apparatus and refinements in surgical techniques that have enormously reduced the mortality rate, subtle cognitive dysfunctions in CABG patients remain to be observed. This might be associated with the occurrence of cerebral microemboli generated during CPB.[2] Several investigators[1,14] have demonstrated that patients who receive less cerebral microemboli during CPB (on-pump surgery) have a lower incidence of postoperative neuropsychological impairment. It is assumed that CABG surgery without CPB will diminish the potential for emboli, particularly those associated with the disruption of atheromatous plaques due to cannulation, cross-clamping, and manipulation of the aorta. Moreover, the generation of gaseous microemboli from the CPB circuit and microparticulate emboli from the pump tubing would likewise be avoided. In essence, the avoidance of CPB during CABG surgery would be expected to reduce cerebral injury by reducing the cerebral embolic load, resulting in improved clinical outcomes.

HITS (as indicator of potential cerebral emboli) were observed in all patients, independently of type of surgery during CABG. This is in accordance with findings from the majority of previous TCD studies.[15] The number of HITS was comparable to that of previous studies although methodologic differences have to be taken into account. For example, we defined HITS associated with a procedure if they occurred within 1 min of the latter, whereas other authors[16] used a 4-min interval. Furthermore, in some studies,[16–17] only the right MCA was intraoperatively monitored, whereas in our study a bilateral measurement in all patients was used. Nevertheless, together with Stump et al,[2] we believe that the wide variety of HITS detection equipment used by differ-

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Table 6—*Percentages Changes Over the Operative Periods for the Total Group**

Test/Side	Preoperative (n = 66)	Early Postoperative (n = 63)	Late Postoperative (n = 44)
NLV			
Left	6.15 ± 9.41	6.41 ± 6.75	6.36 ± 9.45
Right	4.21 ± 8.47	4.73 ± 7.07	5.47 ± 7.25
Visual searching			
Left	10.38 ± 7.81	8.56 ± 4.45	8.93 ± 7.15
Right	11.42 ± 8.46	8.93 ± 5.29	10.78 ± 8.15
Syntactic sentence construction			
Left	9.62 ± 6.21	8.55 ± 4.49	8.17 ± 8.5
Right	7.17 ± 7.89	6.52 ± 5.69	6.89 ± 7.35
Three-dimensional puzzle			
Left	14.22 ± 8.70	11.81 ± 6.11	15.00 ± 7.43
Right	17.07 ± 8.43	13.70 ± 7.08	16.85 ± 7.90
Controlled oral word association test			
Left	7.36 ± 10.08	4.79 ± 6.36	7.91 ± 10.75
Right	3.45 ± 9.16	4.15 ± 11.87	5.10 ± 7.22

*Data are presented as mean ± SD. For explanation of tests see Appendix 2.

ent study groups makes comparison across studies on the absolute number of HITS difficult because each instrument produces quite different estimates of the number of HITS depending on the physics of the transducer, the arteries insonated, and the thresholds imposed that define a HITS event.

More important than the absolute number of HITS is the fact that their frequency differed (range, 5 to 1,229) both between patients and depending on the type of surgery being performed (on-pump vs off-pump). Our results showed that CABG without ECC is associated with significantly fewer HITS. This supports the findings from previous TCD studies. Watters et al[17] described in a small study with unilateral measurements fewer emboli in the off-pump group than in coronary surgery with CPB. This was confirmed by Bowles et al[3] with bilateral measurements in a group of 40 patients (20 patients per group). By eliminating the need for ECC, off-pump surgery has theoretical advantages over conventional on-pump procedures, partly due to the reduction of the systemic inflammatory response elicited by ECC during on-pump procedures.[18–19] Adverse effects of ECC can also occur in the CNS. The principal cause of neuropsychological impairment is thought to be diffuse microischemia secondary to cerebral microemboli.[20] As suggested in our previous study,[21] we also performed a battery of neuropsychological tests before and after the surgery to determine if number of HITS could be related to declines in test scores. Although more HITS were detected in the on-pump group, no significant differences on neuropsychological performances on group level were found between both surgery groups. Furthermore, according to our analyses of this (limited) group of patients, we did not find a relation between degree of postoperative neuropsychological impairment and number of HITS. On an individual level, however, fewer neurocognitive tests remained impaired in the off-pump group.

While off-pump surgery continues to be explored as an alternative to conventional CABG surgery in many cardiac units worldwide, this revascularization strategy continues to generate controversy. Several studies[17,22–23] identify no clear superiority of either the on-pump or off-pump procedures. Instead, they clearly suggest that patients undergoing these two techniques are not clinically similar.[24] CPB patients tend to have higher mean numbers of coronary anastomoses, suggesting potential underlying contrasts to off-pump patients. It seems plausible that patients having less coronary artery disease likewise have less cerebrovascular disease and aortic atherosclerosis, logically suggesting that they are less predisposed to subtle neurologic insult following CABG surgery.[4] In our patient group, there were indeed differences between both groups according to a higher number of diseased vessels and a higher number of grafts for the on-pump group. Randomization of patients groups appears warranted in further research.

In contrast to other authors[1,14] who believe that the number of ultrasonically detectable HITS delivered to the brain is the best predictor of neurobehavioral deficits, we suggest that the composition and size of HITS might be more important for the development of neurocognitive decline than is the absolute number of HITS. An argument for this is found in patients undergoing valve operations where, despite the uniformly larger number of HITS, a

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higher incidence of cognitive decline is absent.[12] Emboli can be particulate, air, or gaseous in nature. Obviously, large particulate emboli and massive air embolism will cause more injury than minor embolic events. Particulate emboli can cause stationary obstruction of cerebral vessels, whereas gas emboli have been reported to pass arterioles and capillaries and may pose less risk to the patient than solid atheroemboli dislodged during aortic manipulation. Furthermore, smaller particulate emboli, still large enough to occlude arterioles and capillaries, may not be detected and the total number of emboli would certainly be many times greater than our count. Until lately, it was impossible for TCD to determine the nature of the HITS recorded. A study[24] was published that shows that it is now possible to differentiate between solid and gaseous cerebral HITS with multifrequency TCD. Although specific CPB components may be associated with increased risk of brain injury, it must be noted that non-CPB patients are not immune to neuropsychological deficits. It might be that other factors independent of CPB impart a greater independent risk than CPB alone such as hospitalization, sleep deprivation, and potential adverse effects of anesthesia.[23]

We were also interested when and where cerebral HITS occurred. Previous research has demonstrated the occurrence of cerebral HITS in association with specific "surgical" events, *ie*, aortic cannulation and decannulation, ECC start and end, cross-clamp application and removal, partial-occlusion clamp release, start of cardiac ejection after cross-clamp removal, and perfusionist interventions.[2,14–16,20,25,26] In our study, the aortic cannulation was the most important HITS-prone surgical maneuver. Although manipulation does account for some of the emboli during on-pump surgery and especially during aortic manipulation, the vast majority (86.1%) occurred when no specific surgical manipulation was identified. This percentage is comparable to that of the study of Bowles et al.[3] In the study of Stump et al,[27] more than one third of HITS were not associated with any specific period or surgical manipulation, and occurred when the observer could not associate any act of the surgeon, perfusionist, or anesthesiologist as having a temporal relationship with the embolic signal. These data suggest that there are two separate major sources of emboli: (1) those secondary to surgical and manual manipulation of the heart and arteries and, (2) emboli from a nonobvious source.

The question remains where HITS occur in the brain? In our study, we found a tendency in the occurrence of HITS in the right MCA but only in off-pump surgery. This is in contrast with what would be anatomically expected. It is the left hemisphere that should have an increased susceptibility for receiving cardiogenic emboli caused by the asymmetrical anatomy in the branching patterns of the extracranial arteries on the aortic arch. Emboli coming from the heart have to pass through the brachiocephalic trunk that only exists on the right side. This divides the chance of embolization between the right subclavian artery and the right common artery, whereas the left common carotid artery of most individuals immediately originates from the aortic arch. Furthermore, the left internal carotid artery almost vertically originates from the arch and is therefore situated in the direct flow direction caused by every systolic contraction. Other authors[28–30] reported an asymmetric distribution side difference for emboli, with a higher incidence of HITS in the left MCA.

On an individual test level, 60% of the patients showed cognitive decline 6 days after surgery. Six months after surgery, most patients returned to baseline level. We found that cognitive decline remained in 24.2% of the patients. In particular, domains of nonverbal immediate memory and attention, visual attention, visual search, and mental flexibility were impaired. This is in accordance with other studies. In the study of Borger et al,[31] worse performance on tests of learning and memory and attention and concentration were seen. We agree with McLean et al[32] and Shaw et al[33] that the cognitive domains of learning, memory, and concentration are sensitive to the deleterious effects of CPB, but based on this study we add that the effect was also seen in patients without CPB.

Studies have been performed to evaluate the effect on CBF before and after the surgery. Abildstrom et al[34] found a significant, uniformly distributed decrease in CBF after coronary surgery that was not correlated to postoperative cognitive dysfunction. Smith and associates[35] found a decrease in CBF in some patients 8 days after surgery. We studied the BFV, which is related to the CBF. We found no BFV differences between the on-pump and off-pump groups and no differences over the different time intervals. Interestingly, preoperative BFV during activation appeared to be a predictor, together with number of diseased vessels and left ventricle ejection fraction for the number of HITS. Since our patient group remains rather small, the relation between BFV and HITS load justifies further investigation before preoperative BFV may be employed as a predictor for HITS load during the operation. As far as we know, this is the first study that examines the association between the number of HITS and the BFV.

Our conclusions may be limited by several factors. First, we believe that the clinical relevance of cog-

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nitive dysfunction is still uncertain. The real clinical impact of cognitive dysfunction, especially regarding quality of life and rehabilitation, needs to be confirmed by further investigations.[36] Second, the study was limited by the fact that we investigated nonrandomized patient groups, because the decision regarding the surgical strategy (on-pump or off-pump) was left to the individual surgeon. However, including the patient for the neuropsychological test battery and BFV tasks was done without knowing which technique was going to be used. Third, we have to bear in mind that our patient group was limited to 50 patients. Research that includes more patients would undoubtedly give more representative conclusions.

To conclude, cerebral dysfunction after CABG operations remains an important possible complication of cardiac surgery. We used TCD to detect and quantify the number of microemboli in patients undergoing CABG. The technique may also alert the surgical team when HITS enter the cerebral circulation during surgery, thus allowing preventive measures to be taken. No relation was found between number of HITS and degree of postoperative neuropsychological impairment. We should bear in mind that the occurrence of neurologic complications after cardiac surgery cannot be attributed to a single causative element in most cases. As with most disease processes, the cause is multifactorial.

In the present study, no clear advantage in terms of neuropsychological test performance was demonstrated by the on-pump group when compared to the off-pump group, although less neurocognitive tests remained impaired in the off-pump group after 6 months when assessing the individual level. This supports the assertion that postsurgical neuropsychological deficits may not be so intimately related to the CPB circuit as suspected. Preoperative BFV, which can also be measured with TCD, should be further explored as one of the possible predictors for HITS load. Future research should focus on the relative importance of particulate matter and gaseous material.

Appendix 1: Neuropsychological Tests

1. The Rey auditory verbal learning test assesses verbal memory. The measure retained is the total number of words immediately recalled over the first five trials.
2. The trail-making test (part B) assesses speed for visual search, attention, and mental flexibility. The time to completion is the measure obtained.
3. The grooved pegboard test measures finger and hand dexterity. The sum of the times to completion of the left and right placement of all pegs is the measure taken.
4. The block taps test assesses nonverbal immediate memory and attention. The number of errors is the measure obtained.
5. The line bisection test assesses unilateral visual inattention. Total deviation from the true center is the measure obtained.
6. The controlled oral word association test (orthographic categories) assesses word fluency. The total number of words (with four given letters) is the measure obtained.
7. Judgment of line orientation examines the ability to estimate angular relationships between line segments. The measure obtained is the correct number of answers.

Appendix 2: Cognitively Induced Cerebrovascular Reactivity Tasks

1. Reading. Subjects were instructed to read a list of 50 words aloud. The list was a Dutch version of the National Adult Reading Test (NLV).[8] The end score gives an estimation of the premorbid verbal IQ.
2. Visual searching. This task, which is part of the FEPSY computer program for neurocognitive assessment, consisted of finding a grid pattern (out of 24 similar designs) that matches the one in the center of the screen.[37] Subjects had to point the identical grid with both index fingers simultaneously to avoid unilateral activation of the motor cortex. The quality of performance was expressed as the percentage of the correct answers.
3. Syntactic sentence construction. The words of a sentence were shown in a mixed-up order. Subjects were asked to whisper a grammatically correct sentence using as many words as possible. Whispering minimizes the acoustic interference on the TCD signal by preventing voice artifacts caused by the conduction of the normal voice spectrum via the cranial bones to the temporally placed probes. For the quality of the task performance, the absolute number of words was taken into account.
4. Three-dimensional puzzle. A commercially available three-dimensional puzzle was used (Eureka bvba; Mechelen, Belgium). Subjects were allowed 2 min to try to free the ring from the rope.[13]
5. Word fluency (controlled oral word association test). The subjects were required to whisper as many words as possible (excluding proper names) beginning with a designated letter. For the quality of the task performance, the absolute number of words was taken into account.

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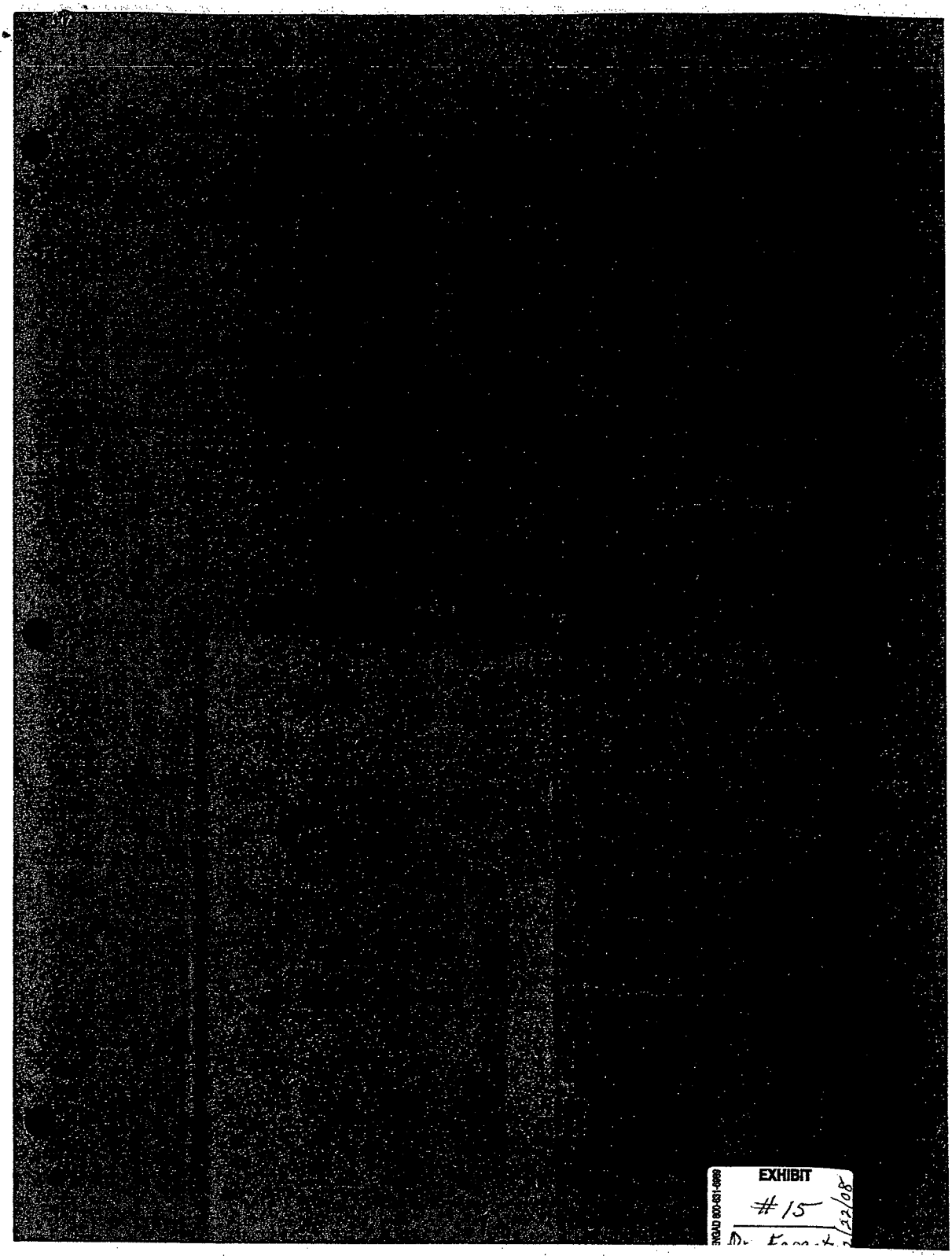

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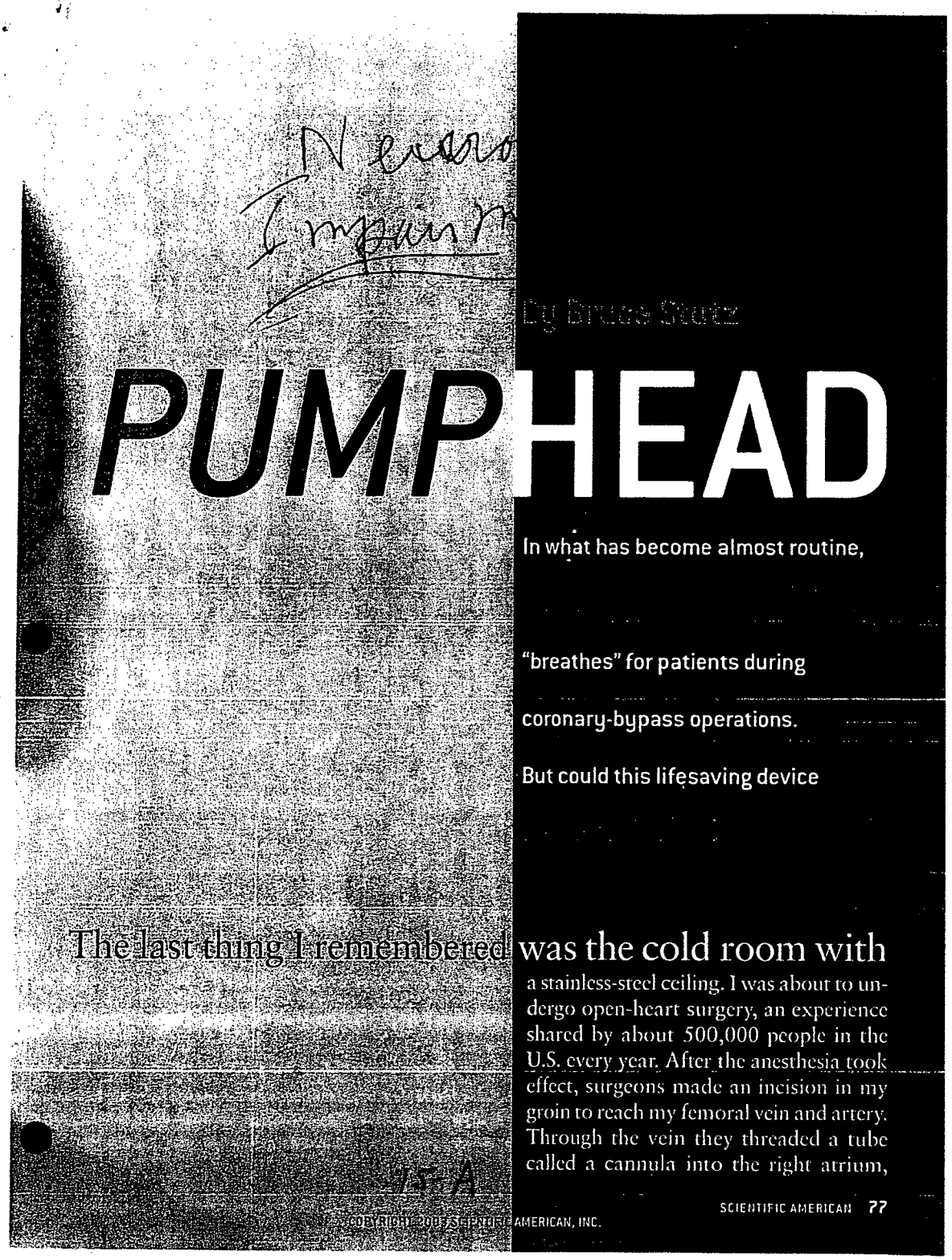

By Bruce Stutz

PUMP HEAD

In what has become almost routine, "breathes" for patients during coronary-bypass operations. But could this lifesaving device

The last thing I remembered was the cold room with a stainless-steel ceiling. I was about to undergo open-heart surgery, an experience shared by about 500,000 people in the U.S. every year. After the anesthesia took effect, surgeons made an incision in my groin to reach my femoral vein and artery. Through the vein they threaded a tube called a cannula into the right atrium,

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an upper chamber inside my heart. This tube, and another attached to the artery, was connected to a cardiopulmonary-bypass pump, also known as a pump oxygenator or a heart-lung machine. A dose of heparin kept my blood from clotting as it traversed the machine's innards. As the venous blood passed through the oxygenator, it was cooled to prevent tissue damage. My body temperature lowered to 25 degrees Celsius (77 degrees Fahrenheit)—deep hypothermia. Surgeons inserted an inflatable clamp into my aorta to seal it off. Two liters of cold potassium solution stopped my heart, and for the next two hours the machine took over. An eight-inch incision below my right breast allowed the doctors to pass cameras and instruments between my ribs and then to repair my congenitally defective heart valve.

I left the hospital a week later. The incision healed quickly and painlessly. In a couple weeks I was out and about on slow but successively longer walks. Within a month I was back in the gym. Mentally, however, I felt a bit hazy, a little disconnected and sometimes even lost. I soon learned that the physician's warning, "You may be a little depressed for a time afterward," would not do justice to the long, dumbfounding struggle against what seemed to be the sudden onset, at 51 years of age, of attention-deficit disorder or incipient senility. Adrift in a clueless no-man's-land, I felt my moods range from querulous to despondent. I couldn't muster the concentration to deal with the problem. I just wanted to be able to think. Think anything.

I didn't know it at the time, but I was suffering from what surgeons among themselves call "pumphead," an all-too-apt appellative that refers to the dimwitted state in which patients seem to linger after being hooked up to a heart-lung machine for open-heart or, in my case, valve surgery. Other symptoms include patchy recall, social difficulties and personality changes. Pumphead was long suspected from anecdotal and journal reports of patients tested soon after their operations. But only recently did a five-year study of bypass patients indicate that after an initial recovery of mental capabilities in the first few months, the condition often worsens later and persists for years. Could the familiar heart-lung machine—which annually provides life-giving oxygen to blood during 900,000 coronary-bypass operations around the world—be at fault?

Adrift in a clueless no-man's-land, I felt my moods range from querulous to despondent.

Making of the Machine

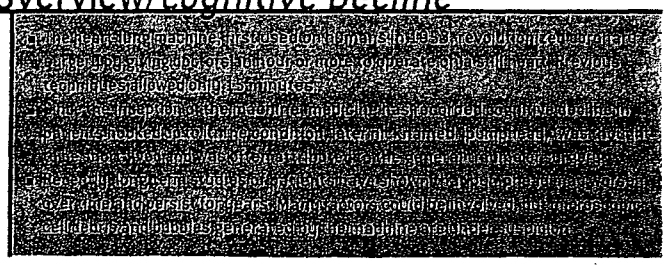
FIFTY YEARS AGO John Heysham Gibbon, Jr., of Jefferson Medical College in Philadelphia performed the first successful human surgery using a heart-lung machine. He had begun developing the device in the 1930s, as a research fellow in surgery at Harvard Medical School. After years of animal trials, and with engineering advice and financing from IBM chairman Thomas J. Watson and others, Gibbon solved what was then the major impediment to heart surgery—giving doctors enough time to operate.

Before Gibbon's pump came into use, induction of, or cooling, the patient's body to slow metabolism and blood circulation gave surgeons a 15-minute window to complete their work. Any longer and the body and brain suffered from a lack of oxygen. Gibbon's machine took blood that would normally go to the heart and lungs, oxygenated it and pumped it back to the arterial system through the aorta. Today the pump's use has become commonplace. Surgeons perform so many coronary-artery-bypass graftings, or CABGs, that they commonly refer to them as "cabbages." But for decades the long-term effects of those operations received little serious study.

That has changed in recent years. In 2001 a *New England Journal of Medicine* article by Mark F. Newman, chair of Duke University Medical Center's department of anesthesiology, and his colleagues revealed that even after five years many coronary-bypass patients still struggled with severe mental impairments. Previous studies had followed subjects for only up to six months. "Adjectives such as 'subtle,' 'transient,' and 'subclinical' have been used to describe the cognitive decline that occurs after CABG, but such descriptions minimize the importance of these changes to clinicians, patients, and their families," the article concludes. Adds Newman: "The month after the study came out, we received 4,000 e-mails from bypass patients. A lot of people were happy just to know they weren't crazy."

In the study, Newman and his group administered five cognitive tests—short-story recall, repetition of number series,

Overview/Cognitive Decline



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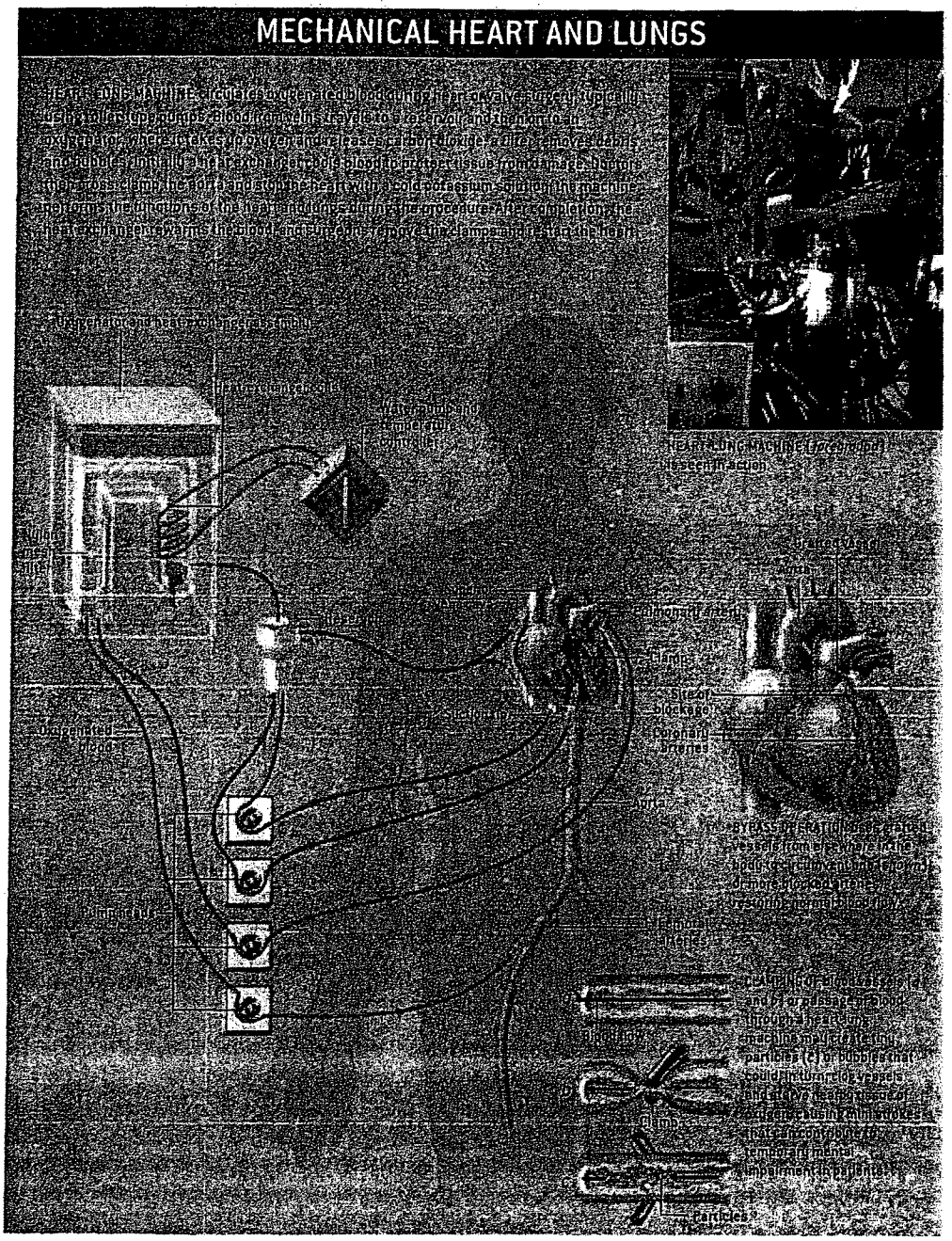
MECHANICAL HEART AND LUNGS



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visual retention, pairing digits with symbols, and connecting a series of numbers and letters—to 261 heart-bypass patients the week before hospitalization, during the week after the operation, after six weeks and again six months later. After surgery, 53 percent of the subjects were unable to match their earlier cognitive performance. Six weeks later, 36 percent continued to be affected, and that number dropped to 24 percent after six months.

Those results surprised no one. Short-term declines in mental function after operations involving the heart-lung machine had been reported in the literature since the beginning, and they were frequently chalked up to the general trauma of surgery. Five years after the first round of tests, however, Newman's team checked in with their subjects once more. Some of them performed about the same as they did originally, but 42 percent fared so poorly that they were again declared cognitively impaired—even after controlling for increased age.

What's to Blame?

ALTHOUGH THE IDEA is not proved, the heart-lung machine is a suspect in cognitive decline for several reasons. Physicians speculate that the pump may cause damage by altering blood flow or by releasing minute debris—fat particles, blood clots, bubbles—into the patient's bloodstream. Or perhaps red blood cells can be damaged as they journey through the machine, losing their capacity to carry sufficient oxygen to the brain and the rest of the body. In Gibbon's original design—which, with refinements, is often still used—the machine pumped blood through tubing that curved around rollers attached to rotating arms. As the arms turned in eggbeater fashion, the rollers pushed the blood through the tubing. Even in today's machines, contact with tubing can damage cells, or they may be sheared or crushed by the roller pumps.

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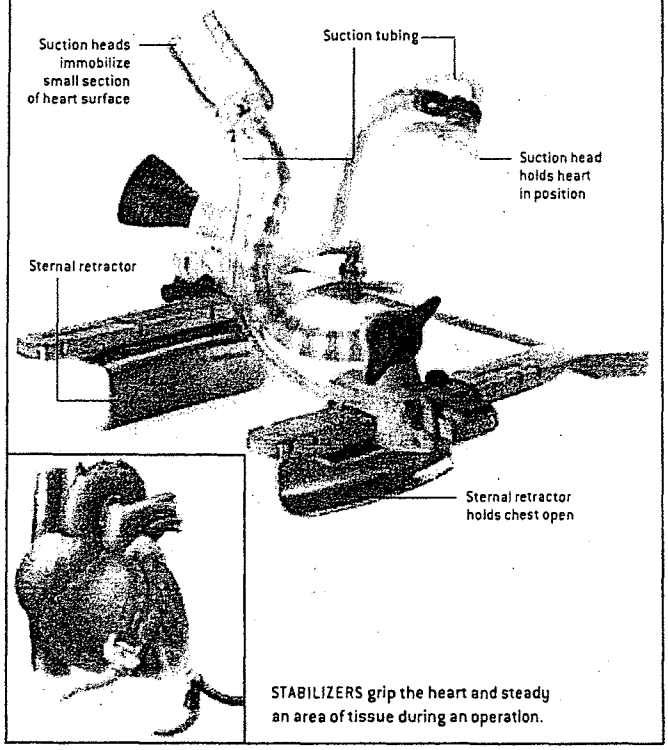
SURGEON'S HELPING "HAND"

OFF-PUMP SURGERY avoids the use of the heart-lung machine. Using suction, a local-tissue stabilizer (*inset*) immobilizes a section of the heart surface, permitting surgeons to work on the beating organ. Whether this procedure prevents pumphead symptoms is still unclear.



STABILIZERS grip the heart and steady an area of tissue during an operation.

MEDTRONIC (devices); ALICE Y. CHEN (illustration)

In Gibbon's models, blood dripped over a wire mesh to expose it to oxygen. But this direct contact often led to too much oxygen being absorbed and resulted in oxygen toxicity. Air bubbles were also common, and they could course through the machine and cause blockages in arteries. To minimize both problems, researchers eventually developed a closer approximation of the lung: a gas-permeable synthetic membrane.

Despite these and other improvements—such as polyvinyl tubing that prevents blood cells from adhering to it, centrifugal pumps that handle cells more gently, gas exchangers that reduce bubble size, and better temperature controls—an intractable problem remains. The entire system, and the surgery itself, can still generate a variety of debris. In addition to bubbles, clotted shards of blood cells, particles of corroded tubing and arterial plaque—all collectively called emboli—can make their way through the pump and cannulae and back into the body. The workings of the pump may loosen debris; some of these materials may also be released when surgeons clamp the aorta to connect the tubing. If the resulting emboli become trapped in small vessels, they can

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block blood flow in a manner akin to a mini stroke, starving or even killing nearby tissue.

Technology has all but eliminated the largest of these emboli. Screens of woven polymer thread placed in the machine filter out particles of 0.2 to 5.0 microns in size from the blood. Sutureless connectors reduce manipulation of the aorta, curtailing specks that might otherwise enter the bloodstream. Doppler ultrasound detectors search for errant microbubbles. If they do appear, the specialist who controls the machine, called the perfusionist, can adjust the flow of blood through the gas exchanger. But microemboli—one tenth the size of the detectable ones and numbering 200 to 300 an hour—may still escape discovery and potentially damage body or brain tissue.

Newman and others believe that these types of anomalies during surgery could cause cognitive problems in patients, but some researchers remain skeptical. For instance, a five-year study of 52 bypass patients at the University of Würzburg in Germany led by Wolfgang Müllges, published last fall in *Neurology*, found essentially no "global decline" in cognitive abilities compared with the baseline (presurgery) test performances of subjects. Nevertheless, a growing concern among surgeons about the machine has led to a demand for improvements in its technology and operation as well as a search for an alternative.

The Off-Pump Option

A "BEATING HEART," or "off pump," coronary-artery bypass may seem, as one surgeon puts it, "like cutting a gemstone on horseback," but new instruments can steady the steed while the rider works [*see box on opposite page*]. The stabilizers are akin to spidery legs with padded feet that grip the heart with vacuum suction. Although off-pump surgery may not be suitable for every situation (it was not in my case), it may be an option for some patients who cannot tolerate the stress of the heart-lung machine. Off-pump surgery now accounts for anywhere from 20 to 80 percent of heart surgeries, depending on the surgeon and the hospital. [For more information about this alternative procedure, see "Operating on a Beating Heart," by Cornelius Borst; SCIENTIFIC AMERICAN, October 2000.]

Off-pump surgery appears to reduce the number of larger emboli. In a 2001 study of 40 patients by B. Jason Bowles and his colleagues at St. Francis Hospital in Honolulu, Doppler ultrasound detected an average of only 27 emboli, compared with an average of 1,766 during on-pump operations. Any cognitive benefits, however, were unclear. Other studies have also produced less than definite—or even conflicting—results.

Experts say that all previous attempts to decide which operation is better have been hindered by studies with too few participants, differing designs or goals or with lingering complexities in assessing the quality of cognition—factors that make valid conclusions problematic. In 2007 the U.S. Department of Veterans Affairs will conclude an extensive $10-million investigation comparing on-pump surgery with off-pump procedures. Led by Frederick L. Grover, chair of the department of surgery at the University of Colorado Health Sciences Center in Denver, the study is monitoring the cognitive outcomes of 2,200 heart patients in 17 V.A. hospitals.

Bearing in mind that off-pump surgery is cheaper and that patients may be ready for discharge faster, is it time to retire the heart-lung machine? No one is ready to say that. Too many other factors that occur during and immediately after heart surgery could also be participants in cognitive decline: inflammation, hypoxia (insufficient oxygen delivery to tissues), lowered blood pressure, irregular heart rhythms, or body temperature that is too warm or too cold. Hilary P. Grocott, associate professor of anesthesiology at Duke, has discovered that patients in whom fever developed within the first 24 hours following coronary-bypass surgery tended to suffer an increased probability of cognitive decline after six weeks; no one is certain whether the fever causes the dysfunction or is a symptom of it.

The overarching question is, What part of what we do is significant with regard to perioperative effects?

The overarching question, Newman says, is "What part of what we do is significant with regard to perioperative effects? If different interventions and improvements can change the early results, we think we can [positively] change the slope of [cognitive] decline." Clearly, medicine will continue to search for better answers.

In the meantime, I have found ways to cope. I've planned shorter work periods. I've walked frequently and gotten off at a subway station many blocks from my destination in order to navigate the long way back. I've played the piano to focus my mind. More than a year and a half after my valve repair, I seem to be returning to life and intelligence as I knew it. Pumpheads, take heart: I wrote this article, didn't I? ■

MORE TO EXPLORE

Longitudinal Assessment of Neurocognitive Function after Coronary-Artery Bypass Surgery. Mark F. Newman et al. in *New England Journal of Medicine*, Vol. 344, No. 6, pages 395–402; February 8, 2001.

Cognitive Outcome after Off-Pump and On-Pump Coronary Artery Bypass Graft Surgery: A Randomized Trial. Diederik Van Dijk, Erik W. L. Jansen, Ron Hijman et al. in *Journal of the American Medical Association*, Vol. 287, No. 11, pages 1405–1412; March 20, 2002.

Protecting the Brain in Coronary Artery Bypass Graft Surgery. Daniel B. Mark and Mark F. Newman in *Journal of the American Medical Association*, Vol. 287, No. 11, pages 1448–1450; March 20, 2002.

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Discussion of POCD part of Cog Deficit

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Sunday June 22nd, 2003

Anesthesia, the aging brain, and the surgical patient

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SORRY to bring you disquieting news but we're not getting any younger. According to the recent US census, there were 4.2 million Americans age 85 or older in 2000, an increase of 30% since 1990, and those 75 to 84 numbered 12.4 million (*vs* 10 million in 1990). The trends in Canada are no different. Many of these people will require anesthesia and surgery. Therefore, inasmuch as the brain is the main target organ for anesthetic and adjuvant drugs, age-associated changes in the brain have important anesthetic implications for this patient population.

The aging brain: "normal" aging

I. Morphologic, physiologic, and biochemical changes

Average brain weight and neuronal number inevitably decline with age beginning in young adulthood and the decline accelerates after age 60.[1] As a result, the ratio of brain volume to skull volume, which is normally about 95%, declines to about 80% in nonogenerians and ventricular volume triples. However, quantification of the extent of neuronal loss with age is imprecise and complicated by technical factors and substantial regional variability. Indeed, newer data indicate the magnitude of age-related neuronal loss is much more modest than the 15% to 50% estimates of earlier studies. Even so, age also affects the business end of a neuron – the dendrites and synapses. There are age-associated decreases in neuronal size, loss of complexity of the dendritic tree, and a reduced number of synapses.[1] In contrast, the physiology of the cerebral circulation appears to be remarkably normal in the healthy aged. Absolute global cerebral blood flow (CBF) is decreased about 10–20%, not because of "hardening of the arteries", but because there is less brain mass to perfuse.[2] Therefore, the lower CBF appears to be a consequence of reduced metabolic demand, not a cause of it. In general, although not as thoroughly investigated as one might imagine, CBF and $CMRO_2$ remain tightly coupled in aging, autoregulation seems to be preserved, and responsiveness to CO_2 and hypoxemia are probably reasonably normal. Finally, numerous neurotransmitter systems are altered during aging.[3] For example, dopamine uptake sites, transporters, and levels are reduced, as are cortical serotonergic, α_2 and β_1, and GABA binding sites. Markers of central cholinergic activity also decrease, which is a finding of particular significance since failure of cholinergic neurotransmission is a central feature of Alzheimer's disease (AD).[4] It would be safe to say, therefore, that nearly every aspect of the brain changes with age.

But all is not bad. There is evidence, for example, that dendritic complexity and growth can increase in cognitively normal octogenarians,[1] suggesting that neuronal mechanisms crucial for learning and memory are retained in the aged but healthy central nervous system (CNS). Moreover, counter to what many of us learned in medical school, the adult brain makes new neurons and this neurogenesis continues into late old age.[5] What's more, these new neurons get incorporated into memory circuits.[6] As one can imagine, there is much excitement about this in the neuroscience world because it provides hope that

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enhancing neurogenesis might be a way to attenuate or reverse age-related cognitive decline. Consistent with this, there is evidence that simple things like physical exercise and intellectual activity maintain and improve cognitive functioning in elders.[7] So, as it turns out, the adage "use it or lose it" is apt even — or especially — for the brain!

II. Cognitive changes

What does all this mean for brain function? Intellectual decline does not invariably accompany aging but it is common. Approximately 5% of persons over age 65 suffer from dementia, which is always a consequence of serious illness, and more subtle cognitive impairment is detectable in nearly two-thirds of all "normal" older people.[8] Such changes can be classified as either disease-related secondary impairment (e.g., related to alcoholism or Alzheimer's) or as primary cognitive decline. However, the line between the two is often hazy.

There are some consistently observed changes in CNS function with "normal" aging.[8] There is a slowing of reaction time and cognitive processing such that there is an inverse relationship between age and speed of motor performance. The more complex the task, the slower the response, presumably due to decreased sensory sensitivity (e.g., reduced auditory acuity) as well as slowed central processing of information. Deterioration in "fluid" intelligence (i.e., the ability to dynamically evaluate, accommodate, and respond to novel environmental events) also occurs. However, some tests used to assess intelligence are influenced by motor speed, so slowed reaction time confounds the assessment. On non-timed tests, vocabulary, verbal information, and comprehension are well maintained. "Crystallized" intelligence (i.e., accumulated knowledge) is also relatively stable into the seventh decade of life. Finally, short-term memory is often impaired. Between 30 and 50% of elders report memory complaints. Much of this impairment is in working memory - which requires not only retention but also manipulation of information. Thus, the ability to store recently processed information while simultaneously acquiring new data is compromised.

Having said all this, it is important to realize that the cognitive decline associated with normal aging is modest and variable. Moreover, as mentioned earlier, it is influenced in a positive way by physical activity and intellectual engagement.[7] In fact, many active elderly individuals remain stable on measures of cognitive performance into their 80s, and even outperform younger but inactive persons on some tests.[8] Consequently, there is no such thing as a "typical" older person from this perspective, making studies of this population difficult because chronological age is often not a predictor of cognitive capability.

Pathological brain aging: dementia

Dementia is a chronic, progressive decline in intellectual function. It can be caused by numerous systemic diseases and neurologic disorders (e.g., stroke, Parkinson's disease) but AD is both the most common cause and a prototype of pathological brain aging.[9] The diagnosis of dementia requires evidence of decline from a higher cognitive level, multiple cognitive defects, among which memory impairment is essential, and the defects must interfere with social or occupational functioning. Criteria stipulate a duration of more than six months and, to exclude delirium, that consciousness be unaltered.

AD is frighteningly common. Ten to 15% of persons older than 65 yr develop AD and by age 85 about 30–50% will be afflicted. The diagnosis is one of exclusion and requires demonstration of neurofibrillary tangles, extracellular amyloid deposits, and neuritic plaques in the brain at postmortem examination.[3,10] Growing evidence suggests these changes may be seminal events in the pathogenesis of AD and not simply markers of it.[11] The brain changes seen in normal aging are present in an exaggerated form in AD. Thus, loss of brain mass occurs at a rate 2.5 times normal in AD[12] and hypofunction of cholinergic neurotransmission is more pronounced, particularly in areas associated with memory and cognition. This cholinergic deficiency is a hallmark of the disease but may not, as once thought, explain the memory deficits because there is no such deficiency in the patient with mild AD.[13] The list of other potential mechanisms of AD is lengthy and includes complement mediated inflammatory responses, oxidative damage to proteins and DNA, and alterations in the hormonal milieu.[10,14,15] Although some of these are being investigated as potential sites for future therapeutic intervention there is as yet no "magic bullet" for AD.

Thus, medical therapy has little or no effect on progression of AD but aims to modify the symptoms. The mainstay of treatment still is anticholineasterases such as tacrine and donepezil,[16] but vitamin E, steroids, and estrogen also have advocates.[10,14] There is some evidence that these drugs may improve memory, attention deficits, and symptoms of AD such as apathy, agitation and hallucinations but none seem to prevent the disease or slow progression.[14] In this regard, probably the most exciting newer

developments in AD treatment and prevention revolve around immunization against ß amyloid and use of anti-inflammatory agents.[14,15] Initial animal work with ß amyloid immunization showed a marked decrease in ß amyloid deposits in brain and a corresponding improvement in cognitive performance. Based on this, a human trial was initiated but was recently stopped prematurely because some patients developed an encephalitic reaction to the antigen. Because the approach seems promising, the search is now on for a different antigen that will prove safer and effective.[14] However, anti-inflammatory agents may be the best of what's available today. It turns out that in addition to anti-inflammatory effects, some non-steroidal anti-inflammatory drugs (NSAIDS; ibruprofen but not naproxen or aspirin) decrease ß amyloid production.[15] Consistent with this action, a few epidemiological and small clinical studies suggest regular use of certain NSAIDS reduces the risk of developing AD. Who knows, maybe all those anti-inflammatory agents we take for age-related aches and pains help our brain as well as our muscles and joints "feel" better!

Aging, anesthesia, and postoperative cognitive dysfunction (POCD)

It has been suspected for at least 48 years that some elderly patients may develop dementia following anesthesia and surgery.[17] Concern that the elderly brain "takes a hit" during general anesthesia and surgery is better justified today but we're still far from sure about the etiology and significance of the problem.[18] This is because we still know so little about the effects of anesthetics on the aged brain. The age-associated structural and functional changes described above imply, however, that the aged CNS has reduced functional reserve and the current assumption is that this makes the elderly more vulnerable to the development of POCD.

I. Delirium

Delirium, defined as acute disturbance in consciousness and cognition that tends to fluctuate throughout the day,[19] is the most common form of perioperative CNS dysfunction. It is twice as common in the elderly, occurring in 10–15% of elderly general surgical patients and as many as 30–50% of those undergoing orthopedic or cardiac surgery.[20,21] The mechanism is unknown but one hypothesis is that it may be related to further decreases in already low levels of neurotransmitters such as acetylcholine. Other etiologic or predisposing factors include hypoxia, drug interactions (particularly anticholinergics, benzodiazepines, and tricyclic antidepressants), alcohol abuse, pre-existing depression or dementia, and metabolic disturbances. Delirium is more than an annoyance; it is associated with longer hospital stay, higher mortality, and may even be a marker for subsequent development of dementia.[22]

Several anesthetic agents, including ketamine, benzodiazepines, and even propofol, can produce delirium but in the elderly the strongest association is with the anticholinergic agents atropine and scopolamine.[19] This is presumably because of the baseline cholinergic deficiency and suggests that with the exception of glycopyrrolate, which does not cross the blood brain barrier, medications with anticholingeric properties should be used sparingly in these patients. Curiously, however, the type of anesthesia does not influence the risk of developing delirium. Specifically, the incidence of postoperative confusion appears to be similar regardless of whether spinal, epidural, or general anesthesia is used.[23] Moreover, postoperative epidural analgesia has proven no better than the *iv* route from this point of view.[21]

What can one do about perioperative delirium? First, identify patients at high risk[24] and avoid or minimize some of the medications just mentioned. In addition, consider obtaining a preoperative geriatric consultation since there is some evidence that such consultation markedly reduces the incidence of delirium, particularly in high risk patients.[25] Second, treat remediable causes of delirium such as hypoxemia or sepsis. Many of the factors contributing to delirium in the hospital setting are not modifiable (e.g., age of patient, type of surgery) so it is especially important to manage those that can be modified. Lastly, when prevention fails, one can manage the symptoms with agents such as haloperidol or atypical antipsychotics such as olanzapine.

II. Prolonged POCD

There is now substantial evidence that many elderly patients experience cognitive deterioration postoperatively. In a prospective, randomized trial of general *vs* epidural anesthesia with sedation for total knee replacement in patients > 70 yr of age, cognitive performance, as assessed with psychometric tests, was worse than the preoperative baseline in 4–6% of patients six months after anesthesia and surgery.[23] However, this study lacked a control group for the effects of time or hospitalization alone. More

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convincing is a large, prospective, controlled international study[26] that demonstrated a cognitive deficit in 9.9% of patients three months postoperatively whereas only about 3% of the age-matched controls were similarly impaired. Among patients over 75 yr of age, 14% had a persistent cognitive deficit after general anesthesia and surgery.[26] Note that although postoperative cognitive impairment is not unique to the elderly,[27] it does seem to be more severe and longer lasting in them. It is also important to recognize, however, that deficits were defined by performance on psychometric tests and that the social or economic significance of the impairment, if any, has not been well examined. Nevertheless, it is clear that prolonged postoperative cognitive impairment is both real and more common than previously realized. The good news is that patients seem to recover completely within one to two years or less, but this is based on data from a small subgroup of patients.[28]

The key question, of course, is what causes it? The short answer is that no one is sure. One old and intuitive hypothesis is that perioperative hypotension and/or hypoxia cause or exacerbate POCD. Like most simple explanations for complex problems, however, this is probably incorrect in most cases. In fact, the largest study of POCD in elderly patients[26] shows that neither perioperative hypotension [mean arterial pressure (MAP) < 60% for ≥ 30 min] nor hypoxia ($SpO_2 \leq 80$ for more than two minutes) are predictors of cognitive decline three months postoperatively, a finding that concurs with older work. Moreover, in a direct test of the influence of controlled hypotension on cognitive outcome in elderly patients under epidural anesthesia, no early or long-term adverse effect of hypotension (MAP 45–55 mmHg) was observed.[29] There could be some patient or procedure – specific causes or risk factors such as a genetic predisposition[30] or cerebral emboli, respectively. In fact, cerebral emboli have been detected during total knee replacement using transcranial Doppler.[31] Finally, there may be factors associated with surgery itself such as stress, immobility, social isolation, and/or inflammation. These are reasonable hypotheses since each factor can influence cognition and is affected by surgery and/or hospitalization but there is presently no direct evidence that they contribute to POCD.

One factor that has received little attention is general anesthesia itself. There are many reasons to speculate that general anesthesia might contribute, not the least of which is that anesthesia is obviously a profound form of CNS dysfunction. However, clinical evidence for this is sparse. First, some data indicate the risk of prolonged POCD is similar with regional and general anesthesia. Thus, in elderly patients undergoing total knee replacement, the frequency of cognitive impairment six months postoperatively was similar (4–6%) between epidural and general anesthesia groups.[23] This is consistent with previous work indicating that shorter term postoperative (one to seven days) cognitive performance in the elderly is typically no better after spinal or epidural than general anesthesia. However, *iv* sedation was used to supplement the regional technique[23] and patients also had a surgical procedure, making it difficult to isolate the influence of anesthesia itself. To circumvent this problem, we have investigated the long-term effects of general anesthesia on learning and memory in rats and, interestingly, found that isoflurane-nitrous oxide anesthesia without surgery impairs spatial learning in aged rats for at least three to four weeks.[32] Because the agents were long cleared from the brain by the time behavioural testing was begun, these data imply that anesthesia itself alters brain regions and neurochemical cascades mediating memory and that this pharmacologic footprint lasts considerably longer than previously recognized. Accordingly, the data suggest that general anesthesia could be a factor in POCD.

In conclusion, the elderly brain is very different from that of young or middle-aged persons both in terms of anatomy and neurochemistry and function. The cognitive consequences of these age-related changes are highly variable and can be influenced by general health as well as mental and physical activity. Delirium and dementia are the result of disease processes that can be unmasked or exacerbated by hospitalization and surgery. However, even apparently cognitively intact elderly patients may suffer POCD. The etiology of POCD is likely to be multifactorial, possibly including a contribution from anesthesia itself, but because the mechanisms are still uncertain it is difficult to identify prevention or treatment strategies. In particular, there is presently no scientific basis for recommending (or avoiding) a specific anesthetic agent or technique in this regard. This may change as further research is conducted on this relatively newly identified and interesting entity. In the meantime, it is reassuring that the prognosis for recovery from POCD appears to be good.

Footnotes

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Why **Postoperative Cognitive Impairment** is Still the Primary Challenge in Geriatric Anesthesia

BY TERRI MONK, MD

ALTHOUGH RESEARCHERS ARE CHANGING THE SHORT-LIVED CONCEPT OF "TOO OLD TO OPERATE," FOR SOME SENIORS, POST-SURGICAL COGNITIVE IMPAIRMENT CONTINUES TO BE PROBLEMATIC.

At present, the number of seniors aged 65 years and older is approximately 35 million in the United States alone. Older adults represent the fastest growing proportion of the population, and their numbers are expected to double to nearly 75 million in the next 50 years. Currently, elders undergo one-third of the 25 million surgical procedures performed annually in the United States and consume one-third of all health expenditures. These numbers will dramatically increase in the future. This rapid growth in the senior population has serious implications for the anesthesiologist, whose practices will increasingly comprise a larger proportion of geriatric anesthesia cases.

It is hard to believe that there was a time not so long ago when older patients were denied surgery solely on the basis of his or her advanced age. Much of the reluctance to operate on older patients was based on a review, published in the Lancet in 1955, of the cerebral effects of anesthesia on senior patients. It is interesting to note that the author, Dr. P.D. Bedford, defined senior as 50 years or older. He determined that 10% of his patients had experienced mental deterioration after surgery, thus concluding that the cognitive problems were probably related to anesthetic agents and hypotension. The final recommendation of this work was that "operations in senior patients should be confined to unequivocally necessary cases." Today, improvements in surgical techniques, anesthesia and intensive care practices have made surgery in patients over the age of 65 years possible. Age is no longer a contraindication to any type of surgery.

> "Anesthetic agents affecting the release of central nervous system neurotransmitters... could potentially impair memory...in senior patients."

POSTOPERATIVE COGNITIVE DISORDERS IN SENIORS

Despite improved operative outcomes in seniors, a significant proportion of these patients experiences postoperative cognitive problems. The most common forms of postoperative cognitive impairment are delirium and postoperative cognitive dysfunction (POCD). The socioeconomic implications of postoperative cognitive decline are unknown, but we do know that abrupt declines in cognitive function in senior individuals living in the community often lead to a loss of independence, withdrawal from society, and death.

Postoperative delirium is common in patients after surgery, with the overall incidence for all age groups estimated to range from 5 to 10% and for seniors from 10 to 15%. Delirium is characterized by fluctuating levels of consciousness, a disturbed sleep-wake cycle, and altered psychomotor activity. Delirious patients often exhibit disorders of cognitive function, thinking, perception, and memory. The etiologic factors associated with this disorder include advanced age, polypharmacy, cerebral damage, surgery and anesthesia, hypoxia, sepsis, sensory deprivation or overload, electrolyte disturbances, pain, and endocrine or metabolic disorders. Delirium is a very costly disorder and Medicare expenditures associated with the diagnosis and treatment of this problem exceed $8 billion per year in the United States.

POCD has been demonstrated in 20 to 60% of patients following coronary artery bypass graft (CABG) surgery and 10 to 16% of senior patients following major, noncardiac surgery. POCD is a "deterioration of intellectual function presenting as impaired memory or concentration." The clinical features of this disorder range from mild forgetfulness to permanent cognitive impairment resulting in a loss of independence.

Little is known about the etiology of POCD and the risk factors for this problem in the aging population. It is likely, however, that the etiology of POCD in senior patients is multifactorial and may include the preoperative cognitive status of the patient, intraoperative events related to the surgery itself, and anesthetic agents.

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PATIENT RISK FACTORS

An emerging concept in neuropsychology and clinical geropsychology espouses a functional cliff hypothesis of cognitive decline and dementia in later adulthood. This is essentially a threshold model, which holds that, with increasing age and normal cognitive declines, individuals move closer and closer to a level that might be considered "impaired" or "demented." As this threshold is approached, individuals enter a high-risk phase that might be considered "preclinical dementia." For patients in this preclinical state, research suggests that the sudden onset of even mild neurological trauma, such as surgery and anesthesia, may move people over the clinical threshold and into the range of functioning that might be classified as "impaired."

There is increasing evidence that CABG surgery can produce long-term cognitive decline. One possible explanation for POCD after CABG is that embolic material is released during crossclamping of an aorta affected by atherosclerosis; this embolic material then enters the cerebral vessels during surgery, resulting in occlusion of both large and small vessels. The incidence of postoperative neurocognitive deficits has been shown to correlate with the number of microemboli detected during CABG. Systemic and cerebral emboli can occur during orthopedic surgery and may represent a possible mechanism for postoperative cognitive decline after noncardiac surgical procedures.

Exposure to anesthetic agents has been suggested as a possible cause of postoperative cognitive dysfunction in senior patients. Anesthetic agents affecting the release of central nervous system neurotransmitters, such as acetylcholine, dopamine, and norepinephrine, could potentially impair memory, especially in senior patients. Inadequate cerebral perfusion and oxygenation during surgery may also be important causes of POCD.

Patients with postoperative cognitive problems need long-term follow-up to determine the mechanisms responsible for this complication and interventions to minimize or prevent these problems. Under the direction of our chairman, Dr. Mark Newman, the Department of Anesthesiology at Duke is leading research efforts in cognitive outcomes research. ▲

Terri Monk, MD, is a professor of anesthesiology at Duke University Medical Center and at the Veterans Affairs Medical Center. She has garnered significant NIH and NIA support to evaluate the mechanisms responsible for intellectual impairment following major, noncardiac surgery. Dr. Monk represents surgery and related medical specialties for the American Geriatric Society. She was recently elected president of the Society for the Advancement of Geriatric Anesthesia (SAGA).

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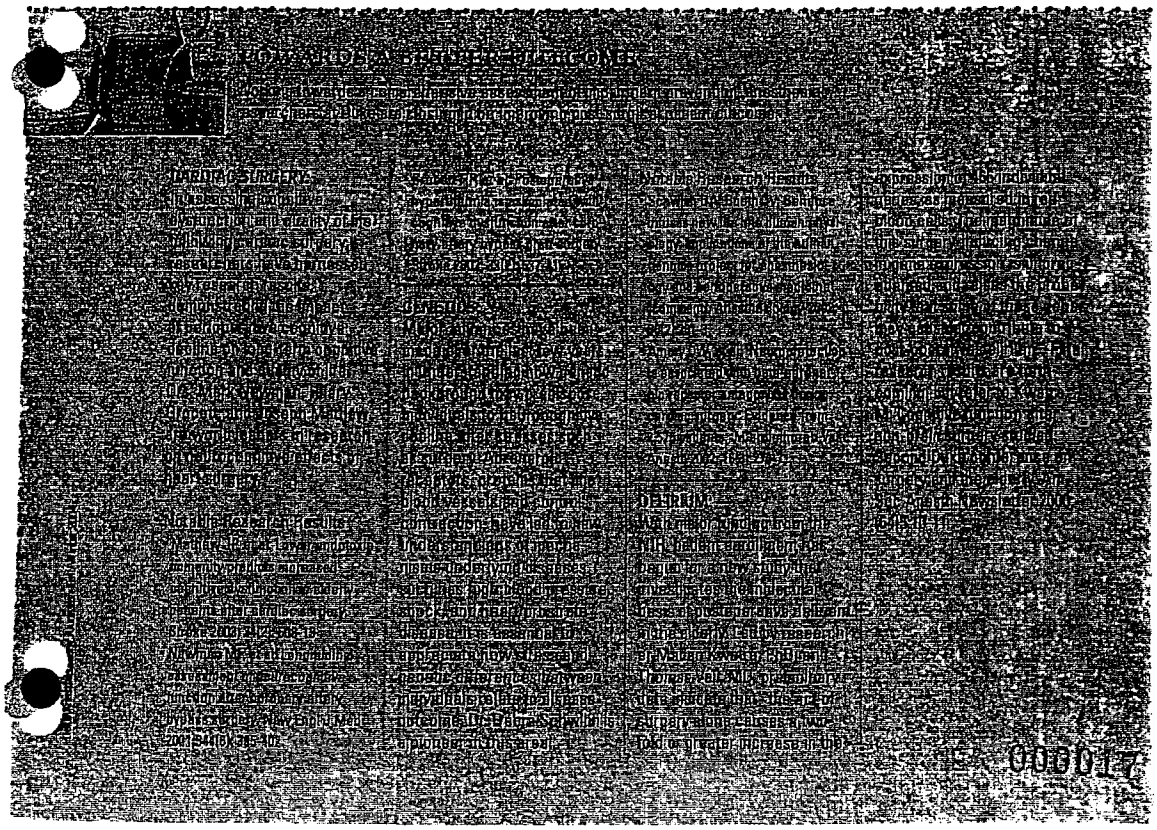

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Subtle Neuro Cognitive Deficits

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Controversies in Off-pump Coronary Artery Surgery

John Pepper, M.Chir, FRCS

Motivated by a desire to reduce the morbidity of a well-established and effective procedure for coronary artery disease, up to 25% of coronary artery bypass operations are being performed without the use of a heart-lung pump. Concerns remain about the quality of the coronary anastomoses and the completeness of revascularization. Randomized trials have not revealed the significant reduction in morbidity or mortality that the early enthusiasts had hoped for. Yet a number of non-randomized studies have shown clinical benefit from the avoidance of an extracorporeal circulation, but these have been criticized for potential bias in patient selection and management.A majority of surgeons have not yet adopted this technique and are waiting for the accumulation of more evidence.

Keywords: Coronary artery bypass; Coronary disease/surgery; Postoperative complications; Vascular patency; Risk factors; Morbidity; Mortality

Coronary artery bypass surgery remains an established form of treatment for coronary artery disease. The majority of coronary surgical procedures are performed for multiple vessel disease. In the United Kingdom, 96% of all coronary bypass surgery involved two or more grafts during the period from 2001 to 2003.(1) Results following multiple vessel coronary surgery are excellent with 2-year re-intervention rates of only 6% and a cumulative risk of death and myocardial infarction of 12% over 2 years post-surgery.(2)

Although the mortality rate of coronary artery surgery is low, at approximately 2%,(1) it is age related and rises to over 6% in those over 75 years of age. This benefit is offset by a complication rate of 20% to 30%. In addition, there is a 2 to 3 month period of recovery from the fatigue that usually follows any major operation. The recent observation of neurocognitive impairment in up to 42% of patients 5 years after surgery has aroused additional concern.(3,4) The functional significance of the neurocognitive findings and the relative contribution of aging, atherosclerotic disease, and surgical procedures to the measured impairment remain unknown.

Patients and their physicians desire a low morbidity procedure, preferably without general anesthesia and in an outpatient setting. These factors together with the avoidance of the adverse consequences of cardiopulmonary bypass have been the driving force behind the development of percutaneous coronary intervention (PCI). Recurrent angina and the need for subsequent re-intervention are more frequent after PCI than after conventional coronary artery bypass surgery, a performance gap that is likely to be narrowed by the emergence of drug-eluting stents.

PCI has had a dramatic effect on coronary artery bypass surgery, arresting the dramatic growth of surgery in the 1980s and shifting the attention of surgeons to patients with more advanced coronary disease and extensive coexisting conditions. This has motivated surgeons to refine coronary revascularization techniques in order to maximize clinical effectiveness, limit costs, and reduce invasiveness.

In contrast to the small incision approaches, off-pump coronary artery bypass surgery through a median sternotomy has gained clinical acceptance and in many centers constitutes 20% to 30% of the total volume of coronary surgery. Creation of the distal anastomoses is facilitated by the use of stabilizers that reduce the motion of the heart in an area of approximately 2 cm(2). The argument in favor of this approach is to avoid the historical, well-documented adverse effects of cardiopulmonary bypass on end-organ function: coagulation, renal impairment, lung injury and, most important in the ageing population, avoidance of stroke, delirium, and more subtle neurocognitive changes. The counter-argument is that potential suboptimal exposure and hemodynamic instability during off-pump procedures could produce inferior short- and long-term outcomes.

Clinical Outcome

The distinction between on-pump and off-pump coronary artery surgery is over-simplistic since both methods encompass a range of techniques. On-pump coronary surgery may be performed on the beating heart without the need for a cross-clamp and at various temperatures. Even when an aortic cross-clamp is employed, myocardial protection can be achieved by a wide variety of cardioplegic techniques or by non-cardioplegic methods. The use of composite arterial grafting can minimize aortic manipulation in on-pump surgery and eliminate it completely in the off-pump situation. Calafiore et al.(5) have shown that avoidance of aortic

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manipulation is at least as important as the avoidance of cardiopulmonary bypass in reducing the risk of brain injury.

Early randomized studies performed on low-risk patients have shown a shorter length of stay, a reduced use of transfusion products, a reduced incidence of coagulopathy, and a lower frequency of atrial fibrillation in patients who undergo off-pump coronary artery surgery.(6-8) Although the use of blood products was reduced in the off-pump group (3% versus 13%) and the release of creatine kinase-MB (CK-MB) isoenzyme was 41% less in the off-pump group, there were no differences in the perioperative complication rates. There was no difference in outcome in the first 1 to 3 years after surgery between off-pump and standard groups.(6,7) A meta-analysis of 6 studies including 558 patients randomized to "on-pump" and 532 to "off-pump" found no significant difference in the combined end-point of death, stroke, or myocardial infarction.(9) However, there is some evidence that off-pump surgery increases the risk of recurrent angina and the need for re-intervention, suggesting poor graft quality or incomplete revascularization.(10,11) In patients with three-vessel disease, the completeness of revascularization is a significant determinant of the relief of symptoms over a 5-year period.(12)

Mack et al.(13) conducted a retrospective review of a 5-year experience with 12,540 patients who underwent isolated coronary bypass grafting; 15% of these patients (n=1,915) underwent off-pump surgery. A gradual increase in the percentage of coronary operations performed off-pump was observed from 1.2% in 1995 to 34.1% in 2000. Individual surgeon adoption rates increased from 1% to 96% by the end of the study period and the mortality rate in off-pump surgery decreased to 3.2% compared with an overall observed mortality rate of 4.0% in the 5 years before the start of their off-pump experience. There was a significant difference in observed mortality between the off-pump and on-pump groups (1.9% versus 3.5%, P<0.001), despite a higher mean predicted risk among the patients in the off-pump group (3.13% versus 2.8%, P<0.004). Furthermore, there was less morbidity in the off-pump group as evidenced by a reduced need for blood products (28.5% versus 54.7%, P=0.0001), prolonged ventilation (5.83% versus 10.93%, P=0.001), and a shorter hospital stay (6 days versus 7 days, P=0.001). One of the questions this study was designed to answer was whether off-pump surgery can be safely incorporated into a surgical practice and be performed by most surgeons. In the Dallas practice studied,(13) there were 22 surgeons of whom 6 were enthusiastic early and persistent adopters of the off-pump approach and who carried out 73% of all off-pump procedures. Eight of the 22 surgeons did fewer than 10 off-pump operations per year. In the 5-year period before the introduction of off-pump procedures, the composite mortality rate of coronary artery surgery for the 3 surgeons with the lowest off-pump adoption rate was 38% greater than the composite mortality rate of the 3 surgeons with the highest rate of off-pump surgery adoption (4.0% versus 2.9%, P<0.001). As Bonchek points out in his accompanying editorial,14 off-pump surgery was being performed predominantly by the most accomplished surgeons. Although off-pump surgery can be safely incorporated into a large practice, it seems unlikely that it will be used on a regular basis by most surgeons. The use of off-pump coronary artery bypass surgery is not widespread and is estimated by the Northern New England Cardiovascular Disease Study Group to be only 8.8%.(15)

In smaller surgical units, unless there is a core of enthusiasm, it seems unlikely that many surgeons will adopt the technique. The exponential rise in the use of PCI with drug-eluting stents gives rise to a situation in which there is a dearth of low-risk patients requiring double or single bypass grafts and who might be considered for off-pump surgery early in a surgeon's experience. An alternative approach is to adopt the technique wholesale after a period of intense training or 're-engineering' as pursued by Sergeant and colleagues.(16)

Mack and colleagues(17) recently reported a large retrospective study encompassing four centers over a 3-year period. The study examined 17,401 isolated coronary artery bypass procedures, of which 7,283 (41.9%) were off-pump and 10,118 (58.1%) were on-pump. Patients were selected for an off-pump procedure on one or more of the following factors: female gender (55% versus 44%), pre-existing renal failure (57% versus 43%), and repeat procedure (52% versus 47%). The operative mortality rate was 1.9% for off-pump and 3.5% for on-pump (P<0.001). To counter the criticism of case selection, 11,548 patients were matched by propensity scoring which produced operative mortality figures of 2.8% off-pump versus 3.7% on-pump (P<0.001).

The use of an on-pump technique was predictive for mortality in repeat procedures, females, and patients over 75 years of age. These authors also found that the use of an off-pump technique was associated with a significantly reduced morbidity. Specifically, there were significant reductions in: the use of blood transfusion (32.6% versus 40.6%, P<0.001), the incidence of stroke (1.45% versus 2.1%, P<0.002), and the incidence of postoperative renal failure (2.6% versus 5.2%, P<0.001). There were reductions in pulmonary complications (4.1% versus 9.5%, P<0.001), the incidence of postoperative atrial fibrillation (21.1% versus 24.99%, P<0.001), and gastrointestinal complications (3.6% versus 4.8%, P<0.02).

The midterm results of a retrospective analysis of off-pump versus on-pump coronary artery surgery were recently published by Sabik et al.(18) The analysis compared 481 patients who underwent off-pump coronary artery surgery with 3,231 who received their grafts on-pump. Propensity matching was used to match 406 patients from each group. Follow-up was 95% complete. Four-year survival was 87.5% after off-pump and 91.2% after on-pump coronary artery bypass grafting (P=0.2). Likewise, there was no significant difference between the groups in freedom from myocardial infarction (92.6% off-pump versus 95.7% on-pump), freedom from PCI (94.3% off-pump versus 95.5% on-pump, P=0.9), or freedom from surgical re-intervention (98.1% off-pump versus 99.0% on-pump, P=0.4). Thus the mid-term outcomes were equivalent, but, interestingly, fewer bypass grafts in the off-pump patients did not decrease survival or increase the incidence of ischemic events.

A recent meta-analysis conducted by van der Heijden et al.(19) examined 18 randomized trials involving 1,584 patients. Favorable results were found for off-pump coronary artery bypass surgery with the combined endpoint of mortality, stroke, and myocardial infarction, although none of the risk reductions reached statistical significance. As the risk of mortality in both off-pump and

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on-pump coronary surgery is around 1%, it is unlikely that a significant difference in mortality will be found in patients who are generally low risk. To find a mortality difference of 0.1%, very large trials of >400,000 patients will be required. Such trials are an enormous and expensive undertaking and, therefore, unlikely to happen.

Completeness Of Revascularization And Graft Patency

In observational studies published before 2000, the number of grafts performed off-pump tended to be less than that on-pump.(20,21) In the recent era this situation has changed. Completeness of revascularization has been reported in only four randomized trials. Czerny et al.(22) reported significantly reduced completeness of revascularization for off-pump versus on-pump, whereas Khan et al.,(23) Puskas et al.,(24) and van Dijk et al.(25) reported no difference. The use of an index of completeness (number of grafts performed/number of grafts planned) is a more precise measure and was similar in the two groups.(23,24)

In a study of 281 low-risk patients randomly assigned to either off-pump or on-pump surgery, Nathoe et al.(26) reported that off-pump and on-pump coronary bypass surgery were equivalent with respect to perioperative and 1-year survival and freedom from stroke, myocardial infarction, and coronary re-intervention. Postoperative angiography was carried out in 64% of the patients one year after operation. The overall patency rates (Fitzgibbon grade A or B) were 93% in the on-pump group and 91% in the off-pump group (table 1). Khan and colleagues(23) showed a significant reduction in graft patency (98% versus 88%) in an off-pump study group. In this randomized trial involving 103 patients, 80% received follow-up angiography 3 months after surgery. The majority of the reduced patency occurred in the radial grafts. These results may reflect the experience of a learning curve, as the surgeons had a 2-year experience preceding the trial during which 13% of their coronary operations had been performed off-pump. Half-dose heparinization at 150 mg/kg was used in this study rather than the full-dose typical of the on-pump technique, and may have played a role in the lower patency rates in the off-pump group.

Table 1. Graft patency after off-pump coronary surgery.

Author	N	% Cohort	Patency on-pump (%)	Patency off-pump (%)	Absolute difference (95% CI)
Nathoe[26]	281	25	93	91	2.0 (5.5-10.4)
Khan[23]	103	80	98	88	10 (3.8-16.2)
Puskas[24]	186	81	95.8	93	2.2 (6.1-1.7)

Puskas(24) reported a single surgeon series of 200 patients in which 81% of 1-year survivors (78% of the enrolled patients) underwent coronary angiography 1-year postoperatively. The overall patency rate was 95.8% on-pump and 93.6% off-pump, an insignificant difference (table 1). Patency between groups was similar at 1-year among all arterial conduits, all vein grafts, and among grafts to all regions of the heart. This is clearly an excellent series, but as a single surgeon experience it may not be generalizable to all surgical practices.

Procoagulant activity may be increased after off-pump surgery.(27,28) This may explain the few isolated reports of reduced vein graft patency after off-pump operations.(29,30) Current practice in experienced centers is to use full-dose heparinization (300 mg/kg) supplemented throughout the procedure and to use aspirin during and after the operation. Because of the hypercoagulable state after off-pump surgery, it may be wise to use postoperative clopidogrel for the first 3 months.(31)

Risk Of Cerebral Injury

Patients of advanced age and those with other risk factors for neurological complications are being referred for coronary artery surgery in increasing numbers. The challenge persists to get these patients safely through their operation without cerebral injury. At the outset, it was hoped that avoiding cardiopulmonary bypass would markedly reduce the stroke incidence, but evidence to support this hope has been slow to emerge. Early studies failed to show a benefit for off-pump surgery, probably because the numbers of patients enrolled were too small.(32) Other studies have shown a stroke benefit, particularly in patients with known cerebrovascular disease.(21,33,34)

Three randomized trials have not firmly established a significant difference in neurological outcomes between off-pump and on-pump coronary artery surgery.(6,35,36) These patients were not stratified according to high-risk aortic disease, so the relative value of off-pump surgery in such patients is not known. But in patients with significant ascending aortic atheromatous disease, it would seem wise to consider an "off-pump" and "no-touch aortic" technique.

Sergeant and colleagues(16) analyzed a consecutive series of 3,333 patients undergoing coronary artery surgery (1,593 on-pump and 1,740 off-pump). They found a trend towards a 60% reduction of stroke, which after risk adjustment, fell below the level of significance for the total population, but the benefit persisted for patients with severe stenosis of the internal carotid artery. In a meta-analysis of 9 observational studies,(37) off-pump coronary surgery was associated with a significantly lower incidence of stroke in patients over 70 years of age as compared to the on-pump technique (1% versus 3%), with an odds ratio of 0.38% (95% CI = 0.22 to 0.65). The incidence of atrial fibrillation was examined in another meta-analysis of eight non-randomized studies, which

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included 3,017 patients (764 off-pump and 2,253 on-pump).(38) The incidence of postoperative atrial fibrillation was significantly less in the off-pump compared to on-pump (odds ratio 0.70; 95% CI = 0.56 - 0.89) in an elderly population over 70 years of age. If this finding can be confirmed by a large-scale randomized trial, it would have major implications for the operative strategy in coronary surgery of the elderly.

Why should atrial fibrillation be more frequent in on-pump versus off-pump patients? There are several potential mechanisms. Ischemia with off-pump is regional, whereas with on-pump it is usually global, which may have a detrimental effect on the atrial myocardium resulting in the generation of arrhythmias. Left ventricular segmental wall motion and blood supply to the sub-endocardium and interventricular septum have been found to be better in patients undergoing on-pump compared to off-pump surgery.(39) This may be important in patients with impaired left ventricular function as atrial dilatation may occur increasing the risk of atrial fibrillation. During off-pump surgery there is less manipulation of the right atrium, as there is no need to insert a cannula. Finally the inflammatory response, which can occur with cardiopulmonary bypass, may result in lung injury and renal injury. The resulting disturbance in acid-base balance and electrolytes may produce atrial irritability leading to atrial fibrillation.

A more common form of cerebral injury is cognitive dysfunction, which affects 40% to 60% of cardiopulmonary bypass patients, but resolves in an overwhelming majority by the third postoperative month.(40) Although it has no obvious immediate impact on clinical outcome, it does correlate with late impairment in quality of life.(5) A third form of cerebral injury is delirium or encephalopathy, which is often thought to be self-limiting. Taggart(40) points out that this is unjustified complacency as revealed by three recent prospective studies(3,41,42) (table 2). A recent prospective study of delirium in a group of 16,000 cardiac surgical patients over a 5-year period has been reported by Bucerius et al.(43) The overall incidence of delirium was 8% and the study confirmed the adverse consequences that follow: ventilator dependency, sternal instability, and prolonged hospital stay. The frequency of delirium varied with the type of cardiac surgery performed: 8% among 8,917 patients undergoing conventional on-pump coronary artery surgery; 11% among 5,424 patients undergoing any type of open heart surgery, including valve replacement; and 2% among 1,847 patients undergoing off-pump coronary surgery. The authors conclude that the off-pump approach should be considered as one of the strategies for minimizing cerebral injury in coronary artery surgery. The only flaw in their argument is that most of the postoperative risk factors for delirium were significantly lower in the off-pump group. Nevertheless, this study is suggestive that an off-pump strategy, especially in the elderly, is an important method for reducing the risk of cerebral injury.

Table 2. Mortality and morbidity resulting from stroke or delirium.

Author	N	Operation	Cerebral Injury	Incidence %	Mortality %
Roach[41]	2108	CABG	None	94	2
			Stroke	3.1	21
			Delirium	3.0	10
McKhann[42]	2711	CABG	None	91	1.4
			Stroke	2.7	22
			Delirium	6.9	7.5
Wolman[3]	279	Open heart ± CABG	None	84	7.4
			Stroke	8.4	20.4
			Delirium	7.2	5.0

CABG, coronary artery bypass graft.

Quality Of Life And Socio-Economic Factors

Three randomized studies failed to demonstrate significant differences in measures of quality of life after 1 to 4 years of follow-up from off- or on-pump coronary artery surgery.(8,25,44) Nathoe and colleagues(26) examined symptoms and quality of life at 1-year postoperatively that were equivalent in the on-pump and off-pump groups. They also documented a significant 14% cost savings with off-pump as compared with on-pump surgery, representing an important cost benefit.

Of four non-randomized trials reporting quality of life, 2 showed no difference(44,45) and 1 showed significant improvement in quality of life(46) with off-pump compared to on-pump surgery. One recent randomized trial(25) reported no significant difference in quality of life 4 to 6 weeks after off-pump versus on-pump. Ascione and colleagues(47) found no significant difference between patients randomized to on-pump or off-pump coronary surgery at 2 to 4 years postoperatively. Questionnaires were sent to 379 survivors who had participated in two randomized trials; response rate was 86.5%. Among those who responded, there was a tendency for questionnaire scores of coronary revascularization outcome (core total, physical and psychosocial functioning, and satisfaction with treatment) to deteriorate with time after the operation ($P<0.05$).

An analysis of two randomized controlled trials showed a significant cost reduction for off-pump surgery.(7) But, due to systematic differences between different health care systems and hospitals, costs are highly variable. It is likely that optimal reduction in resource utilization for off-pump surgery will require significant reorganization of each hospital's cardiac surgery service and

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clinical pathway in order to take advantage of reduced morbidity after off-pump coronary surgery.

Off-Pump Surgery In High-Risk Patients

There are no reports of selected high-risk patients, but evidence from the American College of Cardiology (ACC)/American Heart Association (AHA) 2004 Guideline Update for Coronary Artery Bypass Graft Surgery(48) for mixed risk (high and low) surgical patients shows level A evidence (data derived from multiple randomized clinical trials or meta-analyses) of similar risk of mortality and level B evidence (data derived from a single randomized trial or non-randomized studies) of reduced risk of mortality at 30 days post-surgery for off-pump surgery. At 1 to 3 years of follow-up, mortality is similar between groups (evidence levels A and B). In high-risk coronary patients, the left ventricle is often dilated. The retraction of large beating hearts, necessary for the off-pump technique, is often poorly tolerated and may require inotropic drugs. An alternative approach is to do these procedures on-pump but without a period of global ischemia or cardioplegia. By decompressing the heart with some form of left ventricular vent and using the stabilization devices, excellent exposure is obtained and both mitral regurgitation and subendocardial ischemia are minimized.

Conclusion

The intense interest in the modern development of beating heart surgery for coronary artery disease has been fueled by the expectation that morbidity compared to cardiopulmonary bypass would be dramatically lower. That this has not been apparent from several randomized trials has surprised many, but may reflect all the small, subtle improvements in anesthetic and surgical techniques and equipment (e.g., design of pumps, oxygenators, and cannulae) that have taken place over the last 10 years. In high-risk groups, particularly those with renal impairment, off-pump surgery makes the need for postoperative renal support less likely. In groups over 70 years of age, there is a reduction in the incidence of cerebral injury when an off-pump technique is employed.

It is also apparent that off-pump surgery is an exacting technique that takes time to perfect, but can produce a graft quality equivalent to that obtained on-pump. The only real contraindication to off-pump surgery is poor target vessels with a likelihood to require endarterectomy, but in experienced hands even this is a relative contraindication.

The future of off-pump surgery will probably be a slow increase from the present figure of one-third to possibly two-thirds of coronary surgical candidates in the next 10 years. Off-pump coronary surgery is as safe as on-pump surgery, and in experienced hands offers less early complications, particularly in those patients with significant comorbidity.

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Applied Neuromonitoring and Improving CNS Outcomes

John M. Murkin, MD

Despite an overall decrease in perioperative morbidity and mortality, evidence of some degree of central nervous system dysfunction associated with coronary artery bypass graft (CABG) surgery—with or without cardiopulmonary bypass—has steadily mounted. From preoperative studies of CABG patients, it is apparent that over 50% of patients who present for cardiac surgery have evidence of either extracranial or intracranial atherosclerotic disease. Patient-specific factors thus have a fundamental impact on the risks of a brain injury developing after CABG surgery. Cerebral embolization and/or ischemic hypoperfusion are the most likely etiologic mechanisms for perioperative brain injury associated with cardiac surgery, and these factors are closely interrelated. Various monitoring techniques can decrease risk of intraoperative cerebral embolization and hypoperfusion and are associated with improved outcomes. Ultrasound guided aortic instrumentation (epiaortic scanning) can markedly decrease atheroembolic load and risk of stroke. Unrecognized sources of microgaseous emboli, including air entrainment from surgical purse string sutures and perfusionist interventions, can be identified and reduced by transcranial Doppler monitoring. Cerebral hypoperfusion from unrecognized cerebral venous obstruction, inadequate mean arterial pressure, or from hypocapnic cerebral alkalosis can be identified by multimodality neuromonitoring using regional cerebral oxygen saturation and transcranial Doppler. Overall patient outcomes can be improved, and hospital length of stay shortened, by applied neuromonitoring techniques.

Cardiac surgical procedures are currently being undertaken on increasingly older patients who have a significantly greater burden of disease and associated comorbidity than was the case only a decade ago. Yet despite these increasing clinical challenges, perioperative mortality and overall length of stay have continued to decline. Over the decade from 1990 to 1999, patients' predicted operative risk increased by 30.1%, from 2.6% to 3.4%. Despite higher risk, the observed operative mortality decreased by 23.1%, from 3.9% to 3.0% ($P < .0001$) over this same time period.[1] This is tremendous progress that reflects a variety of factors, including modifications in surgical technique, improvements in anesthetic and inotropic medications, enhanced intraoperative monitoring strategies, and improvements in cardiopulmonary bypass (CPB) equipment and technologies.

Despite an overall decrease in morbidity and mortality, however, evidence of some degree of central nervous system (CNS) dysfunction associated with coronary artery bypass graft (CABG) surgery—with or without CPB—has steadily mounted. Evidence shows that neurologic damage after cardiac surgery remains an important cause of postoperative morbidity.

Many patients have clinically undetectable CNS sequelae, but for a significant minority, the results can be devastating. In one large series, 6.1% of 2100 patients undergoing conventional CABG surgery evidenced clinically apparent CNS injury postoperatively.[2] This was associated with a significant risk of perioperative death. Twenty-one percent of patients with type I (eg, stroke) outcomes died, and the mortality rate was 10% in those with type II (eg, seizures) outcomes versus a mortality rate of 2% in those with no adverse cerebral outcome. In a longitudinal study, Newman and colleagues[3] have further demonstrated that a significant number of surviving CABG patients exhibit ongoing cognitive dysfunction years after their surgery.

From preoperative studies of CABG patients, it is apparent that over 50% of patients who present for cardiac surgery have evidence of either extracranial or intracranial atherosclerotic disease, with over 13% of patients having evidence of both.[4] In a series of 201 CABG patients, 25.4% had single or multiple postoperative CNS complications, and intracranial atherosclerotic disease was found to have a strong independent association with the development of CNS complications. The presence of both extracranial and intracranial atherosclerotic disease was even more strongly associated with adverse CNS outcomes than was intracranial atherosclerotic disease alone.[4] This strongly suggests that in addition to procedural risks, patient-specific factors have a funda-

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mental impact on the risks of brain injury developing after CABG surgery.

Various studies would indicate that cerebral embolization and/or ischemic hypoperfusion are the most likely etiologic mechanisms for perioperative brain injury associated with cardiac surgery, and that these factors are closely interrelated.[5] Gold et al[6] have reported a lower incidence of morbidity, including stroke, in patients undergoing conventional CABG in whom mean arterial pressure was maintained at greater than 80 mm Hg. This may imply a requirement for higher mean arterial pressure to better optimize collateral cerebral perfusion during CPB.

Cerebral venous hypertension from caval obstruction may be another unrecognized yet equally injurious contributor to cerebral hypoperfusion.[7] Detection and correction of this complication can be facilitated by a variety of techniques, including observing low ipsilateral middle cerebral artery flow on transcranial Doppler (TCD), progressive decline in regional cortical oxygenation (rSO_2), and increased slow wave activity on electroencephalographic (EEG) monitoring. Of interest is that the original report of this phenomenon was made over 40 years ago in the context of applied intraoperative EEG.[8]

Other potentially deleterious intraoperative conditions that have been detected by various neuromonitoring modalities during CABG surgery include hypocapnic ischemia, uncompensated anemia, aortic cannula malposition, air embolization, and CPB vaporizer malfunction, among others. The incidence of CNS risk averted through detection of these procedural complications is independent of those patients in whom routine anesthesia and CPB perfusion parameters may be suboptimal, yet otherwise unrecognized, due to underlying extracranial and intracranial atherosclerotic disease.

Various monitoring techniques can decrease the risk of intraoperative cerebral embolization. Ultrasound-guided aortic instrumentation, such as epiaortic scanning, can markedly decrease the atheroembolic load and risk of stroke in CABG surgery.[9,10] Unrecognized sources of microgaseous emboli, including air entrainment from surgical purse string sutures and perfusionist interventions, can be identified and reduced by TCD monitoring.[11] Hypoperfusion from unrecognized cerebral venous obstruction, inadequate mean arterial pressure, or from hypocapnic cerebral alkalosis can be identified by multimodality neuromonitoring using cerebral rSO_2, EEG, and TCD.[12,13] Overall patient outcomes can be improved, and hospital length of stay shortened, by applied neuromonitoring techniques.[14]

Within limits, the use of intraoperative TCD detects embolic events in real time and allows modification of perfusionist and surgical technique. It has been shown that the numbers of emboli generated by perfusionist interventions such as drug injection, blood return, as well as episodes of entrainment of air from the surgical field are rapidly identified and corrected by TCD detection of intraoperative emboli.[11]

Similarly, clinical management, even in the postoperative interval, can be optimized by the reliable detection of cerebral emboli as reported by Naylor et al[15] at a previous Outcomes meeting. In their report of 700 patients, TCD detection of cerebral emboli after carotid endarterectomy triggered Dextran anticoagulation resulting in a significant decrease in perioperative stroke.[15] As discussed by Doblar,[16] further refinements in TCD technologies have resulted in multigating techniques to enhance noise artifact rejection, whereas the use of multifrequency TCD appears able to discriminate between gaseous and particulate emboli.[17]

These more recent developments will further increase the diagnostic importance of TCD emboli detection and enhance the detection of real-time changes in cerebral blood flow velocity with direct clinical applications, including preoperative assessment of the adequacy of the cerebral circulation, monitoring cerebral perfusion during adult and pediatric circulatory arrest procedures, as well as intraoperative and postoperative monitoring for carotid endarterectomy.[16]

Currently, near infrared reflectance spectroscopy can be used to provide noninvasive bihemispheric measures of cerebral rSO_2 through the intact skull and tissue. Though a potential limitation is the fact that the cerebral sample volumes are on the order of 1 cm^3 of tissue, thus rendering them highly localized in nature, a body of literature is developing that indicates a predictive value for near infrared reflectance spectroscopy in patients undergoing CPB procedures.[18]

Previous studies have indicated a positive predictive value between low rSO_2 and adverse CNS outcomes.[19] The use of cerebral oximetry identifies a number of otherwise unrecognized causes of cerebral hypoperfusion, both during conventional CPB[12] and during beating heart surgery.[20] Various causes of cerebral hypoperfusion, including inadvertent positioning of the head turned to

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extreme left side, cannula-obstructed venous outflow from brain, hypocapnia, low perfusion pressure, and inadequate hemoglobin concentration, have all been detected and successfully treated by applied cerebral oximetry.[13,21]

Compromised cerebral perfusion can occur relatively frequently, even during beating heart procedures. Combined EEG and cerebral oximetry identified episodes of cerebral ischemia in 15% of a series of 550 beating heart patients; all were treated successfully by a combination of pharmacologically-improved cardiac output, increased perfusion pressure, and cardiac repositioning.[20] Interim analysis of our own randomized, prospective, blinded study has demonstrated a significant shortening of length of stay associated with intraoperative rSO_2 monitoring and directed interventions in patients undergoing CABG surgery.[14] In an important development, as reported at the Outcomes 2004 meeting, we have demonstrated prospectively in our just completed randomized, blinded study of 198 CABG patients that rSO_2 monitoring is associated with a significant decrease in major morbidities (Figure 1).[22]

Consistent with this result, in a recent large, nonrandomized series of 1698 cardiac surgical patients reported by Goldman and colleagues,[24] a significant reduction in perioperative stroke rate, from 2.01% to 0.97%, was observed in patients in whom rSO_2 cerebral oximetry was used to optimize and maintain intraoperative cerebral oxygenation versus an untreated comparator group of 2077 similar patients operated on in the immediately preceding 18-month interval.[24]

Currently, best clinical practice for reduction of perioperative CNS injury involves minimization or avoidance of secondary exacerbating factors such as hyperglycemia and hyperthermia, as reflected in the PICS Consensus Statement, but does not address primary patient-specific risks of macro- and microemboli and disease-related hypoperfusion. The limitations of most current CNS monitors reflect that they are either highly regional and may miss significant localized cerebral ischemia or they are global in nature and, thus, relatively insensitive to regional ischemia. Despite these limitations, it does appear that cerebral oximetry is highly beneficial in decreasing postoperative stroke. Multimodality CNS monitoring,

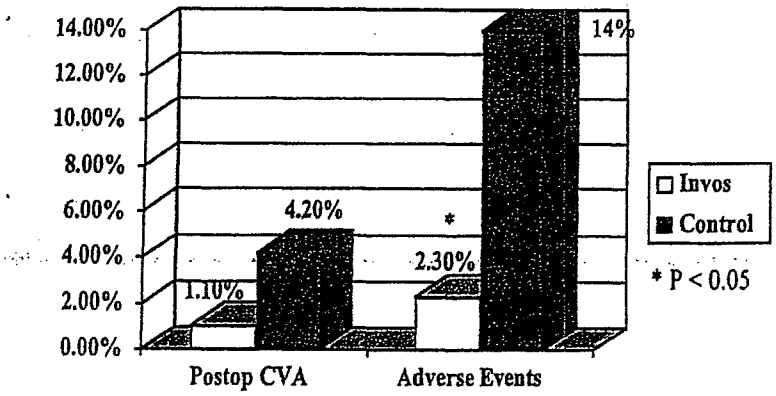

Figure 1. The incidence of postoperative cerebrovascular accident (CVA) and cumulative adverse events in patients undergoing coronary artery bypass surgery in whom cerebral oximetry was actively monitored and treated (Invos) versus patients in whom oximetry display was recorded but blinded (Control), demonstrating a statistically significant decrease in adverse events and a nonsignificant but numerically lower incidence of CVA in the Invos group.

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incorporating different complementary techniques to assess CNS functioning, would appear to be the most appropriate approach to the systematic detection and avoidance of adverse perioperative cerebral events.[12,13]

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Abstracts on Patient Safety Presented at the 2004 American Society of Anesthesiologists Annual Meeting

by Glenn S. Murphy, MD, and Jeffery S. Vender, MD

Over 1,600 abstracts were presented at the 2004 American Society of Anesthesiologist Annual Meeting in Las Vegas, NV. As in previous years, a number of these abstracts examined issues directly related to patient safety. This brief review will highlight some of the important abstracts discussed at the meeting.

Postoperative Neurocognitive Dysfunction

Several investigators examined the incidence and causes of postoperative neurocognitive decline in elderly patients undergoing anesthesia and surgery. In an ongoing prospective study in 130 orthopedic patients older than 65 years of age, Jankowski et al. (A-40) examined the predictors and consequences of postoperative delirium. Neuropsychological and functional testing were performed preoperatively and 3 months postoperatively, and patients were examined daily throughout the hospital stay for the presence of postoperative delirium. Patients who developed postoperative delirium tended to be older and had fewer years of formal education. In addition, an association between postoperative delirium and other major complications (myocardial infarction, dysrhythmias) was observed. An investigation from the University of California (San Francisco) examined the influence of pain medications on postoperative delirium in patients 65 years of age scheduled for major noncardiac surgery (A-39). A structured interview was conducted preoperatively and for the first 2 days following surgery to detect the presence of delirium. Multivariate logistic regression analysis revealed age >80 and lower education level were independently associated with increased delirium risk. The use of oral narcotics was associated with a decreased risk of delirium (OR 0.44, CI 0.23-0.85); narcotics administered by other routes did not affect delirium risk. These findings suggest that the method of postoperative pain relief may influence the occurrence of delirium.

Monk and colleagues conducted a prospective, longitudinal study to evaluate the long-term effects of postoperative neurocognitive dysfunction in elderly patients (A-62). Using a battery of tests, the investigators examined 354 patients undergoing major noncardiac surgery preoperatively, at hospital discharge, 3 months, and 2 years after surgery. The cognitive deficit rate was 59% at hospital discharge, 34% at 3 months following surgery, and 42% at the 2-year measurement period. Analysis of the data revealed that cognitive decline at discharge was a significant predictor of long-term cognitive impairment. This well-designed study reveals that many elderly patients are discharged from the hospital with neurocognitive dysfunction, and that this dysfunction may persist for up to 2 years.

Investigators from Parma, Italy, conducted a prospective, randomized trial to evaluate the impact of interventions to improve regional cerebral oxygen saturation (rSO_2) on cognitive dysfunction in elderly patients presenting for abdominal surgery (A-61). In the intervention group, rSO_2 was maintained above 75% of preinduction values by increasing blood pressure, $PaCO_2$, and FiO_2 and by decreasing brain oxygen consumption with a bolus of propofol. In the control group, clinicians were blinded to rSO_2 data. In the intervention group, the incidence of postoperative cognitive decline was reduced (35%) and length of stay shortened (9 days), compared to the control group (54% and 13 days, respectively). The authors conclude that techniques to increase rSO_2 can potentially improve outcomes in elderly patients.

Use of Perioperative Beta-Blockers

The use of beta-blockers in the perioperative setting has been shown to reduce cardiac morbidity and mortality. Despite clear scientific evidence of the benefit of beta-blockers in appropriate patient populations, few hospitals have protocols for administration of beta-blockers, and many patients at risk for cardiac events do not receive these agents. Two studies from Yale University School of Medicine examined whether the publication of guidelines promoting the use of perioperative beta-blockade increased the use of the drugs at the institution. In the first investigation, data were collected on a cohort of patients (n=230) scheduled for intermediate-to high-risk noncardiac surgery prior to the publication of ACC/AHA guidelines (A-1302). These patients were compared to a similar cohort of subjects operated on following the publication of the guidelines. Nearly half of the patients in each group who were eligible to receive perioperative beta-blockers did not receive them. Approximately three-quarters of each cohort was evaluated by a medical service prior to surgery, yet beta-blocker therapy was recommended by only 51% of consultants. In a similar investigation, the medical records of patients undergoing major vascular surgery were reviewed prior to (n=172) and after (n=197) the publication of the ACC/AHA guidelines (A-204). As demonstrated in the previous investigation, only about one-half of eligible patients received beta-blockers perioperatively in each cohort. In addition, only a small percentage of patients in each group achieved target heart rates 60 bpm (22-29%) as recommended by the ACC/AHA. Vigoda et al. examined the resting heart rate of high-risk patients receiving beta-blockers in a preoperative clinic, and compared this to their average heart rate in the operating room (A-1381). Only 27% of patients on chronic beta-blocker therapy had resting heart rates 60 bpm in the preoperative clinic, and only 19% had a resting heart rate 60 and average intraoperative heart rate <66 bpm. These studies demonstrate that there has been little improvement in the use of beta-blockers in patients at risk for adverse cardiovascular events, and that only a minority of patients receiving this therapy are adequately beta-blocked.

Trace Anesthetic Gases

Current recommendations from OSHA and the ASA state that trace anesthetic gases should be monitored at all anesthetizing locations.

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Ohmura and colleagues measured trace gases in the patient wards of a cancer institute, a large general hospital, and a small community hospital (A-1329). Measurements were obtained in the morning and afternoon of 3 consecutive days in the operating rooms and in patient wards above and below the ORs. The highest levels of sevoflurane detected in the OR areas were 1.1-1.3 ppm, and in the patient wards, 1.2-1.6 ppm. Trace gases were consistently detected in the wards, even on floors several levels above and below the ORs. The results suggest that other areas of the hospital should be monitored for trace anesthetic gases.

Sleep Apnea

Patients with sleep apnea are at risk for adverse cardiovascular and respiratory events in the perioperative period. Previous studies suggest that a large percentage of patients with sleep apnea remain undiagnosed. In a study from Ontario, Canada, the authors examined the prevalence of sleep apnea in patients presenting for elective surgical procedures (A-13). The Berlin questionnaire was used in patients at a preoperative assessment clinic. This 9-item questionnaire has a high sensitivity and specificity for identifying patients at high-risk for sleep apnea in the primary care setting. The Berlin questionnaire identified 23.9% of all patients at the preoperative clinic as being high-risk for sleep apnea. It also identified all patients in whom a previous diagnosis of sleep apnea had been made. The authors conclude that approximately one-quarter of surgical patients are at high-risk for sleep apnea, and that the Berlin questionnaire can be used to identify those at risk.

Central Line Infection

Berenholtz et al. conducted a prospective cohort study in an intensive care unit setting to determine whether the introduction of a multifaceted systems intervention would reduce the incidence of catheter-related blood stream infections (A-3). All clinicians were educated about evidence-based infection control practices (hand hygiene, chlorhexidine skin prep, maximal barrier precautions, subclavian vein placement). In addition, a checklist to ensure adherence to these practices was used, a central line cart was created, providers were asked daily whether catheters could be removed, and nurses were empowered to stop the procedure if improper techniques were observed. The introduction of these interventions reduced the number of catheter-related blood stream infections from 11.3/1000 catheter days (prior to interventions) to 0/1000 catheter days. The findings from this study demonstrate that strict adherence to an evidence-based infection control policy can markedly reduce the incidence of catheter-related infections.

This brief review summarized only a small number of the important abstracts on patient safety presented at the 2004 Annual Meeting. To view other abstracts on patient safety, or to obtain further information on the abstracts discussed in this review, please visit the Anesthesiology website at http://www.anesthesiology.org.

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Anesthesiology's Important Role in Postoperative Cognitive Impairment Research

Terri G. Monk, M.D.
Committee on Geriatric Anesthesia

Less than 50 years ago, surgery was considered hazardous for patients 50 years or older. In 1955, Bedford published a retrospective review of 1,194 elderly patients (50 years or older) who had surgery under general anesthesia during a five-year period.[1] He found cognitive impairment in 10 percent of patients and concluded that the effects were related to anesthetic agents and hypotension and recommended that "operations on elderly patients should be confined to unequivocally necessary cases."

Today the fastest growing segment of the United States population includes people 65 or older, and it is estimated that more than half of these individuals will require some form of surgery in their lifetime.[2] Improvements in surgical techniques, anesthesia and intensive care units have made surgery in these elderly patients possible. Despite improved operative outcomes in the elderly, a significant proportion of these patients experience postoperative cognitive impairment.[3-7] The most common forms of postoperative cognitive impairment are delirium and postoperative cognitive dysfunction (POCD). The socioeconomic implications of postoperative cognitive decline are unknown, but abrupt declines in cognitive function in elderly individuals living in the community often lead to a loss of independence, withdrawal from society and death.[8]

Postoperative delirium is common in patients after surgery with the overall incidence for all age groups estimated to range from 5 percent to 10 percent and for the elderly from 10 percent to 15 percent.[8] The rate of delirium in the elderly varies with the type of surgery and is reported to be 1 percent to 3 percent following cataract surgery, 10 percent following general surgery, 28 percent to 61 percent following major orthopedic surgery (e.g., joint replacement, fracture) and as high as 47 percent after cardiac surgery.[8] Delirium is characterized by fluctuating levels of consciousness, a disturbed sleep-wake cycle and altered psychomotor activity. Delirious patients often exhibit disorders of cognitive function, thinking, perception and memory. The etiologic factors associated with this disorder include advanced age, polypharmacy, cerebral damage, surgery and anesthesia, hypoxia, sepsis, sensory deprivation or overload, electrolyte disturbances, pain and endocrine or metabolic disorders. Delirium is a very costly disorder, and Medicare expenditures associated with the diagnosis and treatment of this problem exceed $4 billion per year (1994 dollars).[7]

POCD has recently been demonstrated in 20 percent to 60 percent of patients following coronary artery bypass (CAB) surgery and 10 percent to 16 percent of elderly patients following major, noncardiac surgery.[3-5]

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POCD is defined as a "deterioration of intellectual function presenting as impaired memory or concentration."[9] The clinical features of this disorder range from mild forgetfulness to permanent cognitive impairment resulting in a loss of independence. POCD is considered a mild neurocognitive disorder, and the diagnosis can only be made if the cognitive decline can be corroborated by the results of neuropsychological testing (presurgical and postsurgical). In addition testing must demonstrate that the individual has a new onset of cognitive deficits in at least two areas of cognitive functioning lasting two weeks after surgery or longer.[9]

"An emerging concept in neuropsychology and clinical geropsychology espouses a 'functional cliff' hypothesis of cognitive decline and dementia in later adulthood. ..."

While it is now accepted that POCD is a real entity, little is known about the etiology of POCD and the risk factors for this problem in the aging population. It is likely that the etiology of POCD in the elderly patient is multifactorial. Potential risk factors for the development of this problem include the preoperative cognitive status of the patient, intraoperative events related to the surgery itself and anesthetic agents.

The preoperative cognitive state of the patient may be linked to the development of postoperative cognitive function. An emerging concept in neuropsychology and clinical geropsychology espouses a "functional cliff" hypothesis of cognitive decline and dementia in later adulthood. This hypothesis is essentially a threshold model that argues that, with increasing age and normal cognitive declines, individuals move closer and closer to a level that might be considered "impaired" or "demented." As this threshold is approached, individuals enter a high-risk phase that might be considered "preclinical dementia."[10] For individuals in this preclinical state, research suggests that the sudden onset of even mild neurological trauma such as surgery may be a sufficient proximal cause to move people over the clinical threshold and into the range of functioning that might be classified as "impaired."

Systemic and cerebral emboli can occur during surgical procedures and may represent a possible mechanism for postoperative cognitive decline. One possible explanation for POCD after CAB is that embolic material is released during crossclamping of an aorta affected by atherosclerosis and that this embolic material enters the cerebral vessels during surgery, resulting in occlusion of both large and small vessels.[3] The incidence of postoperative neurocognitive deficits has been shown to correlate with the number of microemboli detected during the CAB grafting procedure.[3]

"Exposure to anesthetic agents has been suggested as a possible cause of POCD in elderly patients."

Microemboli also are common during orthopedic surgery and may be responsible for the cognitive decline seen after this type of surgery.

Exposure to anesthetic agents has been suggested as a possible cause of POCD in elderly patients. Anesthetic agents affecting the release of central nervous system neurotransmitters such as acetylcholine, dopamine and noradrenaline could potentially impair memory, especially in elderly patients. There are no definitive conclusions on the effects of anesthesia on learning and memory.

There is wide variation in the reported incidence of POCD in the literature.

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Much of this variation is due to methodological differences between the studies such as the use of varying test batteries, inadequate statistical power, the lack of adequate control subjects in the studies and the lack of a standard criteria for diagnosing POCD.[9] Rasmussen et al.[9] demonstrated that the incidence of POCD in a group of 176 volunteers could vary between 0 percent and 40 percent if 10 different commonly used criteria for POCD were utilized.

Long-term follow-up of patients with POCD is needed to provide insight into the financial and emotional burden of this problem and the impact of this problem on the patient, the patient's family and society at large. Future research should identify which neuropsychological tests are best for the diagnosis of the problem and which of the varying criteria for POCD is associated with functional impairment. Additional research also is needed to gain an understanding of the etiology of POCD and to develop interventions to minimize or prevent this serious complication.

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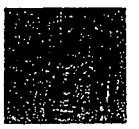

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Chronic neurocognitive effects of critical illness.

Current Opinion in Critical Care. 11(4):369-375, August 2005.

Hopkins, Ramona O ab; Brett, Stephen c

Abstract:

Purpose of review: Until relatively recently critical care practitioners have focused on survival of their patients and not long-term outcomes. An increasing body of research has examined patient outcomes beyond discharge from the intensive care unit and hospital. One area of focus is neurobehavioral outcomes including neurocognitive sequelae and neuropsychiatric disorders such as depression and anxiety. Cognitive functions are brain-based or mental activities that involve acquiring, storing, retrieving, and using information and include domains such as memory, attention, executive function, mental processing speed, spatial abilities, and general intelligence. It is known from other medical specialties that impaired cognitive function can have a broad, substantial, and long-lasting impact on a patient's life. This paper examines the current evidence for neurocognitive impairments in survivors of critical illness.

Recent findings: Recent studies support the hypothesis that critical illness can lead to significant impairments in neurocognitive function. Current work indicates that the neurocognitive impairments can last for months or years after a patient arrives home and may have important consequences for quality of individual and family life and for ability to return to work as well as substantial economic costs. The mechanisms of neurocognitive impairments are not fully understood, but in acute respiratory distress syndrome hypoxemic burden appears important.

Summary: Among the potential consequences of critical illness are now included neurocognitive impairments. Future research should include the search for strategies for the early identification of neurocognitive impairments, mechanisms of brain injury, and therapeutic modalities designed to prevent or decrease neurocognitive morbidity.

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Cognitive Function After Non-Brain Surgery Studied: Second Duke Conference on Surgery and the Elderly

Madan M. Kwatra, Ph.D.

It is well known that the elderly population in the United States is increasing rapidly, and the implications of this trend for surgery on the elderly are being examined. Five years ago, Duke University Medical Center established the Gerontological Research in Anesthesiology and Surgery Program (GRASP) to identify areas of basic and clinical research that will reduce the incidence of adverse postsurgical outcomes in the elderly. In addition to holding monthly meetings and developing research projects, GRASP organizes biennial conferences on surgery and the elderly. The second such conference was held at Duke University Medical Center on September 30, 1999. Titled "Cognitive Function After Surgery: What Do We Know? What Do We Need to Know?," the conference brought together anesthesiologists, basic scientists, geriatricians and surgeons. It was co-hosted by Duke's departments of anesthesiology, surgery and the Duke Center for the Study of Aging and Human Development. Funding was provided by the American Geriatrics Society/John A. Hartford foundation and Abbott Laboratories.

Ronnie Rosenthal, M.D., Yale University, New Haven, Connecticut, said that the percentage of surgeries performed on people over the age of 65 (currently at 40 percent) will increase substantially over the coming decades as the elderly population increases. Although surgery is beneficial even for octogenarians, the incidence of adverse outcomes is much higher due to existing co-morbidities. Dr. Rosenthal provided data implicating nutritional status measured by serum albumin levels and intraoperative hypothermia as the two most important factors affecting postoperative outcomes. Further, she reported that the incidence of major complications including deaths were significantly higher in patients that have postoperative delirium.

Paula Trzepacz, M.D., who is affiliated with Eli Lilly, distinguished delirium from dementia. The hallmarks of delirium are disorientation, attentional deficits and clouding of consciousness. Demented patients, on the other hand, can pay attention but cannot remember. Delirium also develops over a short period of time (hours or a day), whereas most dementias develop over a longer period. The risk factors for delirium in the perioperative period include advanced age, male gender, history of alcoholism, polypharmacy (especially anticholinergic agents), pre-existing dementia or cognitive impairment, metabolic disturbances and low serum albumin.

Three presentations focused on cognitive dysfunction after cardiac, hip and other surgeries. Mark Newman, M.D., Duke University, Durham, North Carolina, discussed his team's study that followed cognitive function up to five years after cardiac surgery. Cognitive dysfunction affected more than half the patients at discharge; this incidence fell to 20-24 percent at six months, but increased to 42 percent at five years. The most significant predictor of cognitive dysfunction at five years was impairment at discharge. To better understand the mechanism of cognitive dysfunction after cardiac surgery, a

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rat model of cardiopulmonary bypass has been developed by Hilary Grocott, M.D., at Duke University.

Kenneth Koval, M.D., New York University, New York, New York, presented data on functional outcomes after hip fractures in patients over the age of 65 who were cognitively intact and lived in community dwellings. In a sample of 921 hip fracture patients, the incidence of postoperative delirium was 5 percent, a much lower rate than that reported by other investigators, possibly reflecting different definitions used for detecting delirium. The predictors of postoperative delirium in this population were gender (male) and general anesthesia.

Terri G. Monk, M.D., University of Florida, Gainesville, Florida, presented details on the International Study of Postoperative Cognitive Dysfunction (ISPOCD) published in *The Lancet* in 1998.[1] Postoperative cognitive dysfunction occurred in 25 percent of patients in the first week after surgery and in 10 percent of patients within three months of surgery. More importantly, the ISPOCD study found that patients over the age of 70 were more susceptible to prolonged cognitive decline after surgery than those in their early 60s. Dr. Monk is currently examining whether the multicenter findings apply to a single institution using ISPOCD methodology, by evaluating 1,500 patients.

Pamela Williams-Russo, M.D., Cornell University, Ithaca, New York, addressed the question of anesthetic technique and cognitive outcome. Because patients undergoing regional anesthesia are alert and awake during and immediately after surgery, it is likely that regional anesthesia could result in less postoperative cognitive dysfunction than general anesthesia. However, the available literature does not provide a clear answer to this hypothesis. Dr. Williams-Russo presented data on a randomized trial of the effects of epidural versus general anesthesia on cognitive dysfunction in 262 older adults (85 percent over the age of 60 and 50 percent over the age of 70) undergoing elective primary total knee replacement.[2] The two anesthesia groups were compared for change in neurocognitive function prior to surgery to six months after surgery using a comprehensive neuropsychologic testing battery. No significant difference in the incidence of postoperative dysfunction was detected between the two groups.

Alexis Carmer, M.D., Duke University, Dunham, North Carolina, discussed an abstract (presented by Stephan A. Schug, M.D., at the 1999 meeting of the American Society of Regional Anesthesia and Pain Medicine) on a meta-analysis comparing regional versus general anesthesia in 107 different trials consisting of more than 8,000 patients. Regional anesthesia patients had a one-third less mortality rate and a significant decrease in the incidence of deep venous thrombosis, pulmonary embolism, pneumonia and respiratory depression. These differences in outcomes, Dr. Carmer suggested, could affect cognitive dysfunction. The group consensus, however, was that anesthesia type does not seem to influence the incidence of cognitive dysfunction, but a larger prospective randomized controlled trial focusing on older patients is warranted to definitively answer this crucial question.

Dr. Trzepacz focused on the cholinergic mechanisms of postoperative delirium. She reviewed the brain areas involved in delirium and highlighted a key role of acetylcholine in the REM sleep, arousal, mood and memory changes seen in delirium.[3] Anticholinergic drugs are known to cause delirium. Dopamine may also cause delirium through acetylcholine because it acts through D_2 receptors and reduces acetylcholine levels. Opiates also cause delirium as they are known to reduce acetylcholine and increase dopamine. Madan M. Kwatra, Ph.D., presented biochemical information on the enzymes and receptors involved in the function of acetylcholine and how the various components of the cholinergic system are affected with age and anesthetics. Muscarinic receptors, a key target through which acetylcholine produces its action, become desensitized with age.[4] Further, anesthetics are known to

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disrupt muscarinic receptor-G protein coupling.[5] Whether the cholinergic system of elderly patients is more susceptible to the detrimental effects of anesthetics is an important question that needs to be addressed.

Lively discussions following the talks identified three key problems. First, the very term "cognitive dysfunction" is confusing. Is it delirium or dementia or both? Precise standard definitions are sorely needed. Second, researchers have used a variety of instruments to detect cognitive dysfunction. Standardization of instruments is needed so that studies from different institutions can be adequately compared. The group consensus was that a standardized and validated delirium score be developed for use in all surgical patients. Finally, many studies have focused on populations consisting of a large portion of patients who are 60 or 65 years old. Since this age group is relatively healthy, more trials should be performed on patients over the age of 75. This group will present the greatest challenge to anesthesiologists.

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Neurocognitive Performance in Older Adults with Postoperative Cognitive Dysfunction (POCD)

Catherine C. Price, Ph.D., Cyndi W. Garvan, Ph.D., Terri G. Monk, M.D.
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Introduction: Older adults are at increased risk for the development of postoperative cognitive dysfunction (POCD).[1,2,3] However, little is known about the type of cognitive problems (memory only, attention only, or a combination of attention and memory) these patients experience. This study evaluated changes in neurocognitive performance of older adults diagnosed with POCD.

Methods: This study included 308 older adults (age 60 or greater) enrolled in a prospective, longitudinal study evaluating POCD following major, noncardiac surgery. [2] Exclusion criteria included cardiac or neurosurgical procedures, central nervous system disorders, drug abuse, severe depression, or a preoperative score <24 on the Mini-Mental State Examination (MMSE). Pre-surgical cognitive function was compared to performance at three months post surgery. 'Attention' was assessed with indices from the *Letter-Digit Coding Test, Stroop Color Word Test , Concept Shifting Task*, while 'Memory' was assessed with immediate and delayed recall indices of the *Visual Verbal Learning Test*.[3] Repeat testing performances from healthy matched controls were used to normalize patient pre-post change scores and compute test Z-scores. Patients were classified as having POCD if a Z score on two individual tests or the combined Z score was > 1.96 indicating a cognitive decline from baseline test scores. Patient test results were used to classify patients into one of five subtypes of POCD: 1) 'Memory' (Z-score > 1.96 on two or more memory indices), 2) 'Attention' (z-score > 1.96 on only two or more attention indices), 3) 'Combined Attention-Memory' (z-score > 1.96 on at least one attention and one memory index), 4) 'Subthreshold' POCD (Z-score between 1 and 1.96 on more than two cognitive indices), and 5) 'No POCD'. Data were analyzed using Chi-square tests with $p<.05$ considered significant.

Results: At three months post surgery, POCD was present in 48 of 308 (16%) older adults. Of these 48 patients, 61% were classified with 'Memory', 10% with 'Attention', 8% with 'Combination Attention-Memory', and 21% with 'Subthreshold' subtypes (Table 1, $p<.0001$). The prevalence of POCD and classification into one of the four subtypes was independent of gender, comorbidity, and anesthesia time.

Conclusions: Older patients who experience cognitive decline three months after major surgery exhibit neurocognitive decline in both memory and attention domains. Our findings suggest that brain regions associated with memory function (i.e., medial temporal lobe structures, basal forebrain) may be most susceptible to perioperative insults. Future studies should evaluate the risk factors and etiologies responsible for interpatient differences in postoperative cognitive decline.

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Patterns of Cognitive Impairment in Patients With and Without POCD

	No POCD N (% of No POCD))†	POCD N (% of POCD)
Memory-only	37 (14%)	29 (61%)*
Attention-only	12 (5%)	5 (10%)
Combined Attention-Memory	0 (0%)	4 (8%)
Subthreshold‡	0 (0%)	10 (21%)
None	211 (81%)	0 (0%)
TOTAL	260	48

† No POCD includes patients impaired on only 1 measure, therefore not meeting study definition of

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Emboli, inflammation, and CNS impairment: an overview.

Hindman BJ

Perioperative stroke occurs in 2-3% of adult cardiac surgery patients, and significant cognitive dysfunction is experienced by 40-60% of patients in the first postoperative week. Perioperative neurocognitive abnormalities are associated with a greatly increased risk of perioperative mortality, lengthy intensive care and hospital stay, and more intensive rehabilitative care. Long-term cognitive dysfunction, ranging from months to years, occurs in 25-40% of adult cardiac surgery patients, resulting in a decreased quality of life. Cerebral emboli are an important cause of perioperative neurocognitive abnormalities. Aortic cannulation, clamping, and manipulation during surgery may dislodge atheromatous materials into the cerebral circulation, leading to perioperative or postoperative stroke. Nevertheless, acute and chronic neurocognitive dysfunction frequently occurs in non-cardiac surgery patients as well, suggesting that some element of surgery and/or anesthesia itself causes or contributes to this phenomenon. One possible cause may be central nervous system (CNS) responses to peripheral tissue injury or inflammation. The CNS is sensitive to systemic pro-inflammatory mediators such as endotoxin and the cytokines interleukin-6 and interleukin- 8, which are activated by surgical trauma. This article discusses the behavior and effects of these inflammatory agents and their intensification in combination with postoperative hyperthermia. The potential beneficial role of pharmacological agents such as heparin, lidocaine, and aprotinin is also examined.

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