Q. The doctor that was caring for you for your heart was also taking care of you for some depression?

A. Mildly, yes.

Q. Sometimes I just don't hear you clearly.

A. He was, yes.

Q. And whatever medicine he put you on, you are no longer on, is that correct, other than the heart?

A. Not on today, no.

Q. And when did you stop taking whatever medicine it was for the depression?

A. Some time last year.

Q. Some time last year. Had you had heart problems prior to being hospitalized?

A. Well, I was only in the hospital for ten hours.

Q. Ten hours, yes, sir.

A. They thought they had it under control. It's been going on since about 1970. Defibrillation, as I recall.

Q. Which hospital did you go to for ten hours, Doctor?

A. A hospital in Poole.

Q. Poole, how do you spell that?

A. P O O L E.

Q. What's the name of the hospital?

A. The Poole General Hospital, and I was under a physician called Dr. Andrew McCloud who I had seen a couple of times about the heart business. They wanted me to see a physician when I first got down there, having left Cardiff, and I saw him then. We had one of these fibrillations occur after that.

Q. After?

A. About two months after I had seen him. No, that's not right. More than two. I saw him in August. August last year, and this occurred in April, this year, so ...

Q. No. I apologize. Apparently in August of last year, you had the heart problem?

A. No. I was referred down to see him because I had had a previous heart problem, and I had come down from Cardiff, Pernarth down to his area. He was recommended as a physician to see me. At that stage I was perfectly fit, and then recently in April, I had another attack.

Q. Last month?

MR. GARRARD: No, April of '89.

BY MR. BRICKMAN:

Q. That's what I'm asking. April of '89?

A. No, this April.

Q. April of '90, last month?

A. I'm sorry, March.

Q. March of this year, 1990?

A. Yes. Quite recent.

Q. Was that when you were hospitalized for ten hours in March?

A. Yes. Either March or April. It was April.

Q. Within the last month or two?

A. Last month or two.

Q. You were hospitalized for ten hours?

A. Yeah.

Q. In the year 1989?

A. In the year 1990.

Q. Okay. But in the year -- let me finish my question. In the year 1989 -- let's go back another year.

A. Yeah.

Q. -- were you hospitalized at all?

A. Not at all.

Q. And you were not under any doctor's care in 1989 for any heart problem?

A. Yes. I was under the local chap there.

Q. Not Dr. McCloud?

A. Not Dr. McCloud. I was seeing him after that.

Q. When you had the problem with the depression, was that based on the 1990 hospitalization or some problem in 1989?

A. '89, just after I saw you.

Q. 1989. Were you having your heart problem then, too?

A. I had it a while, yes.

Q. Were you hospitalized then for that?

A. No. It came on by itself.

Q. So the only time you have been hospitalized for your heart has been in the year 1990?

A. 1990.

Q. And in 1989, you were under the care of a doctor for your heart and depression; is that correct?

A. Yeah, mild depression. Yeah.

Q. Mild depression; is that what you said?

A. Yes.

Q. And you have not been on any medication for the mild depression in the year 1990?

A. No.

Q. Are you in any way restricted as to what you can do because of your heart?

A. No.

Q. Are you restricted in any way or are you under any doctor's instructions with regard to your mild depression you had in '89?

A. No.

Q. Doctor, do you make clinical diagnoses of diseases such as asbestosis, or do you only do so pathologically?

A. Only pathologically. One reads the clinical notes, but mine has always been the pathological.

Q. Can you tell me how you diagnose a mesothelioma pathologically?

A. First of all, the ideal way of doing it is having a microscopic examination and a postmortem seeing the whole body and making sure

no other tumor exists in the other parts.

Q. Okay, wait a minute. Is that the first thing you do or is that the most important thing?

A. This is the ideal way of doing it, would be to see the whole situation, make sure there were no other tumors and then carry out a histological examination of the tissue making sure -- making sure that this was the -- we were taking sections from the whole tumor.

Q. Taking sections from the whole tumor?

A. Taking sections from various parts of the tumor. And one would examine these sections to see the histological features of the mesothelioma.

Q. And which features are those, Doctor?

A. The mesothelioma is a mixture of the type of material which can go two ways. It can go into the sort of epithelial tissue forming glands or masses of cells. It can also go into sarcomas or fibrous or spindle cell type of tumor. And in the ideal case, one should find both of the epithelial type and the spindle cell

type.

Q. When you say ideal, does that mean that's the easiest to identify?

A. That's the easiest to identify. You have various patterns of both the epithelial type.

Q. And the sarcomatous?

A. Sarcomatous type, which would indicate that you're probably dealing with a mesothelioma.

Q. Anything else you do or look for?

A. In doubt, a confirmation, if you have got the tissue fresh, you can look for the hyaluronic acid.

Q. If the tissue is fresh, do you want to look for that?

A. If it's fresh, then you have to put the tissue in a special mixture containing acetic acid and alcohol.

Q. Acetic?

A. Acetic.

Q. How do you spell acetic?

A. A C E T I C.

Q. Acetic acid?

A. Formalin acetic acid and alcohol.

And this keeps the secretion in the tissue. You can then stain for hyaluronic acid, which is soluable. You can do various stains which you stain for the presence of hyaluronic acid, and then you use an enzyme hyaluronidase, which should remove the stains from the tissue if hyaluronic acid is present.

Q. If hyaluronic acid is present, what does that indicate?

A. Indicates it is probably a mesothelioma.

Q. Probably is?

A. If you use a specific hyaluronic -- sorry, it indicates you are dealing with a mesothelioma under these circumstances.

Q. If it turns up positive?

A. Positive.

Q. It's a meso?

A. Meso. Then the other test is the one we also use which is the periodic acid shift, PAS, periodic acid-Schiff. If that stains positively, it's -- identifies the mucin as coming from the epithelial tissue, and what you are dealing with is probably an adenocarcinoma, not a mesothelioma.

Q. If the PAS is positive, it's an adeno?

A. It's an adeno.

Q. Any other things you do?

A. Then one of the more recent ones is the carcinoembryonic antigen.

Q. Spell that?

A. C A R -- it's CEA.

Q. CEA, okay. Now I know what you're talking about. CEA.

A. If CEA is positive or strongly positive, one realizes one is dealing with a tumor which is probably epithelial in origin.

Q. Does that mean it's a meso or not a meso?

A. CEA positive is not a meso. Weak positive, a few cases of meso have been reported.

Q. Weakly positive may be a meso; strongly positive, not a meso?

MR. GARRARD: Said moderately or strongly positive.

BY MR. BRICKMAN:

Q. Okay, moderately or strongly. Any other things?

A. Some people do the keratin test.

Q. Do you do the keratin test?

A. I have done it once or twice. I saw it done in these cases.

Q. Do you rely on the keratin tests?

A. Not nearly as much as on the other two.

Q. And tell me what results should show up for that to determine whether it is a meso or not?

A. Strongly positive keratin would indicate towards a carcinoma.

Q. And not a mesothelioma?

A. And not a mesothelioma.

Q. Anything else, Doctor?

A. Mainly most of the things really -- most of the cases you would do on the histology itself. And you do these tests to confirm it.

Q. When you say the histology, you mean just looking at it?

A. Looking at it, you get most of the answers except when you've got these large secreted areas, and then you have to decide whether it is a mesothelioma or adenocarcinoma.

Q. Just so I know, the most important to you is looking at it?

A. Yes.

Q. And then you do the stains to help confirm or deny or add information?

A. Yeah. I think the reason is so far there is no specific stain -- we all try to find a specific stain for mesothelioma. At the present moment, there is no specific stain but a series of negatives.

Q. With regard to the stains you have mentioned, let's talk about the hyaluronic acid. If that is positive, that would militate in favor of a mesothelioma?

A. Yes.

Q. Is that a 100 percent sure test?

A. No. Because it can occur in certain ovarian tumors. In a male it's 100 percent.

Q. In what?

A. In men.

Q. Males it's 100 percent. So if we have a male and the hyaluronic acid is positive, it's a meso?

A. It's a secretion process. Yes, it's a meso.

Q. Let me --

A. You've got to show -- you've got your areas of specialties or glands; and in the gland-like structures, you have to have hyaluronic acid there.

Q. If it's in the right place, it's a meso?

A. Yes.

Q. The PAS, periodic acid-Schiff, you told me that if that is positive, it's not likely an adeno?

A. Yes.

Q. What percentage do we get false positives on?

A. Very, very low.

Q. What percentage, Doctor?

A. I have only seen one.

Q. You have seen one false positive?

A. I was never convinced that -- it was a borderline case; let me put it that way. Other than that, the PAS is a pretty reliable stain.

Q. You have seen apparently one borderline case that may not have been correct?

A. Yes.

Q. Have you seen reports of others

where the PAS test showed false positives?

A. No, most people are happy about the PAS.

Q. Have you seen reports or false positives in the PAS test?

A. No.

Q. So as far as you are concerned, if the PAS test turns up positive, there is virtually no question in your mind, it's an adenocarcinoma?

A. No.

Q. No, or was what I said correct?

A. In my mind, it's an adenocarcinoma.

Q. So why do you do anything more than the PAS test if that's an absolute indicator whether it's a meso or adeno?

A. Well, I think the other tests, like the CEA, give you an extra --

Q. But you don't need it if it's 100 percent certain, do you?

A. I think one does it because it's an extra confirmatory test.

Q. I don't understand why you need extra confirmation if it's 100 percent correct.

MR. GARRARD: Wait a minute. I think you either are confusing him, or you are

confused. Because what he has said, if it is positive, that shows it's an adenocarciñoma. He has not said that if it is negative that means that it is a mesothelioma.

BY MR. BRICKMAN:

Q. If it's negative, what does that indicate, Doctor?

A. Negative -- well, it can be a malignancy, and some adenocarcinomas you get that are negative, particularly in a rapidly growing tumor.

Q. So an adeno can be negative or positive?

A. Yeah.

Q. But a mesothelioma has never shown positive on a PAS test?

A. Not in my experience.

Q. How about in the literature?

A. I think there -- no, I'm not sure about that. I don't think so.

Q. So any time you do a PAS test, and it turns up positive, you are 100 percent certain it's an adeno?

A. Yeah. But then the confirmatory test is the CEA.

Q. Why would you do the CEA if you were 100 percent sure that the PAS showed up positive?

A. Belt and braces situation.

Q. I don't know anybody that wears both.

A. Pardon?

Q. I don't know people that wear both, Doctor.

A. This is the sort of additional tests. These are the two that are being suggested at the moment.

Q. What I want you to explain to me is why would you suggest doing an extra test if you don't need it? It leads me to believe that the PAS test is not 100 percent certain.

A. I think there are some people who are not 100 percent certain of the PAS test.

Q. How about the CEA test, are there people who say that is not 100 percent certain?

A. There are people who say in certain mesotheliomas, as far as I know, you can get a slight positivity.

Q. You can?

A. Yes, but the majority of the people

say that the PAS is a much more reliable test.

Q. What percentage of CEA testing shows up false positives?

A. Well, the series we have done, I think it's one in 200.

Q. All right, the series that others have done?

A. Some of the other ones have got higher.

Q. Have some of them gone, in fact, as high as 25 percent?

A. I think so, yes. Going into this, and they say this is a slight. You get a slight positivity, the cell gets more and more intense. It's not the intensity.

Q. And how do you determine whether something is moderate or slightly positive with the CEA test?

A. The intensity of the staining.

Q. Be more specific. Does it turn a deeper blue, darker blue, deeper red, darker red?

A. A deeper orange-brown.

Q. Deeper orange-brown.

A. Yeah.

Q. So to distinguish between a slight

and moderate is a matter of how you determine the color?

A. Yeah.

Q. And the keratin test you said you don't rely on; is that correct?

A. Not how it's done.

Q. But that's got a high degree of margin of error, however?

A. It depends upon the fixation of the tissue. I'm not very up on the keratin.

Q. In any of the three cases, did you rely on the keratin test at all?

A. Well, when it is strongly positive, yes.

Q. If it's strongly positive, you rely on it?

A. Yeah.

Q. Is that 100 percent correct?

A. No, I don't think so.

Q. What margin of error is there for the keratin test?

A. Well, I think it depends on when I have reported it, but I am not very happy about it.

Q. When you say you are not very happy

about it, you are not very happy in these particular cases or just in general?

A. In general.

Q. Because it shows a larger margin of error?

A. Because there are so many keratins involved. I think the cytokeratin is strongly positive, is in favor of adeno, of carcinoma.

Q. The cytokeratin test.

What is the margin of error for the percentage of false positives with cytokeratin?

A. I'm not certain.

Q. You don't know one way or the other?

A. No.

Q. There is some margin of error apparently with it?

A. That's what I believe, yes.

Q. Doctor, could you tell me how you diagnose asbestosis pathologically?

A. Well, looking at it microscopically, the fibrosis of the lungs, usually starting at the base of the lower lobe and working upwards. Histologically one has interstitial fibrosis, starting from the smaller

bronchioles or respiratory bronchioles, and spreading out around the lung and in the fibrous tissue, one should find asbestos bodies or fibers.

Q. Do you require a certain number of asbestos bodies or fibers to be found before you would attribute fibrosis to or call it asbestosis, rather?

A. Well, they certainly should be -- the minimal asbestosis, one sees one or two. After serious asbestosis, one sees large numbers of them.

Q. One or two what?

A. Asbestos bodies. This is looking under the light microscope and the equivalent of that is 100,000 on the electron microscope.

Q. 100,000?

A. Fibers or bodies. Looking at the ordinary microscope, one would expect to find -- minimal is about two or three asbestos bodies in the interstitial tissue to take it as a reaction.

Q. Is what you told me, when you see one asbestos body, you typically find 100,000 asbestos fibers? Is that what you just said?

A. Yes. That's if you break down the lung to look in detail.

Q. That's an average breakdown, that for every asbestos body you can expect to see 100,000 asbestos fibers?

A. Yes.

Q. Is that correct?

A. Yes. This is in a case where you do it, you would expect to see 100,000 in the electron-microscopic field. Breaking it down to a gram per dry weight of lung tissue.

Q. Say it for me one more time, Doctor. If you see an asbestos body, what do you expect to see under the electron microscope?

A. Same area. If you took a gram of tissue, you would find at least 100,000 fibers.

Q. Did you discuss these three cases with anyone other than Dr. Gibbs and Mr. Garrard?

A. No.

Q. You have not talked to Dr. Pooley or anybody like that?

A. No.

Q. And you yourself came to the opinion as to how each one of these stains showed up, whether it was positive, strongly positive or negative?

A. Yes.

Q. Those are your opinions and not that of a technician or Dr. Gibbs?

A. No. I agreed fairly well with Dr. Gibbs.

Q. But what I'm getting at is those are your own personal opinions and not those of anyone else?

A. No.

Q. What I'm saying is correct?

A. The ones I did, yes.

Q. And you looked at, for instance, on Mr. Harris. You looked at the mucicarmine stain?

A. Yes.

Q. And the PAS stain?

A. Yes.

MR. GARRARD: Get your Harris report out.

THE WITNESS: Mucicarmine, yes.

BY MR. BRICKMAN:

Q. You looked at the mucicarmine stain yourself?

A. Yes.

Q. And when you wrote on the report, that was your own opinion and not some technician's opinion?

A. No, that was my own.

Q. And the CEA you looked at yourself?

A. Yes.

Q. And the cytokeratin you looked at yourself?

A. Yes.

Q. Do you know where these slides are that were cut by Dr. Gibbs that were stained?

A. Yes. They are in Pernarth.

Q. And were any other tests run or any other stainings done that are not written down here?

A. No. Just the ordinary hemotoxin assay who is the same one that does the routine on the tissue.

Q. That was done also?

A. This was done routinely. It's the routine stain we use.

Q. What did that show in these cases?

A. That showed the histological picture. Call out from the hemotoxin staining.

Q. Is that indicative of anything in particular or just to look at it histologically?

A. Just to look at it histologically.

Q. No other stains were done to your

knowledge?

A. That I was concerned with, no.

Q. Could I see your handwritten -- your reports you have in front of you, Doctor, please, sir?

A. The notes on the cases?

Q. Yes.

A. Which one, sir?

Q. All of them. The typed reports that have some handwritten language at the bottom.

A. All I have that for is to remind me of human chorionic gonadotropin.

Q. What is human chorionic gonadotropin?

A. It's a material which is extracted from the placenta which is used for staining for primitive tumors, germ cell tumors, and teratoma mass. Dr. Gibbs had done it, but I hadn't done it, because it was a test I discovered later when he really explained it to me. Because it occurs in the notes, what actual notes, and in the hospital. The evidence, we get germ cell teratoma as well.

Q. Did you yourself run a human

chorionic gonadotropin?

A. No.

Q. Did Dr. Gibbs?

A. I think it was done for Dr. Gibbs by Dr. Jasani, J A S A N I.

Q. You didn't look at that?

A. I didn't realize its significance.

Q. And what is its significance with regard to whether this tumor is a mesothelioma in Mr. Warrick's case?

A. It doesn't stain positively for mesothelioma, only for germ cells.

Q. Is that a 100 percent positive test?

A. So I have been informed.

Q. Who informed you of that?

A. Dr. Gibbs after reading the literature on the subject.

Q. Could I see the other reports like this?

A. Discussing the carinoembryonic antigen?

Q. Yes.

(Whereupon, a recess transpired.)

BY MR. BRICKMAN:

Q. Dr. Wagner, let's talk specifically about the case of Billy Harris. With regard to Mr. Harris, do you believe that he has mesothelioma?

A. No.

Q. Did you see in the medical records where he was diagnosed as having mesothelioma?

A. He was diagnosed as adenocarcinoma.

Q. Doctor, you didn't see in the medical records where he was diagnosed as having mesothelioma?

MR. GARRARD: You're talking about medical records or the autopsy report?

MR. BRICKMAN: Aren't those medical records? They are all medical records in my book.

MR. GARRARD: Not when the Plaintiffs' lawyer generates it at the funeral home.

THE WITNESS: Maybe I misread it, but I thought he was diagnosed as mesothelioma only at the end.

BY MR. BRICKMAN:

Q. Say that again, Doctor?

A. Mesothelioma at the end.

Q. He was diagnosed as mesothelioma?

A. Cause of death was given-- by Dr. Le Ber, mesothelioma, and he evaluated it on the fact that the earlier PAS was positive. There was no evidence of mucin production.

Q. Let's talk a second.

MR. GARRARD: Did you finish your answer?

THE WITNESS: Yes.

BY MR. BRICKMAN:

Q. You said the certificate of death says carcinoma of the lung. My death certificate doesn't say that. Did yours say cancer of the lung, your death certificate?

A. Yeah.

Q. It did? Okay.

MR. GARRARD: I think it says cardiopulmonary arrest.

BY MR. BRICKMAN:

Q. Mr. Garrard has shown you the death certificate. Is that the same one you saw?

A. Yes, it must be the same one. I thought I saw that the death certificate said carcinoma of the lung.

MR. GARRARD: I think that's

another one of the cases.

BY MR. BRICKMAN:

Q. It doesn't say carcinoma of the lung on that death certificate, does it?

A. No. I apologize.

Q. So in the autopsy report, it diagnosed mesothelioma; is that correct?

A. Yes.

Q. Now, where did this guy go about making his mistake in the autopsy report?

A. Well, the main thing, he said -- he said the PAS was positive, but no evidence of mucin production. The PAS that was done for us showed very marked positivity and also secretion.

Q. Have you looked at the slides he did, the stains -- the slides he did with the stainings on them?

A. No, I'm afraid not. These are going back before I was involved.

Q. Well, let me ask you this. What would account for the difference in the evidence of mucin production in your opinion?

A. It's hard to say, but -- certainly the sections that I saw showed one lump of tissue, one block of tissue, with marked mucin secretion

on the PAS.

Q. If this doctor in Texas was correct that there was no evidence of mucin production, would that then indicate to you it was a mesothelioma, if he is right?

A. If he was right, except we have now got the CEA in strong support of what we have got. Mucin showed a local positivity and the cytokeratins were strongly positive.

Q. So, in your opinion, this gentleman had an adenocarcinoma?

A. Adenocarcinoma, yes.

Q. All right. Now, you only studied the material in which tumor was present; is that correct? I'm reading your report, second sentence.

A. Yeah, with a certain amount of lung on there.

Q. You did not study the lung tissue where tumor was not present?

MR. GARRARD: Said there was a certain amount of lung on there.

BY MR. BRICKMAN:

Q. I misheard him.

A. It showed extensive evidence of the

permeation of lymphatics with carcinoma.

Q. Do you see the second sentence in your report: I only studied the material where tumor was present?

A. Yes.

Q. There was lung tissue that was not tumor that you examined?

A. There was lung tissue infiltrated by tumor which I studied.

Q. Did you have any lung tissue that was not infiltrated by tumor that you studied?

A. As far as I know, no, it was infiltrated.

Q. So you wouldn't be in a position of determining whether this person had asbestosis, would you, based on the material you looked at?

A. There was no evidence of what I had seen that he had asbestosis.

Q. You wouldn't expect to see asbestosis in the tissue?

A. No, this is lung tissue attached to the tissue.

Q. So just so I'm straight, you did see some lung tissue that did not have tumor in it?

A. I saw lung tissue with the lymphatics.

Q. And that didn't have asbestosis, in your opinion?

A. No. No.

Q. Did you see in the autopsy where the doctor found asbestosis, or he found --

A. He found brown granules.

Q. He found ferruginous materials consisting of bedded bodies consistent with fragmented asbestos bodies. Did you see that?

A. No, that I didn't see. I saw a certain amount of iron in the tissues.

Q. Did you find interstitial fibrosis?

A. Interstitial fibrosis I found was involved with the lymphatics being infiltrated with tumor.

Q. And the tumor was on which side, as far as you know?

A. The tumor was the right side.

Q. Right side. Did you look at any of the left lung?

A. No. I don't think I did, no.

Q. And if he found in the left lung areas of interstitial fibrosis, what would account

for that, in your opinion?

A. Well, by the presence of the tumor going through the lungs I saw, once again, this would probably be the continuation of the lymphatic impermeation.

Q. To the other side?

A. Yes. It usually does both sides.

Q. So you're saying there was interstitial fibrosis on the left-hand side, if there was, caused by the tumor?

A. Yeah.

Q. How do you differentiate the interstitial fibrosis caused from asbestosis from that caused by a tumor, Doctor?

A. Well, closely around the vessel, the lymphatics which are infiltrated.

Q. No. No. How do you differentiate between the two?

A. Well, one is much more apparently lymphatic than the other.

Q. One is much more what?

A. Around the lymphatics.

Q. How do you know the fibrosis on the left-hand side was around the lymphatics if you didn't look at it?

A. I thought I had, actually. Actually, I haven't.

Q. So you don't know what that interstitial fibrosis on the left-hand side was, do you, on the left lung?

A. No.

Q. Let me ask you, sir, to assume that this gentleman had asbestosis. Would you then attribute the cancer, as you believe it to be, at least in part to his asbestos exposure then?

A. If there was definitely evidence of asbestosis?

Q. Yes, sir.

A. Well, all I can say, if there was evidence, I should have seen something. I saw absolutely nothing of this.

Q. I am asking you the question, sir: If there was asbestosis --

A. If there was asbestosis, yes. We have got no proof that there was asbestosis.

Q. You didn't look at the left lung, did you?

A. According to this, I thought I had looked at more sections. As I stated, I had only looked at the one section.

Q. Yes, sir. I am asking you to assume, sir, that this pathologist who looked at the left lung said there was fibrosis, interstitial fibrosis. Would you agree with me, sir --

A. Oh, yes, except --

MR. GARRARD: Except what?

THE WITNESS: I thought -- what I say, I saw one lung. I have only got proof that I saw the one section. I thought I saw more.

BY MR. BRICKMAN:

Q. Yes, sir, I understand that. You also thought the death certificate said he died of carcinoma.

MR. GARRARD: I object to that and move to strike it. Inappropriate comment.

MR. BRICKMAN: Why is it inappropriate?

MR. GARRARD: That's just a catty remark.

MR. BRICKMAN: He obviously made a mistake if he didn't look at the lung, and he thought he did.

MR. GARRARD: He is saying it's not on his report.

BY MR. BRICKMAN:

Q. Doctor, do you have any evidence to indicate that you looked at the left side of the lung?

A. There is no evidence here.

MR. GARRARD: But he says he thought he did.

BY MR. BRICKMAN:

Q. Did you, Doctor?

A. I was wondering where I got this thing from. As the report stands now, you are correct.

Q. I am asking you to assume that the gentleman had asbestosis. If he had asbestosis, would you agree with me that asbestos exposure played a role in his, what you think, is an adenocarcinoma?

A. If it was severe asbestos.

Q. Severe asbestos or severe asbestosis?

A. Asbestosis.

Q. What do you mean by severe asbestosis?

A. More than just localized focal fibrosis.

Q. So now you not only have to have asbestosis, but you have to have severe asbestosis for you to attribute a lung cancer to asbestos exposure?

A. I would suspect it to be different from asbestosis. His situation doesn't bring this out.

Q. Whose situation?

A. The previous pathologist.

Q. Well, he writes in here, both lungs demonstrated emphysema and interstitial fibrosis and the presence of asbestos material. Both lungs.

A. Yeah.

Q. Assuming he is correct --

A. Assuming he is correct, it would be.

Q. -- would you agree with me that asbestos played a role?

A. It could have, yes.

Q. What do you believe caused his adenocarcinoma?

A. I think the peripheral adenocarcinoma -- he had had the -- he had respiratory problems right from '64.

Q. What does that have to do with the lung cancer?

MR. GARRARD: Let him finish his answer.

THE WITNESS: One would assume that the lung cancer was an association with his heavy cigarette smoking.

BY MR. BRICKMAN:

Q. What's his cigarette smoking history as you believe it to be?

A. Heavy cigarette smoker up until '79. Two packs a day.

Q. Until 1979?

A. Yeah.

Q. And where did you get that information from?

A. That occurred in the records. I've got it down as 7-24-79.

Q. 7-24-79 is when you have he quit?

A. He was smoking two packs a day and later notes said he stopped smoking, hasn't smoked since his retirement, which was in '79.

Q. Now, Doctor, would you call this cancer a pleural cancer?

A. No. Originated in the periphery of

the lung.

Q. So when some of these other doctors refer to it as a pleural cancer, that would be incorrect?

A. Well, that would be a cancer presenting on the pleura. That would be correct. It wouldn't be a cancer arising from the pleura.

Q. I'm looking at Dr. Binkowitz' report where he says it's a pleural carcinoma. He was the surgeon.

A. Yes, sir, he was talking about peripheral carcinoma presenting in the pleura, in my opinion.

Q. Wouldn't you normally say carcinoma if it was a peripheral carcinoma?

A. Yes, I don't think they are talking about pleural carcinoma.

Q. I'm sorry, I didn't hear that.

A. When he was talking about pleural cancer, I think he was meaning the peripheral cancer.

Q. It had to be the peripheral cancer?

A. That's what he was suggesting.

Q. All he says in my surgical report is pleural carcinoma. Preoperative diagnosis

pleural carcinoma; postoperative, pleural carcinoma?

A. A carcinoma involving the pleura.

Q. Let me ask you this: What are the typical clinical features of a malignant mesothelioma?

A. A tumor completely surrounding the lungs.

Q. Are there any certain signs we would look for that we typically wouldn't have with a peripheral carcinoma?

A. No, the features are very similar. The mesothelioma probably going more into the chest wall.

Q. Are pleural effusions more likely with one than the other?

A. No.

Q. So both adenocarcinomas and mesotheliomas are likely to cause pleural effusions?

A. Yes.

Q. Do you know Oscar Auerbach?

A. Yes, by name.

MR. GARRARD: Is he going to be used as a witness in this case?

MR. BRICKMAN: Might.

MR. GARRARD: I hope so.

BY MR. BRICKMAN:

Q. He says that peripheral carcinomas aren't caused by cigarette smoking. Do you hold to that opinion? He has written an article --

A. Yes, I know. It could or could not be.

Q. Could or could not be. Yes, sir, that's possible. But are you of the opinion that peripheral carcinomas can be caused by cigarette smoking? He is of the opinion that they cannot be. I want to know what your opinion is.

A. I think that they can, but it is an unlikely tumor. But in peripheral carcinoma, it's possible that cigarette smoking played some part.

Q. It's possible. You wouldn't say to a reasonable degree of medical certainty then?

A. No.

Q. Now, with regard to the staining that you did or that you had done, do you recall the precise day that you looked at the staining on the Harris case? Do you have it in your notes anywhere, sir?

A. No, I don't have it in my notes.

Q. Doctor, I am asking you to assume this hypothetical. If this man did have a mesothelioma, would you have attributed his mesothelioma to his asbestos exposure?

A. His asbestos exposure is -- the fact that he got exposed to asbestos fairly late in the story -- he claimed in '69 he had his first exposure to asbestos.

Q. So that would fit within your latency period, wouldn't it?

A. Well, only just, yes.

Q. So the latency was sufficient?

A. Just sufficient, yes.

Q. Just sufficient. Well, it's a couple of years over your timetable, but --

MR. GARRARD: Object to your characterization, Mr. Brickman. He said a typical latency was much longer than that, that some accepted 15 years; but I don't know that he said that is his necessary time frame -- just a moment, please.

MR. BRICKMAN: Is that an objection to the form of the question? It sounds more like your --

MR. GARRARD: I started to add an

objection.

MR. BRICKMAN: It's gone way beyond that.

MR. GARRARD: I wouldn't think so. I overrule you on that.

MR. BRICKMAN: We took it up to a three court judge panel, and they definitely said you were wrong on your ruling.

MR. GARRARD: They were English judges, so they don't know. Some said 15 and some said longer than that. I object to your characterization as fits your parameter.

MR. BRICKMAN: He also said he would go down to 14.

BY MR. BRICKMAN:

Q. Doctor, the latency period was sufficient in this time?

A. I wouldn't be very happy with it, but it has been reported.

Q. I'm sure this man wasn't happy, either. But it is sufficient; is that correct?

A. Right on the borderline of being sufficient, yes.

Q. If this man had a mesothelioma, would you agree with me, Doctor, that the most

likely cause of the mesothelioma was his asbestos exposure?

A. We don't know the extent of his asbestos exposure. We don't know what sort of fiber he was exposed to.

Q. Well, what else would you have attributed it to in this circumstance if it's a meso?

A. It's a hypothetical I don't want to get caught up in, because I don't think it is a meso.

Q. I'm asking you to assume it is a meso. The jury may find it is a meso, and they will want to know what caused that meso. If it is a meso, will you agree with me that his most likely cause is asbestos exposure?

A. If it was a meso. But it is not a meso.

Q. I understand your opinion. But if it is a meso, would you agree with me that the most likely cause is the asbestos exposure?

A. Once again, to what type of asbestos was he exposed?

Q. He was exposed to Mr. Garrard's asbestos which had Amosite in it?

MR. GARRARD: I object to that, because there is absolutely no evidence that he was exposed to asbestos manufactured by anybody I represent.

MR. BRICKMAN: Why are you in the case?

MR. GARRARD: Because the judge won't grant summary judgments, that's why, which are filed. He won't even rule on them.

BY MR. BRICKMAN:

Q. Assuming he was exposed to Mr. Garrard's product which had Amosite, would you agree with me that the most likely cause --

A. You need a tremendous amount of Amosite to cause mesotheliomas.

Q. Maybe he had a tremendous amount. You don't know, either?

A. He denies it himself. He said four or five times a month he supervised --

Q. So in your opinion --

MR. GARRARD: Let him finish.

THE WITNESS: He said he supervised the men replacing the asbestos insulation.

BY MR. BRICKMAN:

Q. So if it was a meso, you would be

of the opinion that it was not caused by his asbestos exposure?

A. I think it would be an open question. Could not be caused by his asbestos exposure.

Q. It could not be caused by his asbestos exposure?

A. Yeah. I think until we know what his asbestos exposure was.

Q. Well, based on the records that you have in front of you and that you reviewed, would you say that the most likely cause of his mesothelioma was asbestos?

MR. GARRARD: Excuse me. The doctor has not said it is a mesothelioma. He has said it is not a mesothelioma.

THE WITNESS: We are getting involved with a very hypothetical situation.

BY MR. BRICKMAN:

Q. Yes, sir, I understand that, but I am asking you to assume that, that it is a mesothelioma. What is the most likely cause of it, sir, under the facts as you know them?

A. If it was --

Q. Yes, sir.

A. -- it's possible that he had sufficient exposure to produce it. Once again, we are in a hypothetical situation. The part -- I would expect to see something in the lung tissues that I saw which would indicate this.

Q. Yes, sir, but you only looked at one side of the lung, correct?

MR. GARRARD: Excuse me. We don't know that, Mr. Brickman. When you say you only looked at one side, he said he thought he looked at both sides, but he doesn't have it written down. I object to you trying to make that into something more positive than what he said by your statement.

BY MR. BRICKMAN:

Q. Doctor, do you normally write down what you look at when you do these reports?

A. Yes.

Q. Did you write down that you looked at the left lung?

A. No.

Q. Ordinarily, if you had looked at the left lung, would you have written it down?

A. What I have got here is the lung, so I think I would have.

Q. You would have written it down?

A. Well, I said the lungs. Should have been -- if I had, it would have said the lung showed evidence.

Q. Doctor, I'm lost. I don't know what you're talking about.

A. As far as I can see from this report, I just say the lung showed evidence.

Q. The lung. That was in the singular?

A. Yes.

Q. And you also said up top, the only material you studied was the one in which tumor was present, and that was only on the right side, correct? And you normally write down, if you look at something, you normally write it down?

A. Yes. I should have written down the lungs.

Q. From looking at your report, does it appear that you only looked at the right lung?

A. It does, yes.

Q. Is there anything else, Doctor, other than what's in your report that makes you think this is an adenocarcinoma and not a mesothelioma?

A. No. All the evidence I got is in the report.

Q. All the evidence you base it on is in your report. That's what I'm getting at, okay?

A. We've got the cellular structure which shows the cells look much more like the adenocarcinoma than the mesothelioma.

Q. In what way, Doctor?

A. You have these -- the glands are lined by about -- mesothelioma, the glands are lined by sort of cuboidal cells. These are lined by these big, tall columnar cells.

It doesn't occur to me he has -- which occurs in carcinoma. And the fact that the cell's nucleus changed, nuclear stating very strongly, and the changes in the cytoplasm.

Q. What would we expect the cytoplasm to look like in a mesothelioma as opposed to an adenocarcinoma?

A. Cytoplasm is very clear in a mesothelioma.

Q. Clear in a mesothelioma?

A. Yes.

Q. What does the word vacuolated mean?

A. Vacuoles are holes.

Q. What does vacuolated cytoplasm mean?

A. Did I use the word vacuolation?

Q. Sir?

A. Did I use the word vacuolation?

Q. I don't know if you do or not. I'm looking at one of the medical records which refers to it as vacuolated cytoplasm. You used a different word, dark cytoplasm.

A. Vacuolated would suggest that there were holes, vacuoles in the cytoplasm. Variance in staining, I presume.

Q. Does that have any bearing on whether it's more likely an adenocarcinoma versus a mesothelioma?

MR. GARRARD: I think if you want to see where he is referring to, Doctor, that's what he is referring to in here.

MR. BRICKMAN: What are you looking at, Henry? I'm not looking at what you're looking at.

MR. GARRARD: What are you looking at?

MR. BRICKMAN: Mine has a different number than yours.

being an adeno or a meso?

A. This would favor it being an adeno.

Q. A vacuolated?

A. Yes.

Q. Okay. And would the size of the cells have any significance here?

A. The meso cells are usually not as large and not as tall.

Q. And are the meso cells normally the same shape, different shapes?

A. Frequently the same shape.

Q. Mesos?

A. Yes.

Q. How about adenos?

A. Adenos tend to vary in size and the shape of the cells.

Q. Okay.

A. Or have more variation than the meso.

Q. The nucleoli, would we expect them to appear one way with mesos and differently with an adeno?

A. They are usually very clear with the mesos.

Q. What is cyto glandular

differentiation?

A. This is where they look as though they are forming glands.

Q. Is that typical of a mesothelioma or adeno?

A. It occurs in both, really.

Q. Both. In your opinion, what was the cause of Mr. Harris' death?

A. Adenocarcinoma of the lung was the cause.

Q. Did you note any emphysema or emphysematous changes in the material you looked at?

A. I didn't mention it.

Q. Well, did you note any or did you recall seeing any?

A. No, I recall seeing what I had described.

Q. So did you not see any emphysematous changes, apparently?

A. No.

Q. Okay. Just for the record, Doctor, would you tell me the exposure history as you believe it to be for Mr. Harris?

A. As far as I know, he was -- when he

was working for ARCO Products as a safety inspector, four or five times a month he supervised men in asbestos installation.

Q. Anything else?

A. That's the only one that was mentioned, since we have no evidence of any other jobs that exposed him.

Q. With the mucicarmine stain, what does it mean to be focal positive as to be just positive?

A. Positive in localized areas rather than generally.

Q. What does that indicate, that it is positive in focal areas as opposed to a generalized area?

A. It suggests mucin is present. It is not as clear as the PAS.

Q. If it was positive all over and not just focally, that would militate more in favor of an adenocarcinoma?

A. I think so. Yes.

Q. Doctor, let me back up just a minute. Have you been deposed at all in the last year, had a deposition like this?

A. No.

Q. Have you testified in court in the last year?

A. No.

Q. Now, doctor, how long did this gentleman live from the time of initial diagnosis to the date of death?

A. He lived from August until October.

Q. Okay.

A. All these people had a very short survival period.

Q. Does that militate in favor of it being a meso versus an adeno?

A. Neither way. If the adeno was pretty much into the pleural cavity, they both would have a very short period of survival.

Q. As a general rule, would you agree with me that mesotheliomas typically take a shorter period of time before onset of death than adenos, as a general rule?

A. As a general rule, I don't know. If the adeno actually -- I presume you are continuing on the pleural surface. I think they are very much the same. Most cases from initial diagnosis, you would expect the adeno to be more rapid.

Q. Let's go to your number one step in determining whether something is an adeno or meso and that is looking for a primary site other than the pleura.

Was that done in this case?

A. As far as what one gathers from the record, the only place he found the tumor was in the lung.

Q. In the lung or in the pleura?

A. Pleura.

Q. Was there anything to indicate that there was a primary site other than the pleura?

A. There were some nodules in the lung, but I don't know whether these played a part in it or not. There was no other mention of any other organ having that.

Q. And you have no evidence of the pathology that you looked at other than to show a site at the pleura, do you?

A. No.

Q. And in the autopsy, the doctor appeared to look at the other parts of the body, did he not?

A. Appeared, yes.

Q. Have any pictures been made of any

of the slide materials, to your knowledge, Doctor?

A. Not as yet, no.

Q. Do you know whether plans are being made?

A. Plans are being made.

Q. They are?

A. Yes.

Q. Who is going to do that, sir?

A. Well, Dr. Gibbs and his team.

Q. Doctor, do you look at chest x-rays?

A. Yes.

Q. Did you look at any chest x-rays in this case?

A. No, just saw the reports.

Q. Did the chest x-ray reports that you looked at in any way assist you in making a determination as to whether this person had a mesothelioma versus an adenocarcinoma?

A. No. There was no indication it wasn't.

Q. Did you already answer that, Doctor? There was nothing in the record?

A. To separate the two. There was some suggestion of a previous disease, and the

nodules in the right lung. The lung had been there so long, it didn't look like it played a part in the tumor.

Q. Now, going back to the stains, Doctor, that you did, there was no staining with hyaluronic acid?

A. No. The tissue -- in all these cases, the tissue had been fixed, blocked in wax. If there had been any hyaluronic acid, it wouldn't have been washed out. Only if we received the tissue directly immediately from the necropsy, you can put it in a special fixative to keep the hyaluronic acid in the tissue.

Q. Now, Doctor, in looking at stains, is there much in the way of interobserver variability, meaning you might say something is positively stained or strongly positive, and somebody else equally as competent might say it's weakly stained?

A. I don't think there is that much. But there maybe -- I think strongly and positively weak are pretty close. I don't think you would have any difficulty there.

Q. Now, with regard to the CEA staining, is it easy to tell the difference

between something that is strongly positive and moderately positive? Is that an easy distinction to make?

A. I think you can make it, yes.

Q. Is there something where there might be interobserver variability where you can make a variation?

A. I think very weakly positive or negative, I think there would be people who would be happy to say whether it is very weakly positive or minus or very positive.

Q. Doctor, with regard to animal experiments, is there any way to look at the latency in animal experiments on things like rats and somehow convert it over to human beings?

MR. GARRARD: Latency?

MR. BRICKMAN: Yes.

THE WITNESS: It's -- people have attempted it. It's extremely difficult. You can -- there has got to be a long latency in animals which suggests there may be long latencies in humans.

BY MR. BRICKMAN:

Q. How about if there is a short latency in animals; would that probably indicate

that there is a short latency in humans?

A. One substance we see a short latency in animals is the Erionite, and we fortunately haven't seen any in humans.

Q. With asbestos, if animal studies showed a short period of time, would that mean that it could cause mesothelioma in a short period of time with humans? Does that mean it could happen?

A. I don't think there is a correlation here. Most asbestos fibers take the same amount of time to cause tumors in animals. Certainly in my experience, if you inject the stuff, between 700 and a thousand days.

Q. Have you ever seen animal experiments where it has taken a day to get a mesothelioma?

A. A day's exposure?

Q. Yes, it's a day's exposure if the latency exposure is a day.

A. No. No.

Q. Where the latency was as short as one day?

A. No, I have never seen that. I don't believe that would occur.

Q. How about if the exposure was only one day's exposure in an animal? Would that have any diagnose -- strike that.

MR. GARRARD: Wait a minute. He struck it. Don't answer it. Saves me an objection.

BY MR. BRICKMAN:

Q. Doctor, with regard to the distinction between pleural mesotheliomas and peritoneal mesotheliomas, do you have any opinions one way or another as to Amosite's ability or likelihood to cause a peritoneal mesothelioma?

A. I don't think it has been reported that they have caused it.

Q. Do you accept those opinions?

A. If they were Amosite exposures, yes.

Q. If they were what?

A. If they were Amosite exposures, yes.

Q. And peritoneal mesothelioma you would look at the same way you would a pleural mesothelioma, same features, same staining?

A. Same, yes.

Q. And the location would be the

difference between a peritoneal and a pleural?

A. Yes.

Q. And you would hold the same opinion with regard to all these matters we have discussed?

MR. GARRARD: Hold on. I object as to all these other matters we have discussed. We have discussed matters from 9:00 AM until 1:00 PM and From 1:00 PM to whatever time you have got back here to 20 minutes to 4:00.

And to ask him do you hold the same opinion with regard to all these matters, I would object to as too broad and ask you to rephrase that in some other fashion.

BY MR. BRICKMAN:

Q. The issue on the staining would be the same with regard to a peritoneal mesothelioma as they would for a pleural?

A. They would stay negative on these stains.

Q. And the histological features would be the same for a peritoneal meso as a pleural?

A. Yes.

Q. Now, there was apparently some sort of bloody -- was it a bloody effusion that this

Mr. Harris had?

A. Yes.

Q. Would you agree with me that that is not diagnostic, but indicative of it being a mesothelioma?

A. No. Could be an adenocarcinoma.

Q. But is that typical for an adenocarcinoma or is that more typical with regard to an adeno?

A. I think the presence of a bloody effusion is a suggestion either way.

Q. So it doesn't make a difference, then. Now, in this case, did the tumor encase the lung, or how did it appear, or how was it described as appearing in this individual?

A. It was described more prominent on the mediastinum.

Q. Is that typical of an adenocarcinoma or a mesothelioma, that appearance you have just described to me?

A. It could occur in either.

Q. Could occur in either. It's not more typical for a mesothelioma to encase the lung? Isn't that a typical description for mesothelioma?

A. Yes, but the peripheral adenocarcinoma can do so as well, but not as common.

Q. Now, was there any metastasis from the pleural area in this case, to your knowledge?

A. Well, I saw one lymph gland that showed a tumor.

Q. Does that indicate to you there was some degree of metastasis?

A. Yes, which would be more common in the adenocarcinoma than mesothelioma.

Q. The fact that there was metastasis?

A. Yes.

Q. Did you find any inflammatory cells in this material you looked at?

A. I have no record.

Q. If, in fact, your records are accurate and there was no inflammatory component to this malignancy, would that militate in favor of a mesothelioma?

A. No, it wouldn't militate either way.

Q. It would not?

A. No, inflammatory changes have nothing to do with the tumor itself. He had this

background of chronic obstructive lung disease.

Q. Now, Doctor, what is basement membrane?

A. Basement membrane is the -- when the cell comes in contact with the connective tissue. It's the membrane between the cell and the connective tissue or on the next cell.

Q. Have you ever seen it reported, Doctor, that in many mesotheliomas, that the cells form a basement membrane?

A. Well, I think any cell would form a basement membrane.

Q. And that basement membrane would stain positive with PAS?

A. If it attached. If it did stain, it would stain very weakly.

Q. It would stain weakly, but it would stain positive for PAS; is that correct?

A. I'm not sure. The only thing that really stains positive for PAS other than the mucin is diastagen. One stains with a diastasis, the diastagen, D I A S T A G E N.

Q. Now, with regard to the CEA stain, I think I got my numbers wrong actually before, Doctor. I said that some studies have shown that

up to 25 percent of mesotheliomas test positive. But actually, one study has shown that almost 50 percent of those studied were positive for CEA. Do you recall that?

A. It was a small study, yes.

Q. Small. They looked at 20 mesotheliomas, and nine of them stained positive for CEA?

A. Which one is that?

Q. I'm referring to a Churg article that cited a Corson article. Corson is the one you're familiar with, aren't you?

A. I thought it was with Churg.

Q. He referred to the fact that in mesotheliomas, in 20 cases, nine stained positive for CEA mesothelioma?

A. Churg goes on to say, if it was strongly positive, he feels much more in favor of the adenocarcinoma.

Q. Would you agree with his statement that this is still an area of great controversy, this immunohistochemistry?

A. On that. But his later articles, I thought he said pretty clearly that it was -- strongly positive, he would be more in favor of

mesothelioma.

Q. But he still says it's an area of great controversy?

A. Is that a recent --

Q. Yes, sir. Do you agree with that?

MR. GARRARD: What's the date on that, Mr. Brickman?

MR. BRICKMAN: I don't have the date on it, Mr. Garrard, but it is recent, I can tell you.

MR. GARRARD: I'm sure it has a date on the article, Mr. Brickman.

MR. BRICKMAN: I don't see it.

MR. GARRARD: If I could look at it, I could probably find it for you. I would be happy to. I don't want to mislead the doctor this is a 1990 article when we both know it's not.

THE WITNESS: My recollection was that Churg said if it was strongly positive, he would be in favor of the adenocarcinoma.

BY MR. BRICKMAN:

Q. That's not my question, though. He has also commented that there is great controversy about the use of immunohistochemical stainings.

MR. GARRARD: Doctor, I am going to

instruct you not to answer that question unless Mr. Brickman gives you the date of that article which he is purporting to read.

BY MR. BRICKMAN:

Q. Do agree there is a controversy or not?

A. Yes, there is a controversy, depending on how strong the stain was, yes.

Q. Now, the histological appearance of this tumor, in your opinion, favored an adenocarcinoma; is that correct?

A. That's correct.

Q. Did it resemble more an epithelial mesothelioma as opposed to a sarcomatous mesothelioma if you had to make that differentiation?

A. Yes, if it was an adenocarcinoma, it certainly was more in favor of a -- be closer to an epithelial mesothelioma.

Q. There was no element in your opinion of any sort of a sarcomatous feature to it?

A. Not in this particular case.

Q. Okay. And the epithelial pattern is the one that is most easily confused with a

metastatic carcinoma?

A. Yes. This is the one we hope the histochemistry is differentiating.

Q. Now, have you also seen it reported, Doctor -- and this is why I asked you about the information -- that CEA will often stain positive where it's done in areas of inflammation?

A. Yes, that's right.

Q. Now, in this case, you were unsure whether there was inflammation or not?

A. No. The CEA was done; there was no inflammation.

Q. How do you know that?

A. There were no -- the sighting around the cells and the area of the acini, I could see no inflammatory cells in that particular section. I said the area where it was staining, it was staining very clearly on the borders of the cells, particularly those in the subliminal area, and there didn't appear to be any infection in that area.

Q. Where would we expect inflammation in mesothelioma cells?

A. One wouldn't. The inflammation is probably bordered by secondary infection or

something of that nature.

Q. Which would be on the border, wouldn't it?

A. No. The inflammatory cells were covering as a mass, yes.

Q. As a what?

A. The inflammatory cells would cover -- the mesothelioma cells, unless they were necrotic would be unaffected by the inflammatory cells. Two different processes.

Q. Would you be able to distinguish inflammatory cells from the mesothelioma cells easily without any problem?

A. Yes.

Q. And in this case, you actually looked at some lung tissue, not just some pleural tissue; is that correct?

A. There was tumor tissue.

Q. From the lung?

A. This was from the tumor.

Q. Do you distinguish between the lung and the pleura?

A. It was the actual one that came from the tumor which was mostly external to the lung in this situation.

Q. That's what I'm asking you. So, you weren't --

A. Yes.

Q. The tumor you saw was tumor from the pleura and not from the lung?

A. As far as I know, the CEA was done on the tumor which was at that site outside the lung.

Q. It was outside the lung.

MR. GARRARD: Wait a minute, so you don't get your record confused here. He is talking about where the CEA staining was done in response to your question, not whether or not he looked at lung tissue at all.

THE WITNESS: Yes.

BY MR. BRICKMAN:

Q. The tumor material that was stained came from where?

A. It came from the tumor tissue which, as far as I know, was the tumor tissue on the surface or outside of the actual lung tissue.

Q. And was tumor tissue apparently on the pleura?

A. Well, you've got two pleural layers, haven't you? It was on the -- as far as I

know, it was on the lung external -- external to the lung. Most of the tumor was outside the lung.

Q. Was there any tumor on the lung itself, on the actual lung tissue?

A. On the actual border, it was hard to distinguish which was what. It seemed to me the tumor was in the lung and going outwards.

Q. It had invaded the lung?

A. It was started off at the surface of the lung and moved out.

Q. What is entrapped alveolar epithelium? What is that, Doctor?

A. That's when the alveolar epithelium gets entrapped in fibrous tissue, and you no longer get the -- as far as you know, you no longer get the normal purposes of the alveolar because the tissue is compressed into the fibrous tissue.

Q. Did you notice any of that in this case?

A. Not in the sections I saw, no.

Q. Now, as I understand correctly, Doctor, the mesothelioma starts out on the pleura and eventually invades the lung itself in some fashion?

A. It can, yes.

Q. Did it do that in this case?

MR. GARRARD: Wait a minute. Hold it. Object to the form of your question, because you are suggesting that he is saying a mesothelioma existed in this case.

BY MR. BRICKMAN:

Q. Did the cancer invade the lung in this case?

A. I was under the impression that the cancer was coming from the surface of the lung more than invading.

Q. Is that the same thing? Does that to you mean it invaded the lung, or it means it did not invade the lung when you say it was on the surface? Did not?

A. It started peripherally in the lung.

Q. But did it invade the lung tissue itself, or did it just stay on the surface?

MR. GARRARD: He answered you that it started in the periphery of the lung. In the periphery of the lung.

BY MR. BRICKMAN:

Q. So does that mean to you that it

was already in the lung, so to speak, and not just on the surface of it?

A. Very slightly.

Q. Slightly what?

A. I mean, all I saw were the sections showing the tumor which I presumed was the adenocarcinoma coming from the lung into the pleura.

Q. So the answer to the question was it was in the lung and not just on the surface of it?

A. It had invaded, yes.

Q. Had invaded.

A. I'm not quite certain which way it went. As I said, a possibility it was arising somewhere else other than the lung. It was being invaded.

Q. But it was inside the lung somehow in your opinion?

A. Yes.

Q. Doctor, was there anything else of significance in Mr. Harris' case that helped you with your diagnosis?

A. No, there wasn't. I was going to say, the evidence of the tumor being inside the

lung was extensive lymphangitis carcinomatosis, what I saw involving the lung.

Q. Okay. That's all the questions I have on Mr. Harris.

MR. BRICKMAN: The only thing I would like to add is the doctor's -- are we going to do this all in one deposition, or are we going to have separate covers? Do you care?

MR. GARRARD: I just assume do one.

MR. BRICKMAN: We have identified for the record and marked as exhibits these three items.

MR. GARRARD: We haven't marked as exhibits.

MR. BRICKMAN: I have marked them as exhibits.

MR. BRICKMAN: Doctor, I need to mark all of your papers if I could. We will substitute copies.

THE WITNESS: Which ones?

MR. BRICKMAN: All of your papers. Hand me all of your papers, and I will identify them in some fashion and then we will make copies.

THE WITNESS: I tried to keep the

information.

MR. BRICKMAN: I'll give them right back to you. Just hand them all to me, and I will identify them in some fashion would be the simplest.

BY MR. BRICKMAN:

Q. Doctor, I think you have a couple of other pages of handwritten notes?

A. Just the human chorionic gonadotropin. It comes in the next case.

Q. I understand. Let me mark them before I go home without marking everything and --

A. A brief thing about bronchoscopy.

Q. Doctor, do you have some other handwritten notes?

A. Just the train timetable.

Q. Oh, we need to have those train times, Doctor. That would be real important for this. We have gone through these.

(Whereupon, an off-the-record conference transpired.)

MR. GARRARD: I am just saying, I am not agreeing to mark them at this point.

THE WITNESS: Can I have my notes back?

MR. BRICKMAN: I have got to identify them for the record.

THE WITNESS: Those are exactly the same.

MR. GARRARD: You are going to get them back.

MR. BRICKMAN: We are going to make copies for the record. Plaintiffs' Exhibit 4 will be the doctor's medical report on Billy Harris with some handwritten notes at the bottom of the page. That will be 4.

Plaintiffs' 5 would be the doctor's one-page of handwritten notes written on both front and back, and Billy Harris Exhibit 6 will be the report of Dr. Wagner on -- typed report on Horace McBryde. That will be 6.

7 would be the two pages of handwritten notes on Horace McBryde, one of which is on front and back. One is just the front.

8 would be the typed medical report on Alvin Warrick.

THE WITNESS: Just the same as the other reports you have got.

MR. BRICKMAN: Yes, sir, I have got to put them in the record, though.

9 would be his handwritten notes front and back on Alvin Warrick.

10 would be a sheet of notes, looks like a cite to a particular article and the spelling of two different types of stains of some sort.

BY MR. BRICKMAN:

Q. Doctor, what is the significance of this article that you refer to at the bottom of this last page which I have just marked Exhibit 10?

THE WITNESS: This is a reference to a paper written by Goodwood -- Greenwood and coauthors in 1971 in the medical journal -- I'm sorry; the Journal of Industrial Medicine. And it just points out the fact that in the germ cells which you're coming to in the later case, you can have a very small small primary in the tests that is quite often missed and can be as little as 1 millimeter in diameter.

MR. GARRARD: Which case do you want to do next, Mr. Brickman?

MR. BRICKMAN: Doesn't matter to me. We can take the Warrick report next.

(Whereupon, Plaintiff's Exhibits 4

through 10 were marked for identification.)

(Whereupon, an off-the-record conference transpired.)

BY MR. BRICKMAN:

Q. Doctor, you have issued a report in the case of Alvin Warrick; is that correct?

A. Yeah.

Q. And in this case, you appeared to have looked at the tumor tissue and the lung tissue?

A. Yeah.

Q. Now, in this case, do you believe he has a diagnosis of mesothelioma?

A. No. I think this is a very unusual germ cell tumor.

Q. Prior to your having made this diagnosis of a germ cell tumor, you apparently had a different diagnosis?

A. No -- oh, the thing was -- yes. Sorry. Comes from the same thing. This was a tumor to be incriminative of an embryonal in nature. This comes down to the same as a germ cell tumor. Very incriminative tumor.

Q. Was this the case that Dr. Gibbs talked to you about where he showed you a certain

report or certain article on germ cell tumors?

A. No. He showed me the --

Q. Or a stain?

A. The stain. He showed me the stain, the human chorionic gonadotropin. It also occurs in the notes. They found it increased in the serum.

Q. What is a teratoma?

A. Teratoma is a primitive tumor but slightly advanced on what I was calling it, in which you pick up three different types of tissue which are not normally expected in that area.

Q. Where does a teratoma arise?

A. Both usually arise in the testes or the ovaries or occasionally in the midline, and they do arise in the anterior sternum of the chest.

Q. Did you do staining of this tissue?

A. I didn't, no.

Q. Did Dr. Gibbs, to your knowledge, do staining?

A. He got the stain for the chorionic gonadotropin, yes.

Q. Why didn't you do stains in this case?

A. I recognized -- I claimed this was a very primitive cell tumor or embryonic tumor; and until it was pointed out to me, I hadn't gotten knowledge of this particular stain.

Q. You hadn't gotten what?

A. Didn't know of this particular stain.

Q. Why didn't you do the other type stains on it, Doctor, or did you?

A. No.

Q. Why didn't you?

A. Because I was sure -- there was no need to use the stains we used to differentiate between adenocarcinoma and mesothelioma.

Q. Dr. Gibbs apparently did some staining on this, didn't he? Do you know why he did the staining?

A. No. No.

Q. You didn't even bother to look at his staining, did you?

A. I haven't recorded on this case.

Q. What?

A. I have no record of date on this.

Q. The fact that the CEA was negative, does that have any significance to you in this

case?

A. I don't know how the CEA goes in these.

Q. But if it was a mesothelioma, we would expect the CEA to be negative, wouldn't we?

A. It could be, yes. And some adenocarcinomas are negative.

Q. And what did this tumor appear like to you? How would you describe it?

A. It was a tumor -- sort of regular large foamy cells. A large hemorrhage and necrosis possibly due to treatment and the large tome cells and these large giant cells without circles which are very primitive. They have no boundaries, no margins, no cell membrane.

Q. And do you have an opinion, Doctor, as to where this tumor arose?

A. Could have arisen from the anterior chest wall. Unlikely -- they did examine his testes several times, but sometimes the primate in this thing could be so small, you could be a millimeter in diameter, yet you would have large tumors within the lung, within the thoracic cavity.

Q. Say that again, Doctor. I missed

it.

A. I was quoting the Greenwood article which did say that in cases, he had seen a case in which the tumor actually of the testis was one millimeter in diameter, and yet the sectile was occupying the whole of the chest, one side of the chest, whole one side of the thoracic cavity.

Q. Who is a Jasani, B. Jasani?

A. He is the authority on doing the more detailed immunohistochemistry in Cardiff.

Q. Is he the one who did the stainings in these cases?

A. I believe just in the one case.

Q. He did it in one case, the Warrick case?

A. The Warrick case, yes.

Q. He is a doctor?

A. Yes.

Q. And you didn't look at his stainings, though?

A. No. Not at that stage, no.

Q. Not at any stage, have you?

A. Well, no. Yes, I have. I looked at it later on.

Q. You did?

A. It stains the giant cells very neatly.

Q. You looked at his staining, but you didn't put it in your report; is that correct?

A. Well, I sent the report off when I came back and had him show me how this thing worked in. I was thinking that we had sufficient on the histology just to make the comment.

Q. Did you see in the autopsy where the pathologists found asbestosis?

A. I couldn't see any asbestosis.

Q. Did you see any asbestos bodies?

A. No.

Q. Is a teratoma a carcinoma of the lungs?

A. No. Teratoma is a primitive tumor of --

Q. Are you --

MR. GARRARD: Wait a minute. Let him finish. Did you finish?

THE WITNESS: It's a primitive tumor of embryonic origin. It's slightly more developed than a germ cell tumor, which is what I always called it.

Q. Are you and Dr. Gibbs the only two

people to say this was a teratoma?

A. In the records, I don't know who else had seen it. I didn't say it was a teratoma.

Q. What?

A. He used the word teratoma. I thought it was an earlier more primitive.

Q. Oh, you don't believe it was a teratoma?

A. It could be a teratoma at the stage I examined it. I thought it was a germ cell tumor which is more primitive than a teratoma. Teratoma, the tissue has organized iteelf in three layers of tissue, whereas in the germ cells, it's even before this happens.

Q. What causes germ cell tumors?

A. These are sort of vestigial clumps of cells left over from the maturation of the fetus, maturation from the earliest part of conception.

Q. So this man had this cancer from the very beginning of his life?

A. No. They develop usually in the -- between 30 and 40 in men. It's there as a group of cells. I'm sure a lot of them they don't develop. If they do develop, this is the usual

age. And also the question, gynecomastia, which is clearly with it.

Q. What is that, sir?

A. That's round developing breast as seen in a woman.

Q. And that's a result of --

A. This is a result of the secretion of the human chorionic gonadotropin.

Q. And that indicates it is a germ cell tumor?

A. Yes.

Q. Does that indicate it's more of a germ cell tumor than a teratoma?

A. It would cover both.

Q. Would it have anything to do with any other type of tumor?

A. No. The answer is no. It's a primitive -- it's primitive to the development of the lung and the organs of the body.

Q. Now, did you note where this gentleman had some prior drug problem?

A. Yeah.

Q. In your opinion, did his drug problem in the past have anything to do with his tumor?

A. Nothing at all. Actually, in the notes, they mention that they think of a germ cell tumor there as well.

Q. What notes are you referring to, Doctor?

A. The notes on -- of Alvin Warrick.

Q. One doctor's notes, you mean?

A. Yes.

Q. Does this type of tumor where there is a teratoma or a germ cell tumor typically cause pleural effusions?

A. If it occurs in the pleural cavity, yes.

Q. The tumor that you saw came from what part of the body, sir?

A. It was certainly coming from the -- in the thoracic cavity, probably from the anterior mediastinum because it described the tumor as being nodules in the anterior.

Q. Did you do any iron stains to look for asbestos bodies?

A. I saw a few fragments of tissue, iron granules. They weren't asbestos bodies.

Q. But did you do any iron staining to see if they were asbestos bodies?

A. No. They didn't have the appearance of the asbestos. They were purely granules without any fiber in between them. There was no fiber there.

Q. Did you see where the pathologist found scattered ferruginous material?

A. Yes. That just means scattered -- scattered iron products in the tissue. That doesn't mean asbestos bodies at all.

Q. Now, did you have an exposure history to asbestos for this individual?

A. It was suggested that his father had worked for Chevron for a while. 38 years. But in the report, it doesn't say where Chevron was or what it is.

Q. Do you believe he was exposed to asbestos?

A. It doesn't sound very likely to me.

Q. So, it's not likely that he had an exposure to asbestos, in your opinion, based upon the records you reviewed?

A. Yes.

Q. Is there any treatment for a germ cell carcinoma?

A. They tried chemotherapy in this

case. It didn't seem to respond.

Q. Is that the typical treatment for a germ cell carcinoma as opposed to an adenocarcinoma?

A. Either try chemotherapy or radiation.

Q. The treatment for a germ cell cancer is no different than that for any other type of cancer?

A. I don't think so. They do respond in some cases. There didn't seem to be any response there. The tumor just went on growing.

Q. Is this typically a fatal or most likely a fatal disease in people who have it?

A. Usually is a fatal disease.

Q. Usually is?

A. Yes.

Q. And is there a timetable between the time of first discovery of the tumor and death?

A. It is very rare. I have no evidence of it.

Q. You have what?

A. No evidence of it, the timetable.

Q. The timetable. Is this type of

tumor easily confused with a squamous cell carcinoma or an adenocarcinoma?

A. It contains bits of keratinized tissue which could be compared to the squamous cell carcinoma, and possibly by itself the structure of these abnormal primitive cells could possibly be mistaken for adenocarcinoma.

Q. For what type of tumor?

A. Adenocarcinoma.

Q. And in this individual, he was first diagnosed as having a squamous carcinoma, and then later the doctors said it was an adenocarcinoma, and then on autopsy, the doctor said it was a mesothelioma?

A. Mesothelioma.

MR. GARRARD: It was also diagnosed as a germ cell tumor in the records.

MR. BRICKMAN: Is that an objection?

MR. GARRARD: A statement. You seemed to be listing --

MR. BRICKMAN: I didn't know you were under oath to tell the truth.

THE WITNESS: I did mention this.

MR. GARRARD: You did. I didn't

want Mr. Brickman to leave that out of his list of mentions in this case.

(Whereupon, an off-the-record conference transpired.)

BY MR. BRICKMAN:

Q. Doctor, the germ cell cancer is not caused by smoking then, I assume?

A. No.

Q. So it's your opinion that smoking played no role in this man's cancer?

A. No.

Q. And a germ cell cancer, are those large cells?

A. They can be large cells.

Q. Were they in this case?

A. Yes, there were these large syncytial giant cells.

Q. What does that mean, syncytial?

A. It means that there is no sort of boundary to the cells, no cell membranes.

Q. What is the significance of there being a minimal alveolar reaction? What does that indicate to you, Doctor?

A. The reaction was in the alveolar, not in the general lung tissue, not in the

interstitial tissues.

Q. Now, if this was a germ cell carcinoma, is that the type of -- and it was in you said the hilar region of the lungs?

A. In the anterior chest wall.

Q. Is that something that one could typically easily find at autopsy and identify as such?

A. No. At this stage, it was a massive tumor. And one would have found the whole tumor occupying the one side, the right side of the chest, as it was in this case. It was presenting more anteriorly than ...

Q. So it's not anything specific in finding it grossly that you could identify it as a germ cell carcinoma?

A. No. No. It was just a huge tumor mass by the time they found it.

Q. This was not, in your opinion, a pleural tumor of any sort then; is that correct?

A. That's correct.

Q. And he died as a result of this tumor?

A. Yes.

Q. Did you have sufficient tissue,

Doctor, in this case for your opinion? I mean, you don't have any problem with the amount of tissue you had? There was a sufficient amount?

A. Yes.

Q. Have you talked to Dr. Jasani about this case?

A. No.

Q. Is there anything else of any significance in the Warrick case that is not contained in your medical report, Doctor?

MR. GARRARD: And that you have not talked about?

MR. BRICKMAN: I'm trying to think what else we talked about.

THE WITNESS: This is my opinion.

BY MR. BRICKMAN:

Q. You did not rely on the stains in this case; is that correct?

A. No.

Q. In fact, you did not even see the stains in this case; is that correct?

MR. GARRARD: Wait a minute. He did not rely on the CEA stain, but he has told you he did rely on the results from the HCG.

THE WITNESS: Subsequent to my

coming down. This was afterwards.

BY MR. BRICKMAN:

Q. You relied on the HCG for what, Doctor?

A. For the evidence of this being a germ cell tumor or teratoma.

Q. Is there a difference between the germ cell and teratoma?

A. Teratoma is slightly more developed. Teratoma is a germ cell tumor. The primitive cell tumor is more primitive than the teratoma.

Q. Based on that staining you did or Dr. Gibbs did, do you now have an opinion it is a germ cell tumor rather than a teratoma?

A. Could be either.

Q. So that stain didn't help you either?

A. Could be positive for both.

Q. How would that stain be for an adenocarcinoma?

A. Negative, as far as I know.

Q. How would it be for a mesothelioma?

A. Negative.

Q. And that stain is called a what

again? Tell it to me again.

A. It's called human chorionic gonadotropin.

Q. That's an HCG stain?

A. HCG stain.

Q. And do you know what the margin of error is or the percentage of cases that show up false positives?

A. No.

Q. And you do not believe that this was a tumor that metastasized from the testicular primary, do you?

A. It could, but -- it could, but there is no evidence there of histological examination of this. Possibly it could, but I don't think this is.

Q. But that's now where you think it came from, from the testes?

A. Probably from the anterior mediastinum. But they had examined fairly well, although not microscopically.

Q. That's all I have on Mr. Warrick. Thank you, Doctor. Let's go to the next one.

(Whereupon, a recess transpired.)

BY MR. BRICKMAN:

Q. Doctor, did you at the request of Mr. Garrard besides looking at the Harris and Warrick tissue also look at the case of Horace McBryde?

A. Yes.

Q. Now, you apparently looked at some stains of Mr. McBryde; is that correct?

A. That's correct.

Q. Was there an autopsy done on Mr. McBryde?

A. I could find no evidence of it.

Q. Okay. And would you agree with me that his treating physicians seemed to indicate that he had a mesothelioma?

A. Yes.

Q. Did you see the death certificate of Mr. McBryde?

A. Yes.

Q. And what did that indicate that he had?

A. On second thought, I didn't see the death certificate. I knew that he died on 3-14-1980.

Q. But did you not see the death certificate?

MR. GARRARD: Do you have a copy of it, Mr. Brickman?

MR. BRICKMAN: Yes, I do.

MR. GARRARD: Could I see it?

MR. BRICKMAN: You mean you don't have it?

MR. GARRARD: No, I don't.

MR. BRICKMAN: I'll think about it. Do you have to know right now whether I'm going to give it to you or not, or can we wait until the end?

MR. GARRARD: It was the order of the judge which you have obviously violated to provide us with all of the records in the case three weeks ago.

MR. BRICKMAN: Your staff obviously must have messed up.

MR. GARRARD: You are obviously in contempt of court.

MR. BRICKMAN: You mean you're not going to turn over your doctor's reports to us?

MR. GARRARD: Already turned them over to you.

MR. BRICKMAN: Not with this one. What is that?

MR. GARRARD: Support notes.

MR. BRICKMAN: You mean you don't have to turn those over to me? (Tendered)

BY MR. BRICKMAN:

Q. Doctor, let me show you the death certificate in case you haven't seen it?

A. Mesothelioma.

Q. Mesothelioma is listed as the cause of death?

A. Yes.

Q. Now, the staining that you did was apparently from a biopsy of subcutaneous nodule. What is that?

A. There is a nodule growing up from the tumor.

Q. Is that a good place to look at the tissue to determine what it is?

A. Yes.

Q. That's not a problem, the fact that you looked at it from a subcutaneous nodule as opposed to the tumor itself?

A. It was done on the pleural biopsy.

Q. No, if you read your report, you appear to say that you could not do histochemistry and immunohistochemistry on the pleural biopsy.

Do you see that?

A. Yeah. Yes, I see that. Well, this would be the best bit of tissue available.

Q. Well, I understand that. But what are the problems of doing it from the tissue that you looked at that you wouldn't have had if you had been able to do it from the pleural biopsy?

A. I don't think -- except we were dealing with the more recent growth of this tumor.

Q. So it wouldn't make any difference at all, would it?

A. I don't think so, no.

Q. Now, in this case, the PAS diastase?

A. Diastase.

Q. Stained negative. That indicates more likely a mesothelioma, doesn't it?

A. It can happen in a rapidly growing adenocarcinoma.

Q. That, however, militates more in favor of it being a mesothelioma than an adenocarcinoma, doesn't it?

A. It's a neutral finding. Because we know rapidly growing adenocarcinomas quite frequently don't have evidence of mucin secretion.

Q. Mesotheliomas however stain negative for PAS with diastase, correct?

A. Yes.

Q. And in this case, it was a negative stain?

A. Yes.

Q. The CEA stain in this case you reported was not strongly positive, but was moderately positive; is that correct?

A. Yes, that's correct.

Q. And were you able to look at this tumor from a histological point of view?

A. Yes. Histological point of view. There was little tissue, and the tumor really showed features which could be of an adenocarcinoma.

Q. Did it also show any features that it was a mesothelioma?

A. Well, in my views, it came out more likely to be an adenocarcinoma.

Q. All right, sir.

A. But obviously we were differentiating on the CEA and the other stains. There wasn't a great deal of tissue to come to diagnosis on.

Q. Did you find that there were atypical cells present?

A. Yes, there were.

Q. And --

A. Undifferentiated tumor which would be atypical cells.

Q. Is that consistent with a mesothelioma?

A. Slightly more to fit in with the adenocarcinoma.

Q. The mesotheliomas show up typically as cuboidal cells?

A. Usually. Usually smaller cells. You can get larger cell varieties of them.

Q. Did you see any cuboidal cells in the material you looked at?

A. Not that I recall, no.

Q. You do not report on what you saw on the pathology labeled S 87-2779.

A. In two of the specimens, four small biopsies in two of them, there was evidence of fragments of undifferentiated tumor.

Q. And what was in the other two?

A. These were, as far as I know, just fragments of connective tissue.

Q. And what did that tumor look like? Did those cells have any particular appearance?

A. According to my notes, no. They looked like a tumor.

Q. Did they appear to have cuboidal cells?

A. The cells were of variation in shape and size. Some small, some large.

Q. I'm sorry, some small, some large?

A. Yeah.

Q. Why do you say that?

A. As I said, the tumor was composed of cells varying in shapes and size.

Q. No, you are looking at a different one than I am.

A. No. Once again, differentiation of the cells. All sizes and shapes.

Q. I'm looking at the pathology marked S 87-2779?

A. There was a picture of sheets of malignant cells. No clear indication which they were.

Q. You just recollect that, or are you reading that in your report?

A. Minute fragments of

undifferentiated tumor.

Q. That's what that means?

A. Yes.

Q. All different sizes and shapes?

A. Just a massive tumor which was hard to --

Q. I'm just curious. You put that, undifferentiated tumor describing the pathology S 87-2779, and you're telling me that means the tumor was composed of cells varying in shapes and sizes?

A. With a lot of activity.

Q. Why when you were describing S 87-4107 did you use the phrase the tumor was composed of cells varying in shapes and size as opposed to undifferentiated tumor? Is there a difference?

A. Not really.

Q. Is there a difference or not really?

A. Forming definite bacilli in the subcutaneous nodule.

Q. Did you see any cuboidal cells in S 87-2779?

A. There may have been, but I didn't

particularly notice that there was a sheet of malignant cells.

Q. You saw cuboidal cells; is that correct?

MR. GARRARD: Wait a minute. He said there may have been.

THE WITNESS: I didn't notice them. Some of the cells in their size differed in shapes and sizes, and some of them may have been cuboidal.

BY MR. BRICKMAN:

Q. Do you recollect that some of them may have been cuboidal, or are you just talking off the top of your head?

A. Cells of different shapes and sizes.

Q. You recollect that?

A. Yeah.

Q. And they may have appeared cuboidal?

A. They may have. The majority, there is no evidence the majority showed any particular pattern.

Q. For mesotheliomas, do they all have to be cuboidal for it to be typical mesothelioma?

A. No, they can vary.

Q. And that's apparently what you saw, that they varied with some of them being cuboidal, correct?

A. Some of them being larger and some being smaller.

Q. Is that typical for a mesothelioma?

A. It could fit in for a mesothelioma, but it would be more particular for an adenocarcinoma.

Q. Even the cuboidal cells?

A. A few of the cuboidal cells vary in size.

Q. Doesn't cuboidal refer to shape?

A. Yes. Can be shape or can be elongated.

Q. Do adenocarcinomas often appear as cuboidal cells?

A. Occasionally. Occasionally they do have cuboidal cells in them.

Q. But more likely if it is a cuboidal, it's a meso rather than an adeno, speaking in general terms?

A. Massive. Sort of massive tumor cells of different shapes and sizes. Some of them

may be small and some of them were large.

Q. Doctor, let me ask my question. Maybe we are not understanding each other.

A. You're saying was this typical of a mesothelioma, I understand.

Q. The fact that there were cuboidal cells, is that more typical of mesothelioma than it is of adenocarcinoma?

A. If the predominant cell was cuboidal, yes.

Q. Now, when you say the specimen had been crushed for the pleural biopsy, are you referring to the tissue in the glass?

A. Where the tissue had been removed. It wasn't a clear biopsy.

Q. Oh, I see. So nobody would have been able to look at that pleural biopsy and make a determination from it?

THE COURT REPORTER: Your answer?

THE WITNESS: My answer is I don't think so. They may have been, but it would have been very difficult to make a diagnosis from it.

BY MR. BRICKMAN:

Q. Did you see where it was done in the records and that they didn't say it was

crushed in any way?

A. This can happen quite often taking a biopsy.

Q. But did you see where the hospital where this man was being treated had this tissue, this pleural biopsy, and looked at it and didn't say it was crushed?

A. I saw that, yes.

Q. So apparently it wasn't crushed at the time they had it?

A. Well, I felt it was difficult to make out details of it.

Q. Well, did you read the report of the doctor that did get a chance to look at it?

A. Yes.

Q. If that doctor is correct, and there were sheets and clusters of large polyhedral cells, is that consistent with a mesothelioma?

A. Large polyhedral cells would be more consistent with a carcinoma. It could be either way.

Q. Could be either way. And the fact that it came in sheets, would that have any significance?

A. No. Undifferentiated. Once again,

this could go either way, but I think slightly in favor of the adeno.

Q. Even the fact that it came in sheets?

A. You can get sheets there. But the fact that they are large polygonal cells.

Q. Polyhedral?

A. Was it polygonal or polyhedral.

Q. Polyhedral. Does that make a difference to you, sir?

A. No.

Q. What's the difference between polygonal and polyhedral?

A. Well, I always thought polyhedral was in three dimensions and polygonal was in two. I may be wrong on this.

Q. Did you attempt to look at the tissue in S 87-2621?

A. Yes, I attempted to look, but I couldn't see any clear differentiating site on the tube. And I referred to the fact that it had been crushed.

Q. Doctor, what do you believe to be this gentleman's exposure history to asbestos?

A. I didn't find any -- he had been in

the Air Force and at NASA. There seems to be no clear suggestion of an exposure.

Q. ... you do not have any evidence of exposure?

A. No.

Q. Did that in any way affect your opinion?

A. No. No, I reviewed his occupation in detail. I received that after the diagnosis.

Q. Did you discuss this case with Dr. Gibbs?

A. Yes, we discussed this case.

Q. And did y'all both agree that it was an adenocarcinoma?

A. Yes.

Q. Do you have an opinion as to where the primary site of this tumor was?

A. No. There was no clear indication where the site was. A massive tumor in the pleural cavity.

Q. What's that?

A. Except it was in the -- there was a tumor in the pleural cavity. It also -- the destruction of the tenth rib, more in favor of an adenocarcinoma.

Q. Doctor, let me go back a minute. Doctor, if the cells are large and polygonal, aren't those the ones that are typical for epithelial mesotheliomas?

A. Not necessarily. Because there are forms of mesotheliomas which this can happen, but the typical one is the smaller cuboidal cells, as we mentioned earlier.

Q. Doctor, what did you believe to be the latency in this case?

A. Let's see. July, '87 to -- July '87 to March '88.

MR. GARRARD: You mean the period of time between diagnosis and death?

THE WITNESS: Diagnosis and death. Was that the question?

BY MR. BRICKMAN:

Q. No, latency. What was the latency in this case?

A. Could you rephrase the question?

Q. What do you believe to be the latency period in this case?

MR. GARRARD: He is talking time from initial exposure to asbestos to diagnosis.

THE WITNESS: I have no evidence of

exposure to asbestos is my problem.

BY MR. BRICKMAN:

Q. Okay. Doctor, would you agree with me that virtually every doctor that was examining him at the end of his life within the last year or so of his life believed he had a mesothelioma?

A. Yes, I would.

Q. And those doctors apparently had the benefit that you did not have, of being able to examine the pleural biopsy; is that correct?

A. Yes. They came to a conclusion on it.

Q. Sir?

A. They came to a conclusion on it.

Q. They had the benefit of being able to look at some material that you apparently could not look at?

A. I didn't have all of it.

Q. Whatever reason, you weren't able to look at the pleural biopsy that they were able to look at; is that correct?

MR. GARRARD: He looked at it. He couldn't make a determination.

THE WITNESS: It wasn't suitable to come to a differential diagnosis or diagnoses.

BY MR. BRICKMAN:

Q. Is there anything else other than what's in your report, Doctor, as to why you believe this to be an adenocarcinoma as opposed to a mesothelioma?

A. No.

MR. GARRARD: You mean inclusive of the things you have talked about here?

MR. BRICKMAN: I don't know what else he has talked about.

MR. GARRARD: It's on the record what he has talked about here. Your question, Mr. Brickman?

MR. BRICKMAN: I'm asking him if there is anything else in his report that he relied on.

MR. GARRARD: I am going to object to the question because the doctor has told you a number of other things as he has testified here that provide some of the bases for his diagnosis. And unless you incorporate that into it, I object to the question.

BY MR. BRICKMAN:

Q. Anything else, Doctor?

A. I was talking about the destruction

of the tenth rib.

Q. Anything else?

MR. GARRARD: That's anything in addition to what you have talked about in your report.

MR. BRICKMAN: That is not my question. You can have whatever question you want later but that is not my question.

MR. GARRARD: I don't think it's a proper question to have asked the doctor questions all along about this case in toto and then say, is there anything in addition to your report that supports your opinion when he has given you other things. I think that's an improper question.

MR. BRICKMAN: That's why we are allowed to make objections, Mr. Garrard.

MR. GARRARD: We are not allowed to create an incorrect record, Mr. Brickman.

BY MR. BRICKMAN:

Q. Go ahead, Doctor.

MR. GARRARD: Don't go ahead. I am telling you not to answer that question unless Mr. Brickman wants to incorporate the report as well as other things you testified about.

MR. BRICKMAN: Are you instructing

him not to answer?

MR. GARRARD: Yes.

MR. BRICKMAN: We will obviously move to have the doctor stricken as a witness.

MR. GARRARD: You can move whatever you want to. That's not a proper question.

BY MR. BRICKMAN:

Q. Doctor, do you intend not to answer that question? Do you intend to follow Mr. Garrard's advice and not answer the question?

MR. GARRARD: Yes.

THE WITNESS: Yes

BY MR. BRICKMAN:

Q. Is Mr. Garrard your attorney?

MR. GARRARD: No.

THE WITNESS: No.

MR. GARRARD: Mr. Garrard does have an obligation to protect the record, however, as an officer of the court.

MR. BRICKMAN: You can do that by objecting to the question, and the question and answer gets struck if you are correct. It doesn't get struck if you are wrong. But I don't believe you have any right to tell the witness not to answer a question like that.

BY MR. BRICKMAN:

Q. Doctor, how many doctors diagnosed mesothelioma in this case?

MR. GARRARD: If you know, Doctor.

THE WITNESS: I don't know. The majority certainly did.

BY MR. BRICKMAN:

Q. Did any of them diagnose adenocarcinoma that you saw?

A. No. Did they?

Q. So the only two doctors that diagnosed adenocarcinoma in this case are you and you believe Dr. Gibbs?

MR. GARRARD: I object to that because that is not correct.

MR. BRICKMAN: I'm asking him. You want to testify, or you want the doctor to?

MR. GARRARD: Just a moment, and I will show him where that is not a correct statement.

MR. BRICKMAN: Apparently the doctor has not looked at the medical records carefully enough.

MR. GARRARD: He has looked at the records. There are a lot of medical records.

This is not a memory test. We don't need to be rude, Mr. Brickman.

MR. BRICKMAN: Who is being rude? I am trying to get the doctor's opinions, not yours.

BY MR. BRICKMAN:

Q. Mr. Garrard is showing you something?

MR. GARRARD: Mr. Garrard is showing you a pathological report that is in the record.

BY MR. BRICKMAN:

Q. Doctor when you give your opinions, do you do it with Mr. Garrard giving you the material and showing you what to find?

A. No. This was either an adenocarcinoma or a mesothelioma.

MR. GARRARD: According to.

THE WITNESS: Dr. Curt Weiss, W E I S S.

BY MR. BRICKMAN:

Q. And what's the date on that report that Mr. Garrard has shown you?

A. 7-16-87.

MR. GARRARD: It's from Saint

John's Hospital, Mr. Brickman. I'll be happy to show it to you.

MR. BRICKMAN: No, that's okay, Mr. Garrard.

MR. GARRARD: I just didn't want you to miss that one.

BY MR. BRICKMAN:

Q. He said it could be either an adeno or a mesothelioma, Doctor?

A. Yeah. This has been the problem throughout this case. We felt it was the finding of the CEA which I couldn't ignore, which is a crucial factor.

Q. But the CEA didn't stain strongly positive, did it?

A. It was a moderate stain. Moderately positive.

Q. If it had been weakly positive instead of moderately positive, would you then have diagnosed this as being a mesothelioma?

A. One was considering this all the way through.

Q. Considering what?

A. Whether it was a mesothelioma.

Q. But if the CEA was only --

A. I think the CEA was the factor which moved -- put him towards the adenocarcinoma.

Q. If the CEA had only stained weakly positive instead of moderately positive, would you then have been of the opinion that it was a mesothelioma and not an adenocarcinoma?

A. If it had been negatively staining, yes.

Q. How about if it had been weakly stained?

A. It would be very hard to make an opinion.

Q. You wouldn't have been able to say one way or the other?

A. No.

Q. That is correct, you mean?

A. We found it very difficult. The thing that's obviously going between the mesothelioma and the adenocarcinoma, this was the one factor which seemed to influence the others, the other diagnoses.

Q. Do you in any way rely upon the document that Mr. Garrard showed you by Dr. Weiss to support your opinion that it is an adenocarcinoma?

A. I think everyone was obviously trying to decide on this, on either an adeno or mesothelioma, according to the tissue they had.

Q. Would you agree with me that everybody in their final analysis came down to the opinion of mesothelioma except for you and Dr. Gibbs?

A. Yes.

Q. Yes?

MR. GARRARD: That's not what that record says he just looked at.

MR. BRICKMAN: I'm asking him whether he thinks that's the case or not.

MR. GARRARD: Let's don't misstate the record.

THE WITNESS: One chap trying to make up his mind, too. I think the decision as far as I was concerned was on the cytochemistry.

BY MR. BRICKMAN:

Q. Yes, sir. But what I'm asking you, Doctor, is every other doctor in the record that looked at the material in deciding whether it was an adeno or mesothelioma came down with the opinion it was a mesothelioma, correct?

MR. GARRARD: I object to the form

of the question because you have just been shown a pathology report where a doctor said either/or. And to say now, with that in the record, that every other doctor has said this is just not a correct statement of the record. That's just not correct, Michael. You don't do things like that. You're too good a lawyer to do things like that.

BY MR. BRICKMAN:

Q. Is what I said correct, Doctor, or is what Mr. Garrard said correct?

A. I think you've got the one chap who hasn't made up his mind entirely.

Q. Did you rely upon that report at all?

A. I saw the report after I made my statement.

Q. Do you think that doctor's report supports you in some way, Doctor?

A. I think he shows the dilemma I was in about this case.

Q. The fact that the tumor was crushed in the pleural biopsy, I can understand how that would affect the histological examination, but how does that affect the use of stainings, Doctor, immunohistochemical stainings?

A. I really don't know. It shouldn't. The small amounts of tissue --

Q. But it shouldn't affect the ability to do immunohistochemical stainings?

A. The tissue -- it would be hard to see where the actual -- if you're working on the fact that the CEA gives the staining around the edge of the cells, around the margins, it would affect that. I don't think it would affect the PAS.

(Whereupon, an off-the-record conference transpired.).

BY MR. BRICKMAN:

Q. Did I ask you, Doctor, what the timetable was between the period of onset of discovery of disease and death in this case?

MR. GARRARD: He told you. You didn't ask him.

BY MR. BRICKMAN:

Q. Would you tell me again?

A. On my notes, he was in the Air Force and there was no --

MR. GARRARD: He is asking you time between diagnosis and when he died.

THE WITNESS: Yes.

MR. GARRARD: You told him that once before, but he didn't hear you. So tell him once again.

THE WITNESS: Between July '87 and March '88.

BY MR. BRICKMAN:

Q. Is that a typical time period for a mesothelioma?

A. They can be -- that's, what, 1 March? Five months which would be a short time.

Q. But typically mesotheliomas have a shorter period of time between discovery and death than adenocarcinomas?

A. Yes. The whole thing is a very short time for a tumor.

Q. Assuming, Doctor -- all these cases are blurring together, and I apologize. You said you did not have any exposure history on Mr. McBryde?

A. Yes.

(Whereupon, an off-the-record conference transpired.)

BY MR. BRICKMAN:

Q. Doctor, the materials you have gotten in these three cases and the other six

cases, when did you first begin work on these cases?

A. It was last month.

Q. Last month? About 30 days ago, approximately?

A. About 30 days ago.

Q. And in that time frame, you gave me a number earlier of having spent over 24 hours, but was that over 24 hours on the three cases or on all nine cases?

A. All nine cases.

Q. All nine cases. So on the average, you only spend about three hours per case, give or take something?

MR. GARRARD: I'm not trying to put words in his mouth, but that wouldn't be correct, because he didn't have full medical records in all the other cases to review.

MR. BRICKMAN: But on the average, he would spend about three hours per case.

MR. GARRARD: The average would be --

MR. BRICKMAN: He might have spent all 20 on this one.

MR. GARRARD: But the average

wouldn't be an accurate statement with regard --

MR. BRICKMAN: It would be an average statement. It may not give an accurate time on what he spent on these cases.

MR. GARRARD: That's what we are after. We don't want misleading averages.

BY MR. BRICKMAN:

Q. Go ahead, Doctor.

A. I'm trying to think when I went up to see the first one.

MR. GARRARD: About a month ago.

BY MR. BRICKMAN:

Q. But you still think you only spent, you said in excess of 24 hours, but you don't know how much in excess? You spent less than 50 hours on these cases, haven't you, on these nine cases?

MR. GARRARD: Before today?

BY MR. BRICKMAN:

Q. Before today.

A. It must be somewhere in the region of more than 50 hours, traveling up and down.

Q. Do you think it's as much as 100 hours for the nine cases?

A. No.

Q. Somewhere around 50?

A. 50, 60.

Q. 50, 60 hours, not including today?

A. No.

(Whereupon, an off-the-record conference transpired.)

BY MR. BRICKMAN:

Q. Doctor, do you plan on coming to wonderful Beaumont, Texas, next month?

A. I would rather not be.

Q. Do you have it presently calendered in?

A. No.

Q. If Mr. Garrard asks you to come to Beaumont, Texas, will you show up next month?

A. If Mr. Garrard asks me.

Q. If he asks you, will you show up next month?

A. Yes.

(Whereupon, an off-the-record conference transpired.)

BY MR. BRICKMAN:

Q. Are you scheduled to be anywhere in the month of June other than perhaps Beaumont?

A. Not June.

Q. So June you have free?

A. June I'm going to Washington and see my daughters in San Francisco.

Q. Well, when you're over in the States, then, you can be testifying in Beaumont. I just want to know. Mr. Garrard played a mean trick on me last time. He had me depose a Dr. Murray and made me come all the way to Beaumont, Texas and never put Dr. Murray up.

Mean trick Henry played. The only comfort I have is that it cost Henry a lot of money to bring the guy over.

That's all I have, Doctor. Thank you very much for your time. I appreciate it. It was nice seeing you again, sir. And tell your wife I'm sorry you had to stay in here so long.

(Whereupon, the deposition was concluded at 5:40 PM.)

SIGNATURE OF DEPONENT

I, the undersigned, J. Christopher Wagner, do hereby certify that I have read the foregoing deposition and find it to be a true and accurate transcription of my testimony, with the following corrections, if any:

PAGE	LINE	CHANGE	REASON

_____

J. Christoper Wagner Date

CERTIFICATE

I, A. William Roberts, Jr., Registered Professional Reporter and Notary Public for the State of South Carolina at Large, do hereby certify:

That the foregoing deposition was taken before me on the date and at the time and location stated on page 1 of this transcript; that the witness was duly sworn to testify to the truth, the whole truth, and nothing but the truth; that the testimony of the witness and all objections made at the time of the examination were recorded stenographically by me and were thereafter transcribed by computer-aided transcription; that the foregoing deposition as typed is a true, accurate, and complete record of the testimony of the witness and of all objections made at the time of the examination.

I further certify that I am neither related to nor counsel for any party to the cause pending or interested in the events thereof.

Witness my hand, I have hereunto affixed my official seal this 5th day of June, 1990 at Charleston, Charleston County, South Carolina.

A. William Roberts, Jr.
Registered Professional
Reporter, CP, CM
My Commission expires
May 20, 1991

Part (4)

biopsy P.M.

MEDICO-LEGAL CASE.
TEXAS SERIES.

Name. HARRIS, Billy

U.S.A.Hospital/Path No. S87-7480

Llandough No.

Slides Received.

2 stains S87-7480
1979 emphysema with chronic bronchitis, rectal polyps
esophagitis lung [illegible] only rectal polyps
[illegible] home with [illegible] for asthma
Rectal polyps benign [illegible]

Blocks Received.

1 block S87-7480

Recuts,H@E.

1939-41 Worked for Gulf Oil [illegible]

1979 suggestive of [illegible] but [illegible] by [illegible] suggested [illegible]
Histo/Immunocytochemistry. both sides of chest [illegible] but no evidence of [illegible]
1975 [illegible] of lower [illegible] no malignant cells seen

51 - 1973 Born 11.5.14

68 - 1987 Retired with COPD in 1976

Mineral Analysis.

Possible exposure to asbestos while working - plastic factory
Safety [illegible] in oil Refinery

Other blocks or slides sent elsewhere.

Rectal polyps but benign

1987 diagnosis of adenocarcinoma with pleural effusion

Death Certificate October 87

2 Packs of cigarettes - day quit 7 years 1979 when diagnosed COPD

[illegible] tobacco

Glazner
Exhibit 1
Date 5/30/90
A.W.R. & Assoc.

[illegible]

LLANDOUGH NO.

- fibrosis

asbestos bodies

other features

Tumour type

Pleura

Histochemistry

Immunohistochemistry

(Probably 1 H&E + 1 PAP)
Blood clot containing some inflammatory &
cells and an occasional very large signet-ring cells with
hyperchromatic nucleus. Appearances suspicious
of malignancy.

Diagnosis:

Is there an asbestos related disease?

Other tissues

Name. HARRIS, Billy S

U.S.A.Hospital/Path No. CY87-1513

Llandough No.

Slides Received.

4 stained [illegible] CY-87-1513

Blocks Received.

1 block [illegible] CY-87-1513

Histo/Immunocytochemistry.

Yes

Mineral Analysis.

Other blocks or slides sent elsewhere.

ADDRESS

LEANDOUGH NO. 64

Lung - fibrosis

asbestos bodies

other features

Tumour type

Pleura

Histochemistry

Immunohistochemistry

Diagnosis:

Is there an asbestos related disease?

Other tissues

CY 87-1513 - Kidney specimen
[illegible]
[illegible]

MEDICO-LEGAL CASE.
TEXAS SERIES. PART 2

Name. HARRIS, Kelly S

U.S.A.Hospital/Path No. 87-119.

Llandough No. 6143/87

Slides Received.

22 slides { 16 stained
3 unstained.

Blocks Received.

10 blocks 87-119 x5
87-119 7½ x5

Histo/Immunocytochemistry.

Mineral Analysis.

Other blocks or slides sent elsewhere.

NAME

ADDRESS

LAB.NO 87-1111 autopsy

LLANDOUGH NO.

Lung - fibrosis

asbestos bodies

other features

Extensive lymphangitis.

Tumour type

Pleura

Tumour shows glandular differentiation - moderately pleomorphic and moderately [illegible] cells. (3 [illegible]) favours adenocarcinoma rather than mesothelioma. A few areas suggestive of squamous diffn

Histochemistry

mucicarmine stains focal positivity.

PAS-D - +++

Immunohistochemistry

CEA - +++ CK - +++

Diagnosis:

~~Large cell carcinoma.~~

Adeno carcinoma

Is there an asbestos related disease?

Other tissues

Spleen - NAD

Liver - NAD

pancreas - NAD

adrenal - NAD

lymph nodes metastatic tumour [illegible]

Kidney - NAD

TEXAS SERIES.

Name. HARRIS, Billy S.

U.S.A.Hospital/Path No. CB87-801
S87-802

Llandough No.

Slides Received.

8 slides C087-801
S87-802 L1, L2 + L3
P87-2960 x4

Blocks Received.

2 blocks, C087-801
S87-802.

Histo/Immunocytochemistry.

Mineral Analysis.

Other blocks or slides sent elsewhere.

NAME [illegible] LAB.NO

ADDRESS LLANDOUGH NO.

Lung - fibrosis

asbestos bodies

other features

Tumour type

Pleura 87-801 - Fluid - numerous mesothelial cells plus groups of malignant cells (adenocarcinoma)

Histochemistry 87-802 - Very small pieces lung tissue + fat - a few groups of malignant cells suggestive either of adenocarcinoma of mesothelioma.

Immunohistochemistry

Diagnosis:

Is there an asbestos related disease?

Other tissues

INFORMATION REQUIRED

Name Billy S. Harris (by Betty Jean Harris

Address 1404 12th St., Nederland, TX

Date of Birth 5/11/19

Occupation Guard dept.; safety inspector

To what materials exposed including non-asbestos materials.

Not specific

Date of first exposure 1969

Duration of exposure 10 yrs.

Intensity of exposure UnKnown

Date of last exposure 1979

Date of present illness and clinical diagnoses Was diagnosed w/pleural mesothelioma at autopsy; thought to be an adenocarcinoma before death

Alive or dead (date of death) Deceased - 10/26/87

Any other non-asbestos related conditions COPD since 1979; Kidney stones; asthma; mild duodenitis

Smoking history 63 pack yrs.; also chewed tobacco

If dead - cause of death according to the death certificate - Cardiopulmonary arrest

Radiological findings - Fibrosis
Plaques
~~Tumour~~ - pleural effusion

Lung function tests
(One representative result)

1979 - VC - 39%
FVC - 51%

POSTMORTEM EXAMINATION REPORT

S.M. Le BER, M.D.
Pathologist
5840 Monroe Street
Groves, Texas 77619

NAME: HARRIS, Billy **AGE:** 67 **SEX:** M. **RACE:** Caucasia

DATE AND TIME OF DEATH: 10-26-87 - 0455 **AUTOPSY NO.** MEA-87-119

PLACE OF DEATH: Residence - 1404 12th Street, Nederland, Texas

DATE AND TIME OF AUTOPSY: 10-26-87 - 1300

PLACE OF AUTOPSY: Nederland Memorial Funeral Home, Nederland, Texas

AUTHORIZATION FOR AUTOPSY: Betty Harris (Wife)

PROSECTOR: S.M. Le Ber, M.D.

ANATOMIC DIAGNOSIS

IMMEDIATE CAUSE OF DEATH: PLEURAL MESOTHELIOMA - RIGHT LUNG

MANNER OF DEATH: NATURAL CAUSES

MECHANISM OF DEATH: PULMONARY INSUFFICIENCY

ADDITIONAL DIAGNOSES:
SECONDARY MESOTHELIOMA IN REGIONAL LYMPH NODES
PULMONARY EMPHYSEMA OF RIGHT & LEFT LUNGS
INTERSTITIAL FIBROSIS OF RIGHT & LEFT LUNGS
ASBESTOSIS
ADHESIVE PERICARDIUM

SML:ms

S.M. Le Ber, M.D.

00001

PRELIMINARY NOTE: The following has been excerpted from notes from the Texas Lung Institute at which Mr Harris was examined on 9-15-87. He apparently worked for Arco, in the Safety Department from 1969 - 1979. During that period he was apparently exposed to asbestos. In late August or early September, 1987 Mr Harris was diagnosed as having a malignancy in his right lung. A needle biopsy was diagnosed as adenocarcinoma. Since that time he apparently had received a number of radiation therapy treatments to the right side of his chest. He died at his son's home in Nederland on 10-26-87. Permission for autopsy was granted by Mrs Harris, wife of the deceased. Postmortem examination was done at Nederland Memorial Funeral Home in Nederland on 10-26-87 at 1300.

EXTERNAL EXAMINATION: The deceased was an adult caucasian male 67 inches in length, and weighing an estimated 170 pounds. He was moderately well developed and well nourished. He had gray-white hair and blue eyes. There were ink mark lines in the form of a rectangle over the right anterior chest such as are placed as aiming point for radiotherapy. No other significant external findings were noted.

INTERNAL EXAMINATION: The body was opened through a high-Y incision, the incision being exteneded to the superior border of the symphysis pubis. The skin flaps were reflected and the sternum was removed in the usual manner. There was no free fluid in the peritoneal cavity, and the organs were in their normal position.

The right pleural space was entirely obliterated by dense fibrous tissue which required mostly sharp dissection to free it. Between this thickened tissue and the underlying lung tissue there were pockets containing coffee-colored fluid together with necrotic lung tissue. The left lung was enlarged and there was a slight shift of the mediastinum to the right. There were no adhesions on the left side of the chest. The organs were removed en-bloc from the larynx to the anus for definitive dissection.

CARDIOVASCULAR SYSTEM: The heart was covered by an adhesive pericardium requiring sharp dissection for its removal. The heart was normal in size and shape. The coronary arteries were patent, large, and demonstrated no significant atherosclerosis. The myocardium showed no evidence of recent or previous myocardial infarcts. The aorta showed moderate degrees of atheroma, present mainly in the abdominal portion.

LUNGS: The tracheobronchial tree contained small amounts of mucus, clear in appearance. Dissection of the bronchial tree revealed no gross evidence of primary neoplasm. The right lung was markedly contracted and was moderately atelectatic. The pleura was densely attached and thickened to an average thickness of one-half to one centimeter. It engulfed the entire lung, and was more dense in the medial aspect. It was yellowish-white in appearance, and portions in the area of the posterior mediastinum, the appearance was that of solid, yellowish-white tumor. The cut surface of the right lung showed atelectasis, hyperemia and edema. The cut surfaces of the left lung were moderately hyperemic and markedly edematous. No gross evidence of tumor was seen in the left lung.

LIVER: The liver was normal in size and shape. It was moderately hyperemic. The gallbladder contained normal bile. No stones were present. No lesions were present.

PANCREAS: The pancreas was normal in size and shape, and demonstrated a normal, creamy-tan lobular architecture.

SPLEEN: The spleen was normal in size. The pulp was [illegible] consistency.

ADRENALS: Both adrenal glands were essentially normal. There was slight postmortem autolysis.

KIDNEYS: Both kidneys were normal in size and shape. The capsules stripped with ease to reveal smooth cortex. The cut surfaces demonstrated normal cortico-medullary markings. There was a slight increase in peripelvic fat. The ureters were norma;. The urinary bladder was normal. The prostate was not palpably enlarged.

GASTROINTESTINAL SYSTEM: The esophagus was normal and was empty. The stomach contained approximately a cup of gray, soupy fluid. The mucosa was intact. The small and large intestines were normal, and contained normal fecal material. The appendix was present.

CENTRAL NERVOUS SYSTEM: No examination of the cranial contents was conducted.

****

MICROSCOPIC:

TUMOR: Sections demonstrate many pleomorphic malignant cells with large vesicular nuclei and prominent nucleoli, irregularly combined with dense fibrous tissue which was taken from the pleura of the right lung. The tumor cells are arranged in columns, cords and nests of pleomorphic cells which show no evidence of aorganoid pattern. The tumor cells are locally infiltrating adjacent lung tissue, and are present in adjacent mediastinal lymph nodes. Special stains show the tumor to be PAS positive, but show no evidence of mucin production. The gross and microscopic findings show that the tumor is a Malignant Mesothelioma.

LUNGS: Both right and left lungs demonstrate patchy areas of interstitial fibrosis with focal emphysema and fairly diffuse pulmonary edema. There is no evidence of pneumonia or tumor in the left lung. Iron stains demonstrate the presence of grouped ferruginous material consisting of beaded bodies consistent with fragmenting asbestos bodies.

LIVER: Sections demonstrate acute hyperemia.

PANCREAS: Sections are histologically normal.

SPLEEN: Sections show no histologic abnormalities.

****

SUMMARY: The deceased was a 67-year-old man who had apparently been exposed to asbestos inhalation in the past. He developed a malignant mesothelioma involving the entire pleura of the right lung. Both lungs demostrated emphysema and interstitial fibrosis, and the presence of asbestos material. The tumor had apparently been treated by external radiation to the chest, and there was moderate necrosis of peripheral tissue of the right lung and areas of loculated fluid.

The immediate cause of death was Pleural Mesothelioma of Right Lung. The manner of death is deemed to be natural causes. The mechansim of death was due to pulmonary insufficiency and terminal pulmonary edema.

****

WEST CARDIFF AREA LABORATORY

HISTOLOGY

6193 AG.

PATIENT'S SURNAME (Block Letters)	FORENAMES IN FULL	AGE	SEX	UNIT No.	PHYSICIAN OR SURGEON
HARRIS	pt 2				
HOME ADDRESS IN FULL		HOSPITAL AND WARD			DATE AND TIME COLLECTED

NATURE OF SPECIMEN

TEXAS CASE. 87 — 119

CLINICAL HISTORY —

Doctor's Signature ..... Date .....

REPORT —

(1) H/E ✓

PAS ± ✓

CEA. —

CYTOK. —

HARRIS, BILLY STEPHEN
0 67871 05-11-19 PWM 68
DR GIRARD
459-03-5167 328E
RT 2 BOX 220
TAVALLA ANGELINA 75980
08-04-87 OCD AC1

AT TYLER

DEPARTMENT OF PATHOLOGY

REQUEST FOR TISSUE EXAMINATION

CASE NO. 67871 SURGEON Girard ATTENDING PHYSICIAN Girard

PATIENT NAME Harris, Billy AGE 68 SEX M RACE W FLOOR 3E 328 DATE 8/4/87

PERTINENT CLINICAL INFORMATION: night sweats, dyspnea

PRE-OPERATIVE DIAGNOSIS: (R) pl. effusion

OPERATIVE FINDINGS: Serosanguinous fluid

POST-OPERATIVE DIAGNOSIS: same

SPECIMEN:
approx 1000 cc red clotted fluid

PATHOLOGY/CYTOLOGY REPORT ACCESSION NO. P87-2960 C887-801

MICROSCOPIC EXAMINATION:

Pap smears of the pleural fluid demonstrate numerous small to medium size clusters of malignant cells. These malignant cells also occur individually and in multi-nucleated forms. The cells themselves have enlarged, pleomorphic, hyperchromatic nuclei and abundant, occasionally vacuolated cytoplasm. The background consists of lymphocytes and there is no tumor diathesis. The cell block similarly displays numerous malignant cells occurring individually and in small clusters. Pseudoglandular differentiation is focally recognized.

Right pleural fluid: Numerous clusters of malignant cells most consistent with adenocarcinoma.

M.F. Fagan MD 8-6-87

M. F. Fagan, M.D. Date
Asst. Chairman, Dept. of Pathology

MFF/jh

459-03-5167 4328E
RT 2 - BOX 220
ZAVALLA-ANGELINA 75980
08-04-87 OCD AC1

DEPARTMENT OF PATHOLOGY

REQUEST FOR TISSUE EXAMINATION

CASE NO. _____ SURGEON _____ ATTENDING PHYSICIAN Jarad

PATIENT NAME _____ AGE ____ SEX ____ RACE ____ FLOOR ____ DATE 8-5-87

PERTINENT CLINICAL INFORMATION: (R) pl. effusion

PRE-OPERATIVE DIAGNOSIS: _____

OPERATIVE FINDINGS: thick whitish pleura

POST-OPERATIVE DIAGNOSIS: same

SPECIMEN: _____

PATHOLOGY/CYTOLOGY REPORT ACCESSION NO. S87-802

GROSS DESCRIPTION:

The specimen is labeled pleura and consists of a few small tan tissue fragments measuring less than 7 millimeters in single greatest dimension. The specimen is entirely submitted.

MICROSCOPIC EXAMINATION:

The pleural biopsy is comprised of skeletal muscle fascicles, fibroconnective tissue and a tag of pleura. Hemorrhage is also present. It is within the areas of hemorrhage that approximately 5 small clusters of malignant cells can be identified. A single cluster of malignant cells is present within the pleura. The malignant cells themselves have large, pleomorphic, eccentric nuclei and abundant, occasionally vacuolated cytoplasm. These cells are identical to the ones described in the pleural fluid (P87-2960/CB87-801) submitted 8-5-87.

DIAGNOSIS:

Right pleura, biopsy: Moderately differentiated adenocarcinoma, see comment.

COMMENT: A malignant mesothelioma can not be excluded from this differential diagnosis if there are no other intraparenchymal pulmonary lesions.

M. Fagan MD 8-6-87

M. F. Fagan, M.D. Date
Asst. Chairman, Dept. of Pathology

MFF/jh

Stock 20844
Rev. 8/11/82

Name. MCBRYDE, Hunter U.S.A.Hospital/Path No. See below.

Llandough No.

Slides Received.

32 slides

S87-4107 x 11
S87-2779 x 4
C87-1848 x 5
C87-1094 x 3
C87-1527 x 2
C88-561 x 1
S85-1974 x 1
S87-2621 x 1
S87-3951 x 4

Blocks Received.

11 blocks

4107 x5
87-2779 x 4
87-3951 x1
S85-1974 x1

Histo/Immunocytochemistry.

Mineral Analysis.

No suitable material

Other blocks or slides sent elsewhere.

NAME McBRYDE, Horace.

ADDRESS

LLANDOUGH NO.

Lung - fibrosis

asbestos bodies

other features

87-2779 (A) Lateral chest wall — some fragments of neoplastic tissue
(B) Diaphragm —) very small
(C) Anterior chest wall) fragments of tumour c̄ some
(D) Pericardium) [illegible]

Tumour type

Pleura

Histochemistry

87-4107 P.A.S.-D neg

Immunohistochemistry

84-4107 { CK +++
CEA ++

Diagnosis:

~~84-4107 CK +++~~
~~CEA ++~~

Adenocarcinoma

87-1527 Pleural fluid — poor quality, ? atypical cells.

87-2621 Pleural biopsy — Small biopsy c̄ foci of tumour [illegible] suggested

87-1848 pleural fluid — unsatisfactory specimen

87-1074 pleural fluid — [illegible] groups of [illegible]

Is there an asbestos related disease?

Other tissues

S87-4107 - Subcutaneous nodule chest wall
RE
"epithelial" tumour showing acinar formation, a small number of cells contain pigment, prominent nucleoli plentiful mitoses

H-F — Stain [illegible], none containing [illegible].

88-1174 - Gall Bladder - Chronic inflammation, a few atypical [illegible] scarring.

86-581 - peritoneal fluid - Some atypical cells and histiocytes, poor specimen.

87-3451 - oesophageal biopsy — Ulcer slough c̄ [illegible] debris

thology No. C-88-561 Hospital No. 155154-156 Room No. 419 Date 3-9-88
tient: MCBRIDE, HORACE Age 59 Sex M Doctor R. RODGERS
ssue:
thologic Diagnosis:

YTOLOGY OF PERITONEAL FLUID: ATYPICAL CELLS DEMONSTRATED CONSISTENT WITH MALIGNANT MESOTHELIOMA (SNOMED T-6X930 M-9050/0)

ytologic smears and cell block preparations demonstrate clusters and individual atypical cells, edium to large size having eosinophilic cytoplasm. There is nuclear enlargement with rregularity of nuclear membrane and clumping of chromatin material including occasional rominent nucleoli. The atypical cellularity is consistent with malignant mesothelioma.

Iver Diaz, M.D.
Pathologist

ID:ch
D&T: 3-11-88

ST. JOHN HOSPITAL OF NASSAU BAY
SURGICAL PATHOLOGY CONSULTATION

athology No. C-87-1848 Hospital No. 155154-123 Room No. 419 Date 11-17-87
atient: MCBRYDE, HORACE Age 58 Sex M Doctor RODGERS
issue: PLEURAL FLUID PREOPERATIVE DIAGNOSIS: MESOTHELIOMA.
athologic Diagnosis:

LEURAL FLUID: NEGATIVE FOR MALIGNANT CELLS (SNOMED T-2Y600 M-00120).

ID:br

ICROSCOPIC:
he specimen received for cytologic evaluation is one cc. amber clear fluid. Cytospin reparations demonstrate scanty cellular material. There is a small population of large cells aving abundant vacuolated cytoplasm and large lobulated nuclei undergoing degeneration. These arge cells are most likely phagocytic histiocytes. There is no evidence of inflammatory or oplastic cellular component.

Iver Diaz, M.D.
Pathologist

:br
I: 11/18/87

SURGICAL PATHOLOGY CONSULTATION

. C-87-1527 | Hospital No.155154-065 | Room No.415 | Date 9/24/87
ARYDE, HORACE | Age 58 | Sex M | Doctor R.ROGERS

ic Diagnosis:

RAL FLUID CYTOLOGY: NO MALIGNANT CELLS IDENTIFIED (SNOMED T-2Y600, M-60120)

KW:jdc

OSCOPIC:
micolaou stained cytocentrifuge preparations of pleural fluid show a moderate amount of ular material. This consists mostly of blood elements. Also seen are some macrophages. cells present are poorly preserved. No malignant cells can be identified on the parations.

Kurt Weiss, M. D.
Pathologist

jdc
: 9-25-87

. C-87-1054	Hospital No.105104-007	Room No.446	Date 7/16/87
BRYDE,HORACE	Age 56	Sex M	Doctor S. Pons

ic Diagnosis:

PLEURAL FLUID CYTOLOGY: HIGHLY SUSPICIOUS FOR MALIGNANT CELLS (CY-87-1054)

Original

MICROSCOPIC:

Cytologic stained smears prepared from pleural fluid specimen received in Cytology. These present numerous clusters of atypical cells characterized by a high nuclear cytoplasmic ratio, by an irregular chromatin structure and by presence of multiple nucleoli or chromatin condensations. Many of these are somewhat degenerated, making classification difficult. These cells are highly suspicious for malignant cells and suggests the presence of either an adenocarcinoma or a mesothelioma.

Kurt Kelly, M. D.
Pathologist

SJOC
DT: 7-17-87

Pathology No. C-87-1054

7

O 46718018

ST. JOHN HOSPITAL OF NASSAU BAY
SURGICAL PATHOLOGY CONSULTATION

/logy No. S-87-4107 Hospital No. 155154-123 Room No. 419 Date 11/27/87
/ent: MCBRYDE, HORACE Age 58 (DOD) Sex M Doctor NATHANSON/ROBBERS
sue:
hologic Diagnosis:

ADDENDUM REPORT

CUTANEOUS NODULE FROM CHEST WALL: METASTATIC MESOTHELIOMA (SNOMED T-Y2130 M-9050/6)
EIGN BODY FROM RIGHT SHOULDER: REMOVAL OF PORT CATHETER

ID:ch

SS:
cimen A is labeled biopsy from chest wall for frozen section. It is comprised of an ellipse skin, 2.5 x 1.5 x 0.3 cm. Also received in the same container is a poorly circumscribed lid nodule, 1 cm. in diameter. Its cut surface is firm, pale gray and solid. Representative tions are taken for frozen section.

ZEN SECTION DIAGNOSIS: METASTATIC MESOTHELIOMA.

e skin surface is light brown and smooth. On cut section, it is grayish-white and remarkable. The specimen is submitted in toto in cassettes A through D. DK:sb

ecimen B is labeled port A catheter, removed from right shoulder. The specimen consists of a tal device attached to a catheter. The catheter is in plastic, measuring 31 cm. in length and 5 cm. in diameter. The catheter is soft, transparent, but having a white line all along the ngth of the catheter. The line measures 0.2 cm. in width. There are ten small holes located one end of the catheter on 6.5 cm. length. These holes are seen at 0.5 cm. apart and appear one line. The tip of the catheter measures 0.4 cm. in diameter. Two portions of Dacron-like terial wrapped around the catheter are seen in two locations, one at 15 cm. from the tip and e second is at 25 cm. from the tip. The other end of the catheter is attached to a metal vice. The metal device is in conic form. The top measures 2 cm. in diameter, showing a rim metal, measuring 0.4 cm. in thickness and plastic material in the center which measures 1.2 . in diameter. The base of the cone is a square metal plate, measuring 2.4 x 2.4 cm. There e four small holes at each angle of the plate from where some sutures are seen. The catheter attached to the device through a metal projection which measures 1 cm. in length and 0.4 cm. diameter. There is no blood clot seen in the catheter lumen. (Gross description only). :sb

ROSCOPIC:
manent sections confirm the above frozen section diagnosis. The tumor is composed of ill fined tubular structures embedded in fibrotic stroma. The tumor cells are polygonal and have larged pleomorphic nuclei having prominent nucleoli. Few mitoses are noted. The subcutaneous ule extends into the dermis of overlying skin.

Iver Diaz, M.D.
Pathologist

:cn
T: 12/1/87
thology No. S-87-4107
6

ogy No. S-87-3951 Hospital No. 155154-125 Room No. 419 Date 11-13-87
t: MCBRYDE, HORACE Age 58 Sex M Doctor MCKINNEY
e: ESOPHAGEAL BIOPSY
logic Diagnosis:

OPHAGEAL BIOPSY: ACUTE ULCERATIVE ESOPHAGITIS (SNOMED T-62000 M-41030).

ID:br

ICROSCOPIC:
icroscopy reveals acute inflammatory-fibrinous exudate admixed with necrotic tissue debris and egenerating squamous cells. The esophageal mucosa is obviously ulcerated and a viable mucosal issue is not identified. Cellular morphology of herpes infection is not noted. Silver stain hows no evidence of fungus organisms.

Iver Diaz, M.D.
Pathologist

ID:br
&T: 11/16/87

ST. JOHN HOSPITAL OF NASSAU BAY
SURGICAL PATHOLOGY CONSULTATION

Pathology No. S-87-2779 Hospital No. 155154-057 Room No. 422 Date 7/29/87
Patient: MCBRYDE, HORACE Age 58 Sex M Doctor YOUMANS/PORG
Issue:

Pathologic Diagnosis:
BIOPSY OF LATERAL CHEST WALL: CONSISTENT WITH MESOTHELIOMA, (SEE COMMENT) (Y220-9053)
BIOPSY OF DIAPHRAGM: NO DIAGNOSTIC ALTERATIONS (Y240-0001)
BIOPSY OF ANTERIOR CHEST WALL: CONSISTENT WITH MESOTHELIOMA (Y220-9053), (SEE COMMENT)
BIOPSY OF APICAL PLEURA: NO DIAGNOSTIC ALTERATIONS (Y220-0001)

KW:jdc

COMMENT: The histological features are similar to the previous pleural biopsy which represents most likely a mesothelioma.

GROSS:
Specimen A is labeled lateral chest wall and consists of small whitish flaky tissue, measuring in greatest dimension 3 mm. The entire tissue is submitted in cassette labeled A.

Specimen B is labeled diaphragm and consists of small whitish flaky tissue, measuring in greatest dimension about 2-3 mm. The entire tissue is submitted in cassette labeled B.

Specimen C is labeled anterior chest wall and consists of whitish tissue, measuring in greatest dimension 2-3 mm. The entire tissue is submitted in cassette labeled C.

Specimen D is labeled apical pleura and consists of a pinkish-white fragment of tissue, measuring in greatest dimension 3-4 mm. The entire tissue is submitted in cassette labeled D.
CR:sb

MICROSCOPIC:
A&C: Sections of biopsies from lateral chest wall and from anterior chest wall shows similar histological features. The biopsy shows numerous proliferating atypical cells with a atypical chromatin structure and irregular nuclear shape as well as numerous mitotic figures. Some of these appear like cuboidal cells. The features of these biopsies are similar to the previous pleural biopsy.

B&D: Sections of biopsy of diaphragm and sections of biopsy of apical pleura are examined at multiple levels and show fibrous tissue with hemorrhage and mesothelial cells. No definite cellular atypia can be demonstrated on these biopsies.

Kurt Weiss, M. D.
Pathologist

Kw:jdc
DAT: 7-30-87

Pathology No. S-87-2621 Hospital No. 155154-057 Room No. 446 Date 7/10/87
Client: MCBRYDE, HORACE Age 58 Sex M Doctor PONG
Issue:
Pathologic Diagnosis:

PLEURAL BIOPSY: CONSISTENTG WITH MALIGNANT MESOTHELIOMA (25-9053)

JA:cn

GROSS:
The specimen is labeled pleural biopsy and consists of multiple light tan to whitish soft tiss fragments, measuring in aggregate 1 x 0.5 x 0.3 cm. The specimen is submitted in toto in a single cassette. BA:sb

MICROSCOPIC:
Sections reveal pleural tissue with attached skeletal muscle fibers. The pleura shows fibrosi and infiltrating within the fibrotic pleura are sheets and clusters of large polyhedral cells with hyperchromatic pleomorphic nuclei. The cytoplasm is abundant. These show no evidence of gland formation. These are arranged as solid sheets of cells. No significant papillary formation is noted. No evidence of psammoma bodies are noted. The morphologic features are consistent with malignant mesothelioma.

COMMENT:
The slides were sent to M.D. Anderson for their opinion and they concurred with the diagnosis malignant mesothelioma.

Jameela Ahmeduddin, M.D.

JA:cn
D&T: 7/22/87

[redacted]

ST. JOSEPH HOSPITAL OF [redacted]

SURGICAL PATHOLOGY CONSULTATION

OLOGY NO. [redacted] HOSPITAL NO. [redacted] ROOM NO. [redacted] DATE

ENT: MCPYDE, [redacted] AGE [redacted] SEX RACE DOCTOR [redacted]

SUE: Gallbladder.

THOLOGIC DIAGNOSIS:

[redacted]

ALLBLADDER: CALCULUS CHOLECYSTITIS (57-3100).

ID:sb

GROSS:
The specimen is labeled gallbladder consisting of an unopened gallbladder measuring [redacted] x 3 x 2.4 cm. On opening at the cystic duct the duct wall is found to be quite thick measuring up to 5 mm. in thickness and there is a stone very low in the neck of the gallbladder which is obstructing the duct. On opening this stone is dark green in color and measuring 1.1 x 1 x .9 cm. It is a mixture of yellow and green crystalline material. On opening the gallbladder contains several smaller stones and mixture of cloudy light brown bile mixed with yellow material. The entire mixture has a consistency of extremely thick and tenacious mucoid material. Mixed within this are several small dark green stones. The serosa of the gallbladder is unremarkable but the wall is appreciably thick measuring up to 3 mm. in thickness and there is dark brown material within [redacted] gallbladder resembling stones measuring up to 4-5 mm. in greatest dimension. The [redacted] of the gallbladder exhibits focal hemorrhage. Representative sections are submitted in one cassette. MY:cm

MICROSCOPIC:
Representative sections obtained from gallbladder demonstrate irregular [redacted] wall showing mural interstitial scarring associated with inflammatory cellular [redacted] and multiple Rokitansky-Aschoff sinuses. The mucosa shows foci of ulceration.

[redacted]
Pathologist

[redacted]

1

PATHOLOGY NO. [redacted]

[redacted]
488-671601 (Rev. 3/82)

LABORATORY COPY

TEXAS SERIES.

Name. WARRICK, Alvin

U.S.A.Hospital/Path No. 88-8

Llandough No.

Slides Received.

29 slides

88-8 H&E Peels x5 (0)
88-8(1) H.E, PAS, Mucin (3)
88-8(2) 2x H.E, PAS, Mucin (4)
88-8(3) H.E, PAS, Mucin (3)
88-8(4) 2x H.E, PAS, Mucin (4)
88-8(5) 2x H.E, PAS, Mucin (4)
Control x1

Blocks Received.

8 blocks

88-8 x3
88-8-7E x5

Histo/Immunocytochemistry.

Yes

Mineral Analysis.

Other blocks or slides sent elsewhere.

age 40 Black male. Drug abuse known in Nelson
Exposure to asbestos via father clothes since 1986
gynaecomastia right side plant Last Cocaine 1986
Tumour initially diagnosed as Sq. Ca. Jan 12 1988
death certificate Carcinoma of lungs
Mesothelioma rib at necropsy
Occupation → Navy 1966-1969
Gulf oil → 1974-1985 Dozer operator

Exhibit 3
Date 5/20/94
A.W.R. & Assoc.

NAME WITKKICK, ALWIN

ADDRESS

LLANDOUGH NO.

Lung - fibrosis 0/1

asbestos bodies 0

other features diffuse alveolar damage + capillaritis.

Tumour type Very necrotic haemorrhagic tumour c̄ polygonal & ~~syncytial~~ deciduoid cells, many grouped around blood vessels — almost choriocarcinomatous but in one block, some areas c̄ giant pleomorphic cells. Endodermal sinus-like areas

Pleura

Histochemistry PAS — +++ globules
PAS-D — +

Immunohistochemistry CEA + ve
CK +++
HCG — +++
α fetoprotein — ±
α1 antitrypsin — +++

Diagnosis: ~~Probable teratoma~~

Poorly differentiated Teratoma

Is there an asbestos related disease? No

Other tissues

POSTMORTEM EXAMINATION REPORT

S.M. Le BER, M.D.
Pathologist
5840 Monroe Street
Groves, Texas 77619

NAME: WARRICK, Alvin **AGE:** 40 **SEX:** M. **RACE:** Black

DATE AND TIME OF DEATH: 1-12-88 - 0300 **AUTOPSY NO.** MEA-88-8

PLACE OF DEATH: Ben Taub Hospital, Houston, Texas

DATE AND TIME OF AUTOPSY: 1-14-88 - 0950

PLACE OF AUTOPSY: Moody-Harris Funeral Home, Port Arthur, Texas

AUTHORIZATION FOR AUTOPSY: Greta Warrick (Wife)

PROSECTOR: S.M. Le Ber, M.D.

ANATOMIC DIAGNOSIS

IMMEDIATE CAUSE OF DEATH: MALIGNANT MESOTHELIOMA - RIGHT LUNG

MANNER OF DEATH: NATURAL CAUSES

MECHANISM OF DEATH: CARDIORESPIRATORY INSUFFICIENCY

ADDITIONAL DIAGNOSES: ACUTE PULMONARY EDEMA
ASBESTOSIS

SML:ms

S.M. Le Ber, M.D.

ADRENALS: Both adrenal glands were normal in size, shape and color. No secondary neoplasm was present.

GENITOURINARY SYSTEM: Both kidneys were normal in size, shape and texture. The capsules stripped with ease to reveal slight retention of the fetal lobular pattern. The cut surfaces showed uniform hyperemia. The archtectural markings were normal. There was no increase in peripelvic fat. The ureters were normal. The urinary bladder was normal and contained less than 10 cc.'s of normal appearing urine. The prostate was not palpably enlarged. Both testes were present and normal.

GASTROINTESTINAL SYSTEM: The esophagus was normal. The stomach contained a small amount of fluid and gastric mucus. The mucosa was normal. The small and large intestines were normal, and contained normal fecal matter. The appendix was normal.

CENTRAL NERVOUS SYSTEM: No specific permission was given for examination of the cranial contents; accordingly no examination was done.

****

MICROSCOPIC:

LUNGS: Sections through the lungs demonstrate acute pulmonary edema, increased numbers of alveolar histiocytes, and patchy interstitial fibrosis. The tumor of the right chest is seen to invade the right lung, and is composed of a haphazard arrangement of cells with no organoid structure. Special stains were used to differentiate these tumor cells from epithelial cells, and identify them as mesothelial in origin. The tumor is identified as a malignant mesothelioma. Iron stains also identify the presence of scattered furruginous material, found chiefly in areas of interstitial fibrosis.

****

SUMMARY: This is the case of a 40-year-old man who died as a direct result of a malignant mesothelioma arising in the right chest.

****

HOSPITAL WARD	PATHOLOGIST	HOSPITAL UNIT NO.	PATHOLOGY NO.	IMMUNOCYTOCHEMISTRY NO.
Llandough	Dr. A.R. Gibbs	. .	88-8 Llandough 6260/89	A 2829/89

NATURE OF SPECIMEN :

Clinical Diagnosis : Lung tumour

Conventional histology : ? metastatic teratoma

Reference Clinicial/Pathologist : Dr. A.R. Gibbs

Hospital :

Specimen details : Llandough

Markers required : Please ring the boxes below

Date received : Processing Details : Fresh Fixed Frozen Spare Sections

Number of specimens/blocks : Two blocks 12 uss on each

Pre-staining Processing :

Results : Key +++ Strong Positive; ++ Positive; + Weakly Positive; ± Equivocal; - negative; x not done; R = Reactive cells only.

OKT 6	RFT 8	RFT 1	WBC	Leu 3a	RFB 4	Y 25a	HLA-DR (LN 3)
LEU M1	MB 2	MT 1	Ki-1	UCHL 1	L 26	M400	KP 1

IgG	IgM	IgA	Sec Piece	J Chain	λ	K	LYZ	α_1 antitrypsin AT	FVIII RAG	Fibrinogen	C3
								-			
GH	PRO	LH	FSH	TSH	ACTH	SOMAT	INS	GLUC	C-Peptide	PP	GAST
HPL	BGP	HCG	AFP	BOM	VIP	CAL	CGRP	CEA	THYR	GCFP-15	HMFG11
		v.focal +++	-ve								
MYOG	MYOS	DES	VIMENTIN	GFAP	NEURO FIL	S100	NSE	Epidermal keratin	Cyto keratin (CAM 5.2)	PaPH	MT
5HT	PSA	Chr A	FX111 A	SAP	SAA	THP	LAMININ	PLAP			

FOR FULL REPORT SEE OVERLEAF.

The tissue in block 88.8 (2) shows a few multi-nucleate cells positive for HCG. Both α_1-antitrypsin and α-feto-protein markers are either negative or show non-specific staining only.

The overall findings are consistent with a tumour of teratoma or germ cell origin.

B JASANI
21.12.89

MEDICAL REPORT ON BILLY HARRIS

My report is based on the examination of the autopsy report of Dr. Le Ber and pathological materials received from Mr. Henry Garrard III. I only studied the material in which tumour was present.

SBT-1480 appeared to be a blood clot containing occasional cells and groups of cells which were suspicious of malignancy.

CY 87-1513 was a cytological specimen containing groups of large cells which appeared malignant.

87 - 119, 87 - 119 7E. This material was from the autopsy. The tumour consisted of masses of vesicular cells many of which appeared to have formed glandular structures. These glands were lined by columnar cells. In foci the cells had small hyperchromatic nuclei and dark cytoplasm. The histological features of this tumour were consistent with those of an adenocarcinoma. This was confirmed by special stains and immunohistochemistry.

Muci carmine - focal positive

PAS Diastase - strongly positive

CEA - strongly positive

Cytokeratin - strongly positive

Exhibit P 4
Date 5/30/90
AWR & Ass.

1 lymph gland showed a metastatic tumour

The lung showed evidence of extensive lymphangitis carcinomatosa. No evidence of asbestosis or asbestos bodies seen.

Comment

In my best medical opinion I consider the tumour to be an adenocarcinoma. This is strongly supported by the results of the histochemistry and immunohistochemistry.

GONADOTROPHIN

β HUMAN CHORIONIC GONADOTHROPIN

CARCINO EMBRYONIC Antige

Billy Harris died age 68 5/11/19 - 10/26/87

Previous CXR 1964 Fibrotic changes noted in both hilar regions particularly on left. Pleural thickening both apical region probably due to a previous inflammatory process. Nodular density in area of right middle also residual of previous infection. Since 1973 had enlarged node in his lung which interfered with pulmonary drainage. Minimal bronchogram [illegible] tubular bronchiectatic change Rt upper lobe. bronchoscopy no [illegible]

11/6/73 CXR Very mild fibrocongestive? sematous change. Minimal apical scarring with associated pleural thickening. A small calcified granuloma is seen on right anteriorly. No malignant cells

4/12/79 admitted with acute bronchial asthma chronic obstructive lung disease. Barrel shaped chest poor excursion found
FVC. 66% FEV1 33%

7/24/79 Severe chronic obstructive lung disease, chronic bronchitis Hypertension, arteriosclerotic heart disease. No evidence of active disease on X-ray. The patient completely disabled by COPD. retired from work and [illegible] smoking was smoking three packs a day. Also rectal polyps (benign) [illegible]. sent home with treatment for Asthma.

8/87 Patient admitted with increased shortness of breath. Thoracentesis followed by pleural biopsy diagnosed as adeno Carcinoma but mesothelioma could not be ruled out

J. CHRISTOPHER WAGNER, MD, FRCPath, MFOM

Tel. 0305 833902

" Foxstones "
69 Coombe Valley Road
Preston, Weymouth
Dorset
DT3 6NL

May 16, 1990

MEDICAL REPORT ON HORACE McBRYDE

My report is based on the examination of pathological materials submitted by Henry Garrard. I was only referred material which was relevant to the diagnosis of the tumour.

Pathology S87 - 2779. This consisted of four small biopsies from chest wall, diaphragm and anterior chest wall and apical pleura. In two of the specimens there was evidence of minute fragments of undifferentiated tumour.

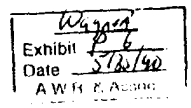
S87-4107. This biopsy of the subcutaneous nodule shows the presence of a small fragment of fibro-fatty tissue in which there was a small focus of tumour on one edge. The tumour was composed of cells varying in shape and size, some of which were forming definite acini.

S87 - 2621. This was a pleural biopsy which consisted of large cells surrounded by fibrous tissue and muscle. The specimen had been crushed and it was not possible to comment on the histology. Therefore histochemistry and immunohistochemistry were undertaken on tissue from specimen S87-4107 with the following results.

PAS Diastase - negative

Cytokeratin - strongly positive

CEA moderately positive



Comment

In my best medical opinion this tumour is an adeno-carcinoma.

CARCINO EMBRYONIC Antigen

Exhibit D-7
Date 5/16/96

Horace McBryde S-4
2/5/21 – 3/14/88

1/7/87 Jan. 87/ comparing X-Ray 1985.

Mild chronic changes – both lungs without evidence of focal consolidation

July 87 Increased density at right base with effusion ? Cause

~~Dr~~ Drainage tube inserted

7/16/87 Fibres of Pleura and right

7/18/87 Fibroptics bronchoscope inserted biopsy taken

Sheets and clusters of large polyhedral cells hyperchromatic pleomorphic nuclei no evidence of gland formation. Mesothelioma confirmed at M.D Anderson suggestive of mesothelioma

Biopsy of subcutaneous nodule for chest wall

7/27/87 C.T.

29/7/87 Further biopsies from Lateral Chest Wall & anterior chest wall apical pleura shows numerous proliferation atypical cells numerous mitotic figures Pleural Plaques.

29/8/87 Acute admission for spinal pain

2/6/88 Increasing destruction of Tenth Rib on Right Side

8/3/88 Reaction to Bruises Tapped

3/14/88 Died ? Neoplasm and small nodule small nodule left upper lobe

1/2/88 } Left lung clear on C.T. Scan
2/10/88 }

Mc Bryde Bronchoscopy

8/22/37 No evidence of tumor endobronchosequestrum
Lung & bronchi appeared normal

7/20/37 No abnormality no specimen obtained.

J. CHRISTOPHER WAGNER, MD, FRCPath, MFOM

Tel. 0305 833902

" Foxstones "
59 Coombe Valley Road
Preston, Weymouth
Dorset
DT3 6NL

MEDICAL REPORT ON ALVIN WARRICK

My report is based on the examination of the autopsy report of Dr. Le Ber dated 1.14.88 and pathological material sent to me by Mr. Henry Garrard III of which I only examined the tumour tissue and lungs.

Slides 88-8 1 & 2

Sections taken at autopsy from the lung and pleura show the presence of sheets of large foamy cells and large syncitial giant cells. These cells are surrounding vesicular spaces in which there is considerable evidence of haemorrhage and necrosis.

The remaining lungs showed evidence of minimal alveolar reaction, but no signs of asbestosis or asbestos bodies have been observed in the sections examined.

In my best medical opinion I consider this tumour to be primitive and embryonal in nature. There is no evidence for the diagnosis of mesothelioma.

Wagner
Exhibit 8
Date 5/30/94

May 16, 1990

Hyaluronic

β HUMAN CHORIONIC GONADOTROPIN

UNIVERSITY HOSPITAL OF WALES PATHOLOGY DEPARTMENT IMMUNOCYTOCHEMISTRY REQUEST / REPORT

NAME (Surname First - Block Letters)	PATIENT'S HOME ADDRESS	DATE OF BIRTH	SEX
WARRICK			

HOSPITAL WARD	PATHOLOGIST	HOSPITAL UNIT NO.	PATHOLOGY NO.	IMMUNOCYTOCHEMISTRY NO.
Llandough	Dr. A.R. Gibbs		88-8 Llandough 6260/89	A 2829/89

NATURE OF SPECIMEN :

Clinical Diagnosis : Lung tumour

Conventional histology : ? metastatic teratoma

Reference Clinicial/Pathologist : Dr. A.R. Gibbs

Hospital :

Specimen details : Llandough

Markers required : Please ring the boxes below

Date received : Processing Details : Fresh Fixed

Frozen Spare Sections

Number of specimens/blocks : Two blocks 12 uss on each

Pre staining Processing :

Results : Key +++ Strong Positive; ++ Positive; + Weakly Positive; ± Equivocal; - negative;

x not done; R = Reactive cells only.

OKT 6	RFT 8	RFT 1	WBC	Leu 3a	RFB 4	Y 25a	HLA-DR (LN 3)
LEU M1	MB 2	MT 1	Ki-1	UCHL 1	L 26	M400	KP 1

IgG	IgM	IgA	Sec Piece	J Chain		K	LYZ	(α_1 antitrypsin) AT	FVIII RAG	Fibrin-ogen	C3
								-			
GH	PRO	LH	FSH	TSH	ACTH	SOMAT	INS	GLUC	C-Peptide	PP	GAST
HPL	BGP	HCG /	AFP	BOM	VIP	CAL	CGRP	CEA	THYR	GCFP-15	HMF G11
		v.focal +++	-ve								
MYOG	MYOS	DES	VIMENTIN	GFAP	NEURO FIL	S100	NSE	Epi-dermal keratin	Cyto keratin (CAM 5.2)	PaPH	MT
5HT	PSA	Chr A	FX111 A	SAP	SAA	THP	LAMININ	PLAP			

FOR FULL REPORT SEE OVERLEAF

Wagner
Exhibit 9
Date 5/30/96
A.W.R. & Assoc.

Alvin KVARRICK 7/26/47 – 1/12/88
40 years

History of drug abuse Heroin now on Methadone previously cocaine IV and Freebase due to Dyspnea
Sept 87 Age 40 presents with tumor in right chest with pleural effusion presents with dyspnea and general fatigue. Has had gynecomastia for about 4 months, X-Ray effusion and opacity right chest. Left no significant signs. Continued growth of opacity on right repeated pleural taps ? adenocarcinoma.
13/10/87. Opacity mainly in right upper lobe ? carcinoma. Needle biopsy Squamous carcinoma Treated with chemotherapy Cis Platinum right hilum Intermediate bronchus blocked on bronchoscopy by acute pneumonia but was managed to pass in abnormalities in other bronchi.
β In view of gynecomastia serum Human CHORIONIC GONADOTrophin estimated and found to be increased.
Germ cell tumour considered but possibly Large Celled Carcinoma would give a similar result.
No evidence of Testicular abnormality
1/12/88 P.M. Large tumour completely filling right chest not possible to separate lung from tumour. Dr. Le Ber states that histologically Correct for Mesothelioma Large nodular tumour
DR. Gibbs the result of β Human Chorionic Gonatrophin which is positive – Syncitial giant cells – the tumour. Diagnosis Giant cell tumour. Le Ber also finds anthracotic pigment granules – interstitial tissues of the lung
Asbestos Exposure Other father who was

Human Gonadotrophin.

Human Chorionic Gonadotrophin

Greenwood ... et al.
1971 Med J. Industrial Med. 5-1 416-422

ENDOCRINE STUDIES IN TESTICULAR TUMOR PATIENTS WITH AND WITHOUT GYNECOMASTIA

A Report of 45 Cases

ANTANAS V. STEPANAS, BMEDSC, MB, BS, FRACP, NAGUIB A. SAMAAN, MD, PHD, FRCP, FACP, PAMELA N. SCHULTZ, BS, AND PAUL Y. HOLOYE, MD

Prolactin (PRL), human placental lactogen (hPL), the β-subunit of human chorionic gonadotropin (βhCG), testosterone (T), estrone (E_1), and estradiol (E_2) were measured in blood samples from 45 patients with testicular tumors, 27 of whom had gynecomastia at some stage of their disease. Forty-two of the 45 patients had at least one abnormal hormone level. The most common abnormality was that of plasma estrone: it was elevated in 32 out of 42 (76%) patients in whom it was measured, suggesting a useful role for E_1 as a testicular tumor marker. Prognosis was notably worse in patients with embryonal carcinoma, teratocarcinoma, and choriocarcinoma, in those with gynecomastia and, particularly, galactorrhea. Such patients also had the highest incidence of hormonal abnormalities as well as the most extreme absolute values. Hormonal mechanisms were implicated in the development of gynecomastia and galactorrhea. Prolactin, βhCG, E_1, and E_2 levels in all permutations correlated significantly among patients with gynecomastia, but not among those without, while estrogen to testosterone ratios were elevated in patients with galactorrhea.

Cancer **41:369-376, 1978.**

ABNORMAL CONCENTRATIONS OF VARIOUS PEPtide,[1,4,6,9,23,32] and steroid[9,12,20,21,23] hormones as well as nonhormonal tumor-related antigens[14,17,30] are an established feature of patients with testicular tumors of germinal cell origin.

In the present study, six hormones, prolactin (PRL), human placental lactogen (hPL), the β-subunit of human chorionic gonadotropin (βhCG), testosterone (T), estrone (E_1) and estradiol (E_2) were simultaneously measured in blood samples from 45 patients with testicular tumors. Twenty-seven patients had demonstrable gynecomastia and four had galactorrhea as well. Our aim was to determine the prevalence of abnormal hormone concentrations in the various types of testicular tumors, assess the prognostic significance of abnormal hormone levels, gynecomastia and galactorrhea, and identify any hormone patterns correlating with the occurrence of gynecomastia or galactorrhea.

MATERIALS AND METHODS

Patients

Fasting, early morning blood samples for hormone assay were drawn from 45 patients with testicular tumors at various stages during the management of their disease.

Patient selection was strongly biased toward those with gynecomastia; its presence was established by palpation of glandular tissue, lipomastia being ignored. Twenty-seven patients had gynecomastia at some stage of their disease. Four patients also had galactorrhea.

Tumors were classified according to the

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We are grateful to Douglas Johnson, M. D., Chief, Section of Urology, Department of Surgery, at M. D. Anderson Hospital, for referring his patients to us for study, and for valuable advice in the preparation of this manuscript. We also wish to thank Mr. Alonzo Guerra, Mrs. Socorro Castillo, Mrs. Elsa Pope, Ms. Laura Smith, and Mrs. Carolyn Marshall for invaluable technical assistance. We are indebted to the British Medical Research Council for supplying prolactin and β-hCG standards, and the National Pituitary Agency for supplying prolactin, β-hCG, and their antibodies for radioimmunoassay.

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0008-543X-78-0100-0369-0085

TABLE 1. Mortality related to Presence or Absence of Gynecomastia in Patients with Testicular Tumors

Group	Pathology Type	No.	Mean age & range at diagnosis (years)	No Gynecomastia No.	Dead	% Dead	Gynecomastia No.	Dead	% Dead
I	Seminoma	9	47 (29-65)	5*	1	20	4	1	25
II	Embryonal carcinoma	16	32 (21-54)	4	3	75	12†	8	67
III	Teratoma	2	24	1	1	100	1	0	0
IV	Teratocarcinoma	10	27 (14-44)	6	3	50	4	4	100
V	Choriocarcinoma	8	32 (20-44)	2*	0	0	6	5	83
TOTAL		45		18	8	44	27	18	67

* One patient living with disease
† Two patients living with disease.

scheme of Dixon and Moore.[6] Among the 45 patients, there were nine seminomas (group I), 16 embryonal carcinomas (group II), two teratomas (group III), ten teratocarcinomas (group IV), and eight choriocarcinomas (group V).

The primary tumors were all of testicular origin, and were treated by orchiectomy and radiotherapy to metastases followed, in most cases, by chemotherapy using various drug regimens. Management details are beyond the scope of this paper. The charts of all patients were reviewed recently to determine current status. Follow-up from date of diagnosis ranges from 10 to 52 months for patients still living, and 2 to 41 months for those who died.

Hormone Assays

Serum PRL, hPL, βhCG, and plasma T, E_1, and E_2 were assayed by specific radioimmunoassays as previously described.[7,10,22,25,29] Blood samples were immediately spun after drawing, and serum or plasma was frozen at −20 C until the time of assay. Hormone measurements were made in several assays, but interassay variability below 10% ensured comparability of results.

RESULTS

Gynecomastia occurred in all tumor types (Table 1). Comments on its prevalence are in-

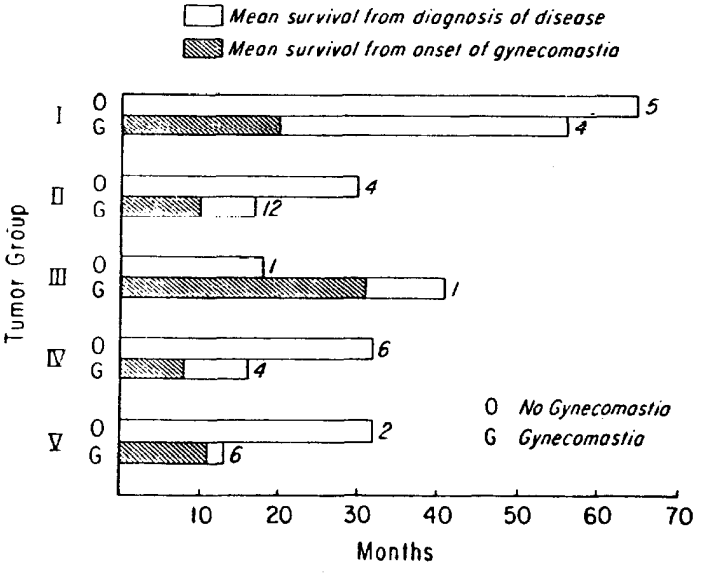

FIG. 1. Survival duration in patients with and without gynecomastia. Number of patients in each group shown to the right of the bars. Tumor types: I, seminoma; II, embryonal carcinoma; III, teratoma; IV, teratocarcinoma; V, choriocarcinoma.

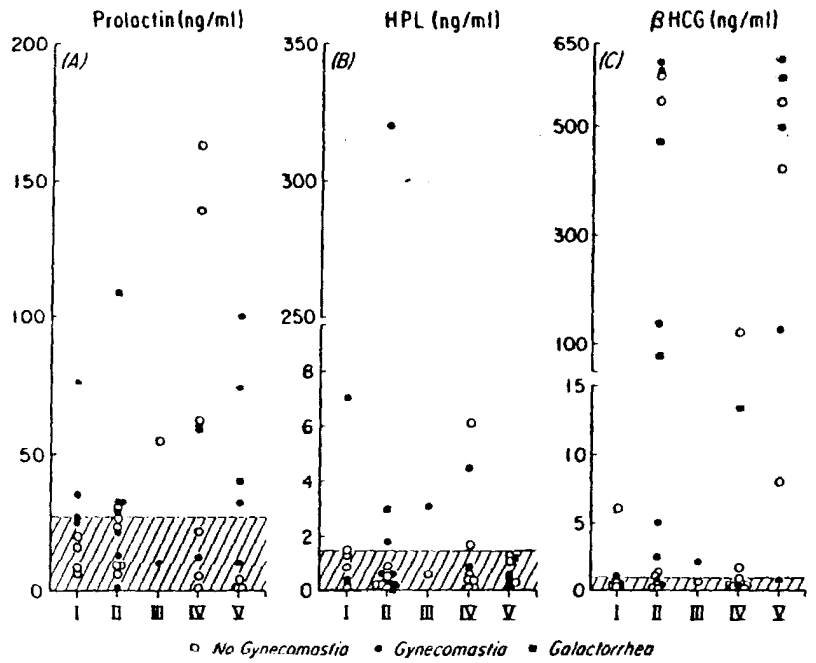

FIG. 2. Peptide hormone concentrations in testicular tumor patients. I-V = testicular tumor types as in Fig. 1.

appropriate because the patients had been selected for the presence of gynecomastia. The mortality was higher in patients with gynecomastia (67%) than in those without (44%). The adverse influence of gynecomastia on survival duration is shown in Fig. 1. Survival was strikingly shortened by the onset of gynecomastia. Conversely, the disappearance of gynecomastia correlated with a good prognosis and coincided with eradication of demonstrable tumor in four patients. Five other patients are still alive with persistent gynecomastia. Two of these (with embryonal carcinoma) also have persistent tumor, but three patients with seminoma are alive and are now free of disease. The latter three patients represent a special case, since all had undescended testicles and two demonstrated other features of feminization (sparse facial hair and redistribution of body fat); thus, persistent gynecomastia without evidence of disease in their case may be attributable to factors other than their testicular tumor.

The levels of peptide hormones PRL, hPL, and βhCG are plotted for the five tumor types (group I to V) in Fig. 2(a-c); those of steroid hormones T, E_1, and E_2 are plotted in Fig. 3(a-c). High concentrations of PRL hPL, βhCG, E_1, and E_2 and low T concentrations were found in all tumor types except for choriocarcinoma, in which hPL levels were normal, and teratoma, in which E_2 and T levels were normal. Extremely high levels of βhCG, E_1, and E_2 were found among embryonal carcinoma and choriocarcinoma patients, while lowest T levels and highest PRL levels were found in teratocarcinoma patients (Figs. 2, 3). Although patients with gynecomastia tended to have the highest hormone values, high concentrations were not necessily associated with gynecomastia. A tendency for very abnormal hormone levels was noted among patients who eventually died: PRL >50 ng/ml: 7 dead (D), 2 alive (A); hPL >5 ng/ml; 4D, 1A; βhCG >50 ng/ml: 13D, 2A; T < 350 ng/100 ml: 9D, 2A; E_1 >200 pg/ml: 8D, 3A; E_2 >200 pg/ml: 5D, 1A.

Because the timing of samples relative to therapeutic events was variable, no attempt was made strictly to relate hormone levels to stage of disease. This will be done in a prospective study now under way.

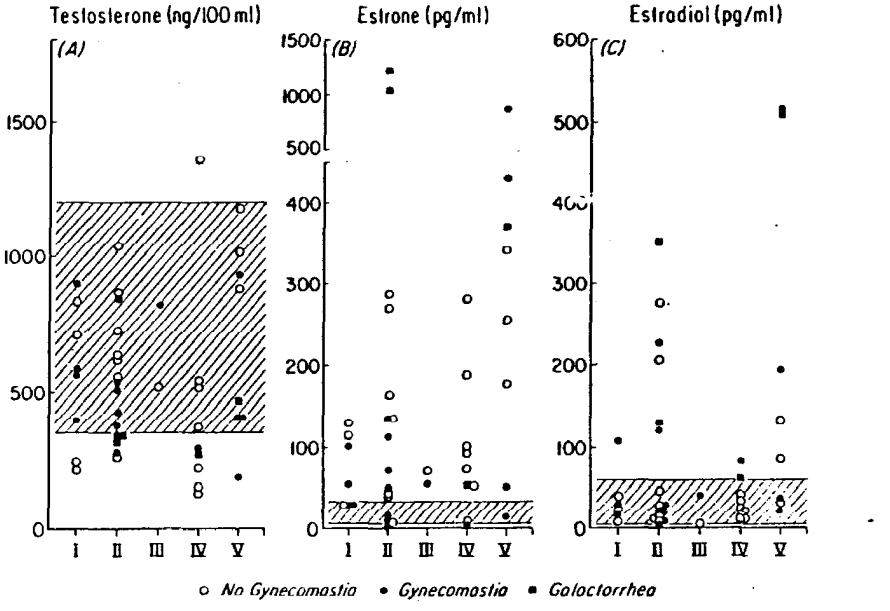

FIG. 3. Steroid hormone concentrations in testicular tumor patients. I-V = testicular tumor types as in Fig. 1.

The percentage incidence of abnormal hormone levels is presented in Table 2. E_1 was the hormone most frequently elevated among all tumor types; 32 of 42 (76%) patients in whom it was measured had high E_1 levels.

The incidence of several abnormal hormone levels occurring simultaneously was higher in patients with gynecomastia than in those without (Fig. 4). Among gynecomastic patients, the mortality increased as the number of coexisting hormone abnormalities increased, a trend which was slightly reversed in patients without gynecomastia.

Features of patients with and without gynecomastia and galactorrhea are examined in Table 3. Fourteen patients presented with gynecomastia, while in 13 it developed subsequently. Those with gynecomastia and galactorrhea tended to be younger than those without. Survival duration was significantly shorter in patients with galactorrhea ($p < 0.05$) when compared with those without.

Factors possibly important in the genesis of gynecomastia were examined. Exposure to phenothiazine antiemetics, which can elevate prolactin levels and induce gynecomastia, did not differ for patients with gynecomastia (96% exposed) and those without (89% exposed). Fur-

TABLE 2. Percentage Incidence of Abnormal Hormone Levels According to Tumor Type, Presence or Absence of Gynecomastia or Galactorrhea, and Fate

	Pathological Type					Gynecomastia			Fate	
	I	II	III	IV	V	GM −*	GM +*	Galact.†	Alive	Dead
PRL ↑	25	46	50	38	50	29	55	100	41	59
hPL ↑	14	20	50	33	0	10	33	25	18	33
βhCG ↑	25	69	50	30	88	40	61	100	44	62
T ↓	25	33	0	44	14	27	33	75	11	36
E_1 ↑	57	75	100	78	88	82	67	100	76	76
E_2 ↑	14	38	0	22	63	18	42	100	35	44

* GM − = no gynecomastia; GM + = gynecomastia.
† Tumor types in patients with galactorrhea: 1 embryonal carcinoma, 2 teratocarcinomas, and 1 choriocarcinoma.

thermore, 52% of gynecomastic patients had not received such drugs prior to developing gynecomastia. Similarly, there was no significant difference between gynecomastic and nongynecomastic patients in the incidence of obesity (our patients as a group, were not obese) or pulmonary metastases. We were unable to demonstrate a significant difference in the E_1/T, E_2/T, E_{1+2}/T ratios between patients with and without gynecomastia. However, in those with galactorrhea, these ratios were uniformly higher, but significantly so only for the E_1/T ratio ($p < 0.05$).

Significant positive correlations were found between certain hormone pairs (Table 4). This was particularly marked between PRL, βhCG, E_1, and E_2 in all permutations in patients with gynecomastia, but not in those without. Notably, E_1 or E_2 levels >100 pg/ml were always associated with βhCG >100 ng/ml in patients with gynecomastia, but not in those without. However, specific hormone patterns could not be defined in relation to particular tumor type, gynecomastia, or mortality.

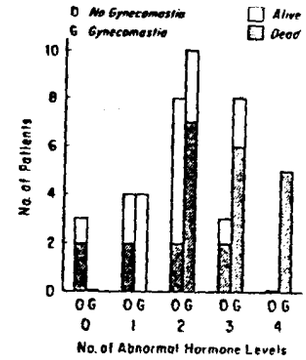

FIG. 4. Concurrent association of abnormal hormone levels in patients with and without gynecomastia. Four patients with galactorrhea each had four concurrent abnormal hormones.

DISCUSSION

The simultaneous measurement of serum PRL, hPL, βhCG, and plasma T, E_1, and E_2 in a large series of patients with testicular tumors has not been reported previously. Our results demonstrate that the concentration of any of these six hormones may be abnormal in any of the five tumor types of Dixon and Moore.[6] Of our 45 patients, 42 had at least one abnormal hormone concentration, this finding being without exception among the 27 patients with gynecomastia.

Abnormal hormone levels were most prevalent among patients with embryonal carcinomas, teratocarcinomas, and choriocarcinomas, which is a predictable consequence of these tumors consisting of trophoblastic cells,[6] or multipotential cells that may differentiate along trophoblastic lines.[6] Multipotential cells are also found in teratomas, but the spermatogonial origin of seminomas[6] precludes speculation of a direct hormone-secreting function. On the other hand, even a small nest of choriocarcinoma cells may elaborate a considerable amount of hormones,[10] and an undetected focus of such cells may be responsible for the endocrine activity observed in some patients with seminoma. Recognition that testicular tumors have a predeliction for mixed histology[6] particularly in metastatic seminoma[11] supports this possibility.

Recent investigations permit fairly confident speculation on the exact origin of abnormal levels of the six hormones measured in our patients. hPL and βhCG are natural secretory products of trophoblastic tissue in health and disease.[19,25,26]

TABLE 3. Features of Patients with and without Gynecomastia and Galactorrhea

	No.	Mean age at Diagnosis (years)	Survival from diagnosis of tumor (months: $\bar{x} \pm SD$)[1]	Prolactin-inducing drugs No.	%	Lung metastases No.	%	$E_1/T \times 10^{-4}$ ($\bar{x} \pm SD$)	$E_2/T \times 10^{-4}$ ($\bar{x} \pm SD$)	$E_{1+2}/T \times 10^{-4}$ ($\bar{x} \pm SD$)
No gynecomastia	18	36	39 ± 29*	16	89	11	61	6.9 ± 3.7*	4.2 ± 5.6	17.5 ± 18.5
Gynecomastia	27	31	22 ± 27*	26	96	20	74	6.8 ± 6.5*	4.6 ± 4.0	12.7 ± 12.8
Galactorrhea	4	30	9 ± 5	4	100	4	100	52.6 ± 43.5	34.5 ± 41.7	90.9 ± 83.3

* $p < 0.001$ compared to patients with galactorrhea.
† $p < 0.05$ compared to patients with galactorrhea.
‡ $\bar{x} \pm SD$ = mean ± standard deviation.

thermore, 52% of gynecomastic patients had not received such drugs prior to developing gynecomastia. Similarly, there was no significant difference between gynecomastic and nongynecomastic patients in the incidence of obesity (our patients as a group, were not obese) or pulmonary metastases. We were unable to demonstrate a significant difference in the E_1/T, E_2/T, E_{1+2}/T ratios between patients with and without gynecomastia. However, in those with galactorrhea, these ratios were uniformly higher, but significantly so only for the E_1/T ratio ($p < 0.05$).

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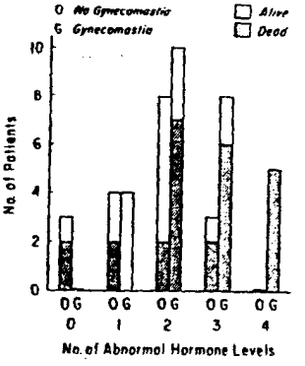

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No gynecomastia	18	36	39 ± 29*	16	89	11	61	6.9 ± 3.7‡	4.2 ± 5.6	17.5 ± 18.5
Gynecomastia	27	31	22 ± 27‡	26	96	20	74	6.8 ± 6.5‡	4.6 ± 4.0	12.7 ± 12.8
Galactorrhea	4	30	9 ± 5	4	100	4	100	52.6 ± 43.5	34.5 ± 41.7	90.9 ± 83.3

* $p < 0.001$ compared to patients with galactorrhea.
‡ $p < 0.05$ compared to patients with galactorrhea.
† $\bar{x} \pm SD$ = mean ± standard deviation.

TABLE 4. Significant Correlation Cofficients (Positive except as shown) between Hormone Pairs in Patients with and without Gynecomastia

Hormone pairs correlated*	No Gynecomastia r†	p	Gynecomastia r	p
E_1/E_2	0.15	n.s.	0.60	<0.01
PRL/E_1	0.03	n.s.	0.79	<0.001
PRL/E_2	−0.11	n.s.	0.49	<0.05
βhCG/E_1	0.75	<0.001	0.48	<0.01
βhCG/E_2	0.35	n.s.	0.67	<0.001
βhCG/PRL	−0.11	n.s.	0.44	<0.05
βhCG/T	0.43	<0.05	−0.16	n.s.
T/E_1	−0.38	<0.05	−0.28	n.s.

* Correlations between T and E_2, T and PRL, and hPL and all other hormones did not reach significance in either group of patients.

† r: correlation coefficient.

The investigations of Kirschner *et al.*[12,13] indicate that high circulating estrogen levels in testicular tumor patients are the result of *in situ* aromatization of $C_{19}O_2$ androgens, principally dehydroepiandrosterone but also androstenedione, produced by steroidogenically competent cells within the tumor tissue itself.

Reduced Leydig cell mass as a result of orchiectomy, radiotherapy, and chemotherapy may account for the low T levels that we and others[12,20,21] have observed. The high LH levels in testicular tumor patients, demonstrated by Cochran *et al.*,[4] may represent a compensatory adjustment by the pituitary to maintain T secretion. Elevated circulating estrogen levels would tend to suppress pituitary secretion of gonadotropins so that LH levels, even though elevated, may represent a compromised pituitary response that is inadequate to restore normal T secretion from the reduced Leydig cell mass. A report of low FSH levels in testicular tumor patients[23] lends support to this suggestion. That the testicles of these patients are refractory to stimulation by the massive concentrations of circulating hCG, but are LH-responsive, was demonstrated by Kirschner *et al.*[13]

Elevated prolactin concentrations are the most difficult to explain. Although spurious elevation may result from administering phenothiazine antiemetics, the possibility of estrogen-stimulated prolactin release at the hypothalamic-pituitary level is supported by our finding of a significant positive correlation between PRL and both E_1 and E_2 in patients with gynecomastia, while in two teratocarcinoma patients without gynecomastia extremely high PRL levels (139 and 163 ng/ml) were also associated with very high E_1 levels (>100 pg/ml). However, prolactin secretion directly by multipotential tumor cells cannot be ruled out in the absence of data on testicular vein samples.

Uniformly normal hPL concentrations in the presence of high βhCG levels in all our patients with choriocarcinoma was an unexpected finding. Elevated hPL concentrations have been reported previously in patients with choriocarcinoma.[9] However, the dissociation of βhCG and hPL in early pregnancy,[24] particularly in molar pregnancy and trophoblastic disease in women is well recognized.[25] A similar situation might exist in our choriocarcinoma patients.

The low incidence of gynecomastia in previous series (reported to be between 2.5% and 6% in patients with testicular tumors[15,16]) may have precluded its recognition as an important prognostic marker in its own right. Among our patients with gynecomastia, its onset frequently heralded a rapid demise, while its disappearance was often associated with eradication of disease.

Abnormal levels of various hormones, particularly PRL, hCG, and estrogens, or an altered estrogen to androgen ratio, are commonly suggested in the pathogenesis of gynecomastia. In our series, patients with gynecomastia had an overall greater incidence of abnormal hormone concentrations, in addition to a greater prevalence of exceptionally high βhCG, E_1, and E_2 (but not PRL) levels. This was not a specific finding, as some patients without gynecomastia had equally high levels of these hormones, and many gynecomastic patients had normal values.

A striking feature was the significant positive correlations of PRL, βhCG, E_1, and E_2 in their various permutations among patients with gynecomastia, but not among those without. Clearly, it is not the mere elevation of one hormone that is important in the development of gynecomastia, but a synchronized elevation of the several hormones maintaining a physiological relationship to each other. The model for such a situation prevails in pregnancy in relation to lactogenesis in the female breast. The interdependence of βhCG and estrogens has been cited before,[12,21] but the statistical significance of this interdependence and the correlation with PRL have not been demonstrated before in either testicular tumor or gynecomastic patients.

The possibility that obesity, prolactin-elevating drugs[8] or pulmonary metastases[27] may play a role in the development of gynecomastia was not supported in our series. Nor did we find evidence for an abnormal estrogen to androgen

ratio, patients both with and without gynecomastia had almost identical mean E_1/T, E_2/T, and E_{1+2}/T ratios (Table 3), which were similar to those reported for normal men.[3,21] This contrasts with previous studies demonstrating high E/T ratios in patients with gynecomastia associated with puberty,[16] Klinefelter's syndrome,[9] cirrhosis,[3] digoxin use,[26] and Graves' disease.[2] However, all three E/T ratios were elevated in four four patients with galactorrhea (significantly so for E_1/T), thereby supporting an etiological role for estrogen-androgen imbalance in the development of inappropriate lactation. Furthermore, it was noteworthy that four patients without gynecomastia but with gross perturbations of PRL, hPL, βhCG, and estrogen levels had the highest T levels observed among our patients (all >1000 ng/100 ml), suggesting that T may play a protective role against the development of gynecomastia.

The search for markers useful diagnostically and prognostically or for following the effects of therapy in testicular tumor patients has recently established the value of the nonhormonal polypeptide, alpha-fetoprotein,[14] particularly when measured together with either βhCG[17] or another nonhormonal protein, carcinoembryonic antigen.[30] To these, we would suggest adding plasma estrone as a potentially useful marker. Estrone levels were more frequently elevated than any other hormone, being high in 32 out of 42 (76%) of our patients both with and without gynecomastia, and with all types of tumor. Its value as a marker will be more critically assessed in a prospective study now under way. Taking E_1 and βhCG together, 37 of 45 (82%) patients had elevated levels.

The prognostic significance of elevated urinary hCG levels in patients with testicular tumors is widely accepted.[6,15,18,32] Except for the measurement of serum βhCG,[4] which is more sensitive than the urine measurement,[1] the prognostic implication of abnormal hormone concentrations in blood had not been systematically studied. Although no prognostically significant "hormone profile" emerged from our series, it was clear that the incidence of abnormal hormone levels, the most extreme absolute values, as well as increasingly complex hormone associations, correlated with gynecomastia and with mortality, all being found more frequently in patients with galactorrhea, and those with embryonal carcinoma, teratocarcinoma, and choriocarcinoma.

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PRIMARY MEDIASTINAL CHORIOCARCINOMA

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Extragonadal choriocarcinoma is an uncommon tumor, and to date only 14 cases of the primary mediastinal form of the disease have been reported in the literature. Because only one of these occurred in a female, it appears to be a disease almost entirely confined to males. A review was undertaken of the cases of choriocarcinoma occurring in males examined at the Mayo Clinic in the period from 1957 through 1967. Of the total of 17 cases diagnosed during this period, 1 was the primary mediastinal form of the disease and is discussed herein.

REPORT OF CASE

A 20-year-old man was seen in October 1967 because of nonproductive cough and chest pain of 3 months' duration. He had had no fever and no other systemic symptoms. Two weeks prior to his admission here, a thoracic roentgenogram had shown an anterior mediastinal mass. The mass had been explored and biopsied through a right thoracotomy incision. The pathologic diagnosis was undifferentiated carcinoma, and the patient had been referred to the Mayo Clinic for further evaluation. The slides from that biopsy were reviewed and a revised diagnosis of primary mediastinal choriocarcinoma was made.

The patient had mild gynecomastia; otherwise, the physical examination gave normal results. The testicles were normal to palpation.

Results of routine laboratory tests were normal except for a sedimentation rate of 88 mm in 1 hour (Westergren). The thoracic roentgenogram showed multiple metastatic pulmonary nodules in both lungs, with a large mass protruding from the mediastinum into the right lung field (Figure). The urinary chorionic gonadotropin level was 6,485 international units/24 hr.

The patient was seen by the oncology consultants, and a program of treatment was outlined to include triple drug therapy with actinomycin D, methotrexate, and chlorambucil.

DISCUSSION

Primary mediastinal choriocarcinoma is characteristically seen in young Caucasian males presenting with the symptom triad of cough, chest pain, and gynecomastia. Most cases have occurred in males 20 to 30 years of age (Table 1). The cough and chest pain are often accompanied by other respiratory symptoms including hemoptysis, dyspnea, hoarseness, and

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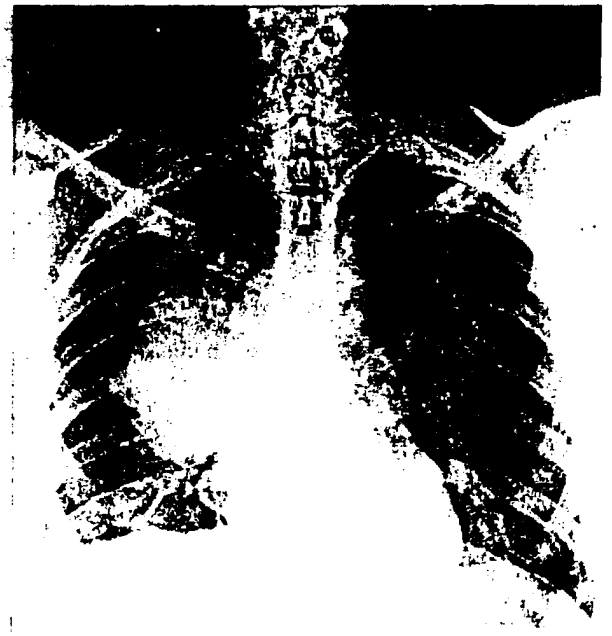


Chest roentgenogram, on admission at Mayo Clinic, shows multiple metastatic pulmonary nodules in both lungs with large mass protruding from mediastinum into right lung field.

stridor. Horner's syndrome and dysphagia have been described. Gynecomastia has been reported in approximately half the cases. Nonspecific symptoms include generalized malaise, anorexia, and weight loss.[1,13-15]

Roentgenographically, primary mediastinal choriocarcinoma presents as a well-defined anterior mediastinal mass characterized by rapid growth but without cavitation. It must be differentiated from other anterior mediastinal tumors including other germinal tumors (teratomas), thymomas, intrathoracic thyroid adenomas, pericardial cysts, lipomas, lymphangiomas, and parathyroid adenomas (listed in order of decreasing frequency[1]). A roentgenogram revealing an anterior mediastinal

Table 1.—Summary of Reported Cases of Primary Mediastinal Choriocarcinoma*

Author	Date	Age, yr; sex	Gynecomastia	Pregnancy test	Histology†	
					Primary	Metastasis
Arendt[1,2]	1931	20M	Yes	...	...	...
Kantrowitz[4]	1934	22M	No	Pos.	Complex teratoma and chorio	Chorio
Lapply and Shipley[5]	1945	13M	Yes	Pos.	Complex teratoma and chorio	Chorio
Hirsch et al.[6]	1946	25M	Yes	Pos.	Undifferentiated cells and chorio	Chorio
Giroux and Desmeulest[7,8]	1947	12M	No	Pos.	Chorioepithelioma in a dysembryoma	Chorio
Shlimovitz and Van Brown[9]	1950	27M	Yes	Pos.	Complex teratoma and chorio	Chorio
Zorzi and Piacentil[2,3]	1952	29M	Yes	Pos.	...	...
Nielubszye[2,10]	1952	38M	Yes	Pos.	...	...
Fanger and MacAndrew[11]	1952	44F	...	...	Complex teratoma and chorio	Granulomatous lesions typical of TB in liver and mediastinal lymph nodes
Lynch and Blewett[12]	1953	26M	Yes	...	Chorio	Chorio
Magovern and Blades[3]	1958	20M	?	Pos.§	Seminoma, embryonal cell cancer, chorio	Chorio
Yurick and Ottoman[1]	1960	26M	No	...	Chorio	Chorio
Fine et al.[13]	1962	49M	Yes	Pos.	Chorio	Chorio
Bennington et al.[14]	1964	44M	No	Pos.	Chorio	Chorio

*This table is a modification of that published by Yurick and Ottoman.[1]
†Chorio = choriocarcinoma.
‡Cases abstracted from Magovern and Blades.[3]
§At autopsy.

mass in a young male patient with the above triad of symptoms is strongly suggestive of primary mediastinal choriocarcinoma.

The finding of a high titer of gonadotropin in a male, as occurred in our case, is of itself diagnostic of choriocarcinoma, whether it be of gonadal or extragonadal origin. The hormone is presumably produced by the trophoblastic element of the tumor and is biologically similar to the chorionic gonadotropin of normal pregnancy in the female.[15] Consequently a pregnancy test is also positive in patients with choriocarcinoma.

The gynecomastia observed in males with primary mediastinal choriocarcinoma is undoubtedly related to the production of gonadotropin. Circulating gonadotropin may stimulate the Leydig cells of the testicles to increase not only testosterone synthesis but estrogen production as well. The increased blood level of circulating estrogen could account for the adverse effect noted on the testicular germinal epithelium as well as the hypertrophy of the mammary glands. Leydig cell hyperplasia was reported to have been found in 30 to 40 cases of extragonadal choriocarcinoma studied by Fine and co-workers.[13]

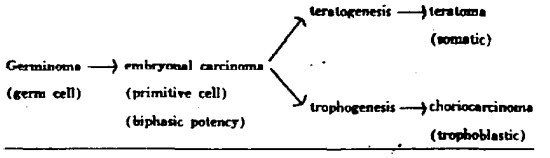
Much of the controversy concerning extragonadal chorio-

carcinoma regards the location of the primary site of the neoplasm. Certainly, gonadal origin of the primary lesion must be excluded before one can conclude that a choriocarcinoma is of extragonadal origin. Fine and co-workers[18] and others[5,16] have made a careful study of multiple serial sections from each testicle and have advocated that this must be done before the testicle can be excluded as the primary site. The testicles should also be free of cysts, scars, or tumors. Some authors[1,3,6] question the spontaneous involution which these scars are said to represent. Fine and co-workers think that mediastinal choriocarcinoma can be metastatic as well as primary. There are those, however, who doubt the possibility of metastatic choriocarcinoma in the mediastinum.[6,12] This controversy regarding exact criteria for the diagnosis of primary mediastinal choriocarcinoma has made the validity of case reports difficult to ascertain.

The pathogenesis of this tumor has also been of considerable interest. Several theories have been proposed in the literature, none of which has been totally accepted. The primitive germ cell rest theory has received the widest acceptance.[1,13-15,17] This theory states that, as the primordial germ cell migrates along the urogenital ridge to the primitive gonad, it either goes astray or does not complete the journey. The theory is supported clinically by at least two observations. First, extragonadal tumors develop in midline structures such as the mediastinum, retroperitoneal space, and abdominal or pelvic viscera. Second, the appearance of these tumors in the second, third, and fourth decades of life can be explained by the fact that the primitive gonadal germ cell remains dormant until puberty. Other theories that should be mentioned are the included twin theory, the included zygote theory, and the somatic cell rest theory.

Friedman[16] does not think that the primordial germ cell originates from the urogenital fold. Rather, he believes that the mediastinal teratomas and chorioepitheliomas may arise from germ cell rests in the anlage of the thymus gland. This is based on his observation of similar histopathologic features in thymic teratocarcinomas and germinomas seen in the mediastinum. He suggested a scheme (Table 2) for the histogenesis of these tumors based on studies of testicular and extragonadal teratomas and epitheliomas and their metastases. This scheme of development could certainly explain the preponderance of mixed teratomas and trophoblastic tumors seen clinically. The histogenesis of extragonadal choriocarcinoma remains an unsettled issue in need of further investigation.

Table 2.—Origin of Teratomas and Choriocarcinomas According to Friedman*



*(From Friedman, N. B.:[34] The Comparative Morphogenesis of Extragenital and Gonadal Teratoid Tumors. Cancer 4:265-276 [Mar.] 1951. By permission of J. B. Lippincott Company.)

Prognosis with choriocarcinoma is very poor, and most patients die rapidly of metastasis. Surgical treatment is of little value because of the rapidity of the growth and the invasive nature of the tumor. Deep radiation (cobalt therapy) has been of little success because chorioepitheliomas are highly radioresistant.[3] Methotrexate, although highly effective in female choriocarcinoma arising from fetal tissue, is much less effective in primary mediastinal choriocarcinoma. To date, the most effective treatment is triple drug therapy with methotrexate, actinomycin D, and chlorambucil. Most patients have died in 4 to 6 months.[18]

SUMMARY

During the period 1957 through 1967, 17 male patients with choriocarcinoma were seen at the Mayo Clinic. One, with primary mediastinal choriocarcinoma, is described, bringing the number of such cases in the literature to 15 (including only 1 female) for the primary mediastinal form. This patient presented with cough, chest pain, and gynecomastia and had a positive pregnancy test and high chorionic gonadotropin titer. Roentgenographically, primary mediastinal choriocarcinoma presents as a well-defined anterior mediastinal mass. Gonadal origin of the primary lesion must be excluded before one can conclude that the choriocarcinoma is of extragonadal origin.

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