UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF LOUISIANA

JOYCE BARROIS, ET AL	)	CIVIL ACTION NO:
PLAINTIFFS,	)	09-380
	)	
VS.	)	SECTION: R
	)	
FIREMAN'S FUND INS. CO.,	)	JUDGE: VANCE
ET AL	)	
DEFENDANTS.	)	MAGISTRATE: KNOWLES

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ORAL AND VIDEOTAPED DEPOSITION
OF
ETHAN A. NATELSON, M.D.
FEBRUARY 10, 2010
Volume 1 of 1 Volume

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ORAL AND VIDEOTAPED DEPOSITION OF ETHAN A. NATELSON, M.D., produced as a witness at the instance of the Plaintiff, and duly sworn, was taken in the above-styled and numbered cause on the 10th of February, 2010, from 1:38 p.m. to 3:09 p.m., before Minnie Cadena, CSR, RPR, RMR, in and for the State of Texas, reported by stenographic method, at the Marriott Hotel, 6580 Fannin Street, Houston, Texas, pursuant to the Federal Rules of Civil Procedure and the provisions stated on the record or attached hereto.

ORIGINAL

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INDEX

	Page
Appearances	2
Stipulations	4
Testimony of ETHAN A. NATELSON, M.D.	
By Mr. Williams	4
By Mr. Scott	36
By Mr. Asher	61
FURTHER EXAMINATION	
By Mr. Williams	65
By Mr. Scott	68
By Mr. Asher	71
By Mr. Scott	71
Witness' Signature Page	73
Reporter's Certificate Pages	74

EXHIBITS

		Page
No. A	Subpoena to Testify.....	4
No. B	Testimony Given by Dr. Ethan A. Natelson.....	4
No. C-1	Original Petition.....	4
No. C-2	Preliminary Trial Witness List.....	4
No. C-3	June 22, 2007, Letter to Kevin Parks from Dr. Natelson.....	4
No. D	Copy of Depo of Dr. Natelson, 9/17/07.....	4
No. E	Subpoena to Produce Documents.....	4
No. F	E-mail from Kindy to Williams.....	25
No. G	Copy of BLOOD Cover.....	42
No. H	Hematopoietic Malignancies and Related Disorders.....	47
No. I	Chemico-Biological Interactions.....	51
No. J	Myelodysplastic/ myeloproliferative neoplasm, unclassifiable.....	56
No. K	Invoice.....	67

(Exhibit A-E were marked.)

THE COURT REPORTER: Will the witness read and sign his deposition?

THE WITNESS: Read and sign.

THE VIDEOGRAPHER: We're on the record. The time now is 1:38, Wednesday, February 10, 2010. 01:38

ETHAN A. NATELSON, M.D.,

having been first duly sworn, testified as follows:

EXAMINATION

BY MR. WILLIAMS: 01:39

Q. Good evening, Dr. Natelson. Would you please state your full name and address for the record?

A. Yes, Ethan A. Natelson, N-A-T-E-L-S-O-N; and my address is 6550 Fannin Street, Suite 1001, Houston, Texas 77030. 01:39

Q. And, Doctor, I'm going to show you a subpoena; and I want you to tell me whether or not you received a subpoena to appear here today.

A. Yes, I did.

Q. Okay. And earlier we had an opportunity to go over some of the documents, and I'll get to that in a minute. 01:39

Can you briefly tell us your educational background?

A. Yes, I went to college at Haverford College 01:39

which is outside Philadelphia and had a bachelor of science degree; and then in 1962, came to Baylor College of Medicine in Houston where I graduated in 1966 from medical school, getting an M.D. degree. And then I did an internship at the Methodist Hospital from '66 to '67 and then a residency in internal medicine in what were then called Baylor affiliated hospitals, which are the Ben Taub Hospital, the Veterans Hospital and the Methodist Hospital, to a slight extent, St. Luke's Hospital. 01:40

Following that, I did a fellowship in hematology at Baylor College of Medicine for one year; and then I was in the service and assigned under what's called the Barry plan to the Wilford Hall Hospital in San Antonio, which is the referral hospital for hematology for the Air Force or was at that time. And so, I did purely hematology for two years in the service and then came back to join the faculty at Baylor College of Medicine. 01:40

Q. And you are a hematologist? 01:41

A. Yes.

Q. Doctor, do you do expert witness work?

A. Yes.

Q. Earlier you provided me with a list --

MR. WILLIAMS: And we're going to have to 01:41

mark this as B.

Q. (By Mr. Williams) And if you could, tell us how many cases you've identified that you've served as an expert witness.

A. This is a record of the cases I've given testimony in since 1992 to the present, and there are a total of 74 cases. 01:41

Q. And can you tell me how many of those cases involved myelodysplastic syndrome?

A. Yes, ten of those cases did. 01:41

Q. And can you tell me how many involved refractory anemia with ringed sideroblast?

A. Five of the 10 cases that have to do with MDS.

Q. And can you go through the list and identify the name of the case and tell us who you worked for and tell us what the disease -- as far as the ten we just discussed? 01:42

A. Yes.

MR. SCOTT: Have you marked this as an exhibit? 01:42

MR. WILLIAMS: B.

A. The first one is No. 22 on this list, which is Donald Ward v. Atlantic Richfield Company; and that was an RARS case.

Q. (By Mr. Williams) What date was that? 01:42

A. That would be January 18, 2002.
Q. Could you tell us the next case?
A. The next case is No. 24, which is Howard Collins v. American Petrofina; and that case was in May of 2002. 01:42
Q. Okay. Could you tell us the next case?
A. The next case was No. 35, which is Federico Tagle v. Citgo Refining & Marketing; and that was in October of 2004.
Q. And, Doctor, did you work on 30 and 31? Were they myelodysplastic syndrome cases, too? 01:43
A. Yes, I thought you were asking me about RARS in particular.
Q. I'm asking you about all of them.
A. I'm sorry. Yeah, I was looking at them as just RARS cases. I have them marked here in yellow if they are MDS. 01:43
So, I mentioned the Ward case; the Collins case. No. 30 is the James Cowey v. Radiator Speciality Company. That was in 2003. 01:43
No. 31 was the Ronald Awalt, A-W-A-L-T, v. Applied Energy Services & Company Incorporated; and that was in December of 2003.
Then the Tagle case, which I mentioned; and that's in October of 2004. 01:43

And then Guy Hamman v. American Oil Company, and that was in July of 2007. That's No. 52 on my list.

And then No. 54, Charles Wilson v. Rycoline Products Incorporated. That was in 2007, 9-17-2007. 01:44

And then No. 62, Connie Lea Gibson Andrews v. United States Steel Company; and that was in August of 2008.

Then the Bonnie L. Mallory case. That's No. 68. Bonnie L. Mallory v. The GoodYear Tire & Rubber Company. That was in June of 2009. 01:44

And then Mary Ellen Hall v. Radiator Specialty Company, which was in January of 2010.

Q. And, Doctor, in all ten of those cases, did you work for the defendants? 01:45

A. Yes.

Q. And in all ten of those cases, did you find that the benzene exposure caused the person's myelodysplastic syndrome? 01:45

MR. SCOTT: Object to the form of the question.

Q. (By Mr. Williams) Did you find that the benzene exposure caused anyone's myelodysplastic syndrome in those ten cases? 01:45

A. I don't know that they all had to do with benzene. There may be optional chemicals. Some may have been butadiene. I don't know if they were specifically noted as benzene, but I didn't find that the alleged chemical exposure caused the disease. 01:45

Q. Okay. In the case identified as No. 22, Donald Ward v. Atlantic Richfield and Howard Collins v. American Petrofina, in either of those RARS, we can call them, cases, did you find -- did you opine that benzene does not cause RARS in either of those two cases? 01:46

A. I don't recall in detail, but I'm sure that that was correct. I don't believe benzene causes RARS; so, that's what I would have said.

Q. And when did you formulate that opinion?

A. I can't tell you exactly. Probably many years ago because the original work by Dr. Wintrobe on that, which I've referenced in that article you have, Dr. Wintrobe considered benzene as a cause of RARS and rejected it. So, I think the literature for many years has not suggested RARS can be caused by benzene. 01:46 01:46

Q. Doctor, would you say that the majority of your cases in the 74 that you have provided were blood malignancy cases?

A. I would think the majority are. Some are malpractice cases. Some have to do with residency 01:47

training programs and other things, but the majority probably are to do with blood diseases.

Q. Were you paid as an expert witness in all of these cases?

A. Not all of them because some of them, for example, residency training programs, I wouldn't have been paid; but if they had to do with either testifying in malpractice or testifying in, let's say, a benzene-related issue, yes. 01:47

Q. And how much do you charge an hour, Doctor? 01:47

A. To review records, $250 an hour; and to testify at trial or deposition, $400 an hour.

Q. Have you ever opined that a plaintiff's blood malignancy or blood cancer was caused by benzene?

A. No. 01:48

Q. Have you ever opined or testified that benzene can cause myelodysplastic syndrome?

A. Yes.

Q. Is myelodysplastic syndrome the same thing as myelodysplasia? 01:48

A. Yes.

Q. Would you say myelodysplasia, myelodysplastic syndrome, myelodysplastic disorder are all the same thing?

A. Well, they are a classification of a group of 01:48

illnesses.

Q. Okay. What level and part per million years is required for benzene to cause myelodysplastic syndrome?

MR. SCOTT: Objection, form.

A. I don't know that it's known with absolute certainty. It's very, very high levels. I think in one article I wrote I said, I'd like to see at least higher than 40-part per million years as accumulated dose recognizing that in many instances the levels are not accurately measured. In many other areas of literature, the 200-part-per-million year accumulated dose is used; but I simply say it's very, very high doses. 01:48 01:49

Q. You think 370-part-per-million year dose is a high dose?

A. Yes. 01:49

Q. Doctor, I'm going to direct you to an article which is in Exhibit A, if you would flip the pages, please, entitled Benzene Exposure.

A. Yes, you have a copy of that.

Q. And it's attached to your subpoena. Benzene Exposure and Refractory Sideroblastic Erythropoiesis. 01:49

Did you write this article?

A. Yes.

Q. And can you tell us what journal this is published in? 01:49

A. This is in the AMERICAN JOURNAL OF THE MEDICAL SCIENCES.

Q. And is there a citation for this article?

A. Yes, it was published. It's Volume 334, Year 2007, Page 356 to Page 360. 01:50

Q. And, Doctor, when did you start working on this article?

A. Probably -- let's see. I submitted this, according to the paper, in January of '07. Probably several months prior to that submission date. 01:50

Q. Several months prior to January of '07?

A. Yes. In other words, it's marked -- on the paper it says, submitted January 16, 2007. And so, therefore, I would likely have worked on it for, perhaps, three, four months or so, at least, before submitting it. 01:50

Q. Okay. What process did you go through in submitting this article to the journal?

A. Well, I've been interested in sideroblastic anemia for many years, actually, since my training because two of my professors were heavily involved in 01:51 studying sideroblastic anemia; and I frequently did bone marrows on those patients and saw them clinically. So, I've been interested in the disease for many years.

As I -- as I began to give testimony in benzene-related cases and actually was asked to review 01:51

certain allegations of causation, I realized that this would be an interesting article to write because, No. 1, I had a lot of background with this illness. I enjoy this illness. I've always wanted to write a paper on the illness, and I have access to a lot of references that would bear on this question. And so, I thought it would be a good paper to write. 01:51

Q. Were there any rules for submitting this article to the journal?

A. I don't know of exactly what you mean by that. Most journals -- and today, things have changed. Everything is submitted electronically. But at this point in time, you would type up a manuscript. You would put a cover letter to the editor; and you would say, Dear Editor, this is a manuscript. I'd like to seek publication in your journal. Here it is, and you would mail it in. 01:52

And then after some period of time, you would hear something back from the Journal about whether they were interested in publishing it, whether they had corrections they would like you to make, whether they rejected it and so on. 01:52

Q. Does this journal, the AMERICAN JOURNAL OF MEDICAL SCIENCES, require disclosing potential conflict of interest at the time you submit the article? 01:52

A. Yes, I think all journals would say that, disclose a conflict of interest to that form.

Q. At the time you submitted this article, Doctor, were you serving as an expert witness in any benzene cases? 01:53

A. I don't know, probably so.

Q. At the time you submitted this article, were you serving as an expert witness on any Benzene cases that involved myelodysplastic syndrome?

A. I don't know; but possibly so, depending on what those lists of cases are that we went through. 01:53

Q. And at the time that you submitted this article in the journal, were you involved in any cases where your opinion was that RARS was not caused by Benzene in the case? 01:53

A. Well, I -- as we went through those cases, some of those cases, I think, dated back to 2002 or earlier, long before I wrote this article; and that was my opinion that RARS was not a benzene-related illness.

Q. Doctor, I want to show you a petition -- we have this marked as C-1 to a case, and I believe -- could you read the caption to that case? 01:53

A. It says: Now comes Charles Wilson and Laura Wilson, hereinafter referred to as Plaintiffs, complaining of Rycoline Products, Inc., Rogersol, Inc. 01:54

Q. I'm sorry, Doctor, the top, the caption, Charles Wilson v. Rycoline Products. I apologize.

A. Charles Wilson and Laura Wilson, Plaintiffs v. Rycoline Products, Inc., Rogersol, Inc., Hostman-Steinberg, Inc., IC Compound Company, Ashland, Inc., Company Individually, Ashland Oil & Refining Company and Ashland Oil, Inc., Allied Photo Offset Supply Corporation, Day International, Inc., Individually and d/b/a Varn Products, Allied Photo Offsets Supply Corporation; and Lastra American Corporation. 01:54

Q. Okay. And, Doctor, can you tell me the date on the top of that petition that it was filed?

A. Filed 7-13-2006.

MR. WILLIAMS: Okay. We're going to mark that as C-1, Ms. Reporter. 01:54

Q. (By Mr. Williams) And that's the case you have listed as No. 54 on your expert summary?

A. Yes.

Q. Doctor, I'm going to next show you a witness list to the case of Charles Wilson v. Rycoline Products, and can you tell me if your name is listed as a witness on that case? 01:55

A. Yes, it is.

Q. Okay. And could you tell me what date is on the top of that witness list that it was filed? 01:55

A. It says filed 7-17-2007.
Q. Okay. Do you recall being a witness in this case?
A. Vaguely.
Q. Okay. And that's marked as C-2. 01:55
Next, I'm going to show you a report from that case, Doctor. Can you tell me if you recognize that report?
A. Yes, this is a report on my letterhead.
Q. Can you tell me the date of that report, 01:55
Doctor?
A. June 22, 2007.
Q. Okay. And, Doctor, on the first page, it is your opinion, the highlighted portion, that there are several names for what we talked about earlier, ringed 01:56
sideroblast or RARS? Can you tell me what your opinion is?
A. Yes, as I have written here: It is alleged that his hemologic illness of refractory anemia with ringed sideroblast, also known as acquired idiopathic 01:56
sideroblastic anemia, sideroachrestic anemia and by the initials RARS and AISA has occurred subsequent to his exposure in the workplace to benzene-containing solvents.
Q. And, Doctor, I want to return to Page 4 of the report, you have a highlighted bolded portion. Can you 01:56

read that out loud, please?

A. Yes. In fact, I am not aware of a single epidemiologic study or even an isolated case report in the world's medical literature that shows RARS/AISA to be a consequence of benzene exposure. 01:57

Q. And there was a reference number that you have there?

A. Yes, No. 14.

Q. Can you tell us what No. 14 is?

A. That's the article that we've talked about Benzene Exposure and Refractory Sideroblastic Erythropoiesis: Is There an Association. And that was the AMERICAN JOURNAL OF MEDICAL SCIENCE. At that time, it was in press, in 2007. 01:57

Q. And "press" means that it's not published yet; is that correct? 01:57

A. Well, it often is published on -- E-published. In other words, you can see the article; but the journal hasn't made the streets yet.

Q. Okay. Thank you. 01:57

Were you paid for preparing that report there, Doctor?

A. I'm sure I was.

MR. SCOTT: Which exhibit is that?

MR. WILLIAMS: That's C-3. 01:58

Q. (By Mr. Williams) Were you paid to be an expert in that case, Wilson v. Rycoline Products?

A. Yes.

Q. Do you remember how much money you were paid in the Wilson case? 01:58

A. No.

Q. How long does it usually take you to review records and write a report in a case like that?

A. It's variable from case to case because some cases have a small amount of information, other cases 01:58 have a staggering amount of information. And once I have all of the information together and then I sum up what references I'd like to put into the letter and by the time I go through revisions to the letter and modifications of it, it might be from, starting a letter 01:58 to finishing a letter, easily seven or eight, ten hours.

Q. Okay. Doctor, I want to show you the next exhibit, Exhibit D, a deposition from the Wilson v. Rycoline Oil Products case; and if you turn the page to the tabbed page. In the deposition are you offering 01:59 opinions that benzene does not cause RARS?

A. Yes, that's correct.

Q. Okay. And if you flip the page, in that deposition, do you also testify that your journal article will be published in November of 2007? 01:59

A. Yes.
Q. And what's the date of that deposition, Doctor?
A. 9-17-2007.
Q. Were you paid for that deposition in that case, Doctor? 01:59
A. I'm sure I was, yes.
Q. Okay. Thank you, Doctor.
Doctor, I'm now going to show you a subpoena that was issued to the -- David Ploth, the editor of the AMERICAN JOURNAL OF MEDICAL SCIENCES, along 02:00 with a copy of your published paper.
Have you ever seen that subpoena before?
A. No.
Q. Do you know who David Ploth is?
A. Is his name written? 02:00
Q. Ploth, I think I'm mispronouncing, on the front page. David Ploth, I apologize.
A. According to this thing, he is the current editor of the AMERICAN JOURNAL OF MEDICAL SCIENCES.
Q. Doctor, I'm going to provide you with a copy of 02:01 the response that we received.
It's a copy of the response that we received from the journal; and if you flip the page, there is a document -- the second page right there. Is that your handwriting, Doctor? 02:01

A. It is.

Q. And can you identify the title of this document?

A. It says: Authorship responsibility, financial disclosure and copyright transfer form. 02:01

Q. And, Doctor, you filled out this form and submitted it to the AMERICAN JOURNAL OF THE MEDICAL SCIENCES; is that correct?

A. Yes.

Q. Okay. Doctor, if you go down to Section 2 under financial disclosures, the highlighted section, and read that into the record for us? 02:01

A. I certify that any affiliations with or involvement, either competitive or amiable, in any organization or entity with a direct financial interest in the subject matter or materials discussed in the manuscript, for example, employment, consultancies, stock ownership, honoraria and expert testimony, are noted below. Otherwise, my signature indicates that I have no such financial interest. All financial research or project support is identified in an acknowledgment in the manuscript. 02:02

Q. Okay. And my question to you is, Doctor, I don't see where you disclosed that you had any expert testimony relating to the subject matter in that 02:02

document?

MR. SCOTT: Object to the form of the question.

A. That would be true.

Q. (By Mr. Williams) Okay. And I don't believe the article identifies that you were serving as an expert witness in RARS cases; is that correct? 02:02

MR. SCOTT: Objection, form.

A. That's correct.

Q. (By Mr. Williams) And am I correct that you were serving as an expert witness in benzene, RARS cases prior to starting the article? 02:02

A. Yes.

Q. As we have just evidenced through the depositions and the reports, while the article was under publication; is that correct? 02:03

A. Possibly. Look at those dates. As I say, we have the date I submitted it, yes.

Q. And you were serving as an expert witness in benzene, RARS cases after the article was published; is that correct? 02:03

A. Yes.

Q. If you flip the page please, Doctor --

A. (Witness complies.)

Q. -- and let me ask you one more question. What 02:03

did you understand "certifying" to mean, under oath, or do you know what certifying means?

MR. SCOTT: Object to the form.

A. I'm not sure I know what it means. In other words, this article was a review. It was not original work. It's a review of literature and I'm just putting it together and I don't see that that offers any conflict of interest to anybody. And it's a common practice in writing articles that one reviews other people's work and puts it in there and that, to me, is not considered a conflict of interest. 02:03 02:03

Q. (By Mr. Williams) And you don't agree that the Journal required you to identify any potential conflict of interest?

MR. SCOTT: Object to the form. 02:04

A. Well, I look at that as, was that article being written about information in a particular case that I'm testifying in? This is a general subject matter, and I don't see that it has anything to do with a conflict of interest. 02:04

Q. (By Mr. Williams) Doctor, do you know a gentleman by the name of David Pyatt?

A. I've actually never met him but I've corresponded with him and I've spoken with him on the phone once or twice. 02:04

Q. Did you speak to him relating to this article that you published?

A. I don't know that. I mean, at the time I wrote it, I think that would be doubtful; but I couldn't say "yes" or "no." 02:04

Q. Do you know if you've ever served as an expert witness on a benzene myelodysplastic syndrome case with David Pyatt who is a toxicologist?

A. Yes.

MR. SCOTT: Objection, form. 02:05

Q. (By Mr. Williams) Can you tell me which ones you've served on? If you'd like to look at your list, that would be fine.

A. I wouldn't be able to tell you that from this list. 02:05

MR. SCOTT: Eric, I'm sorry. I've got some objections to these questions.

And, Doctor, if you will let me --

THE WITNESS: I'm sorry.

MR. SCOTT: No, that's all right. If 02:05 you'll just pause for a second after his question is done, I'll get my objection in and then I won't be prancing all over your words; but I object to the form of the last question.

Q. (By Mr. Williams) Doctor, have you ever told 02:05

the AMERICAN JOURNAL OF MEDICAL SCIENCES up until today that you do work involving benzene RARS cases?

A. No.

MR. SCOTT: Object to the form.

Q. (By Mr. Williams) Can you tell me how many benzene myelodysplastic syndrome cases you worked on with Dr. Pyatt? 02:05

A. I couldn't.

Q. Can you tell me how many benzene cases you've worked on with Dr. Pyatt? 02:06

A. I don't know.

Q. Can you tell me if it's more than ten?

A. I can't tell you that. I don't know. He's been an expert witness on several cases; and, in fact, I've written a paper with him, but I actually have never met the man. 02:06

There are two papers. One is a paper that he was the primary author that has to do with formaldehyde, and it's in my CV. And the other is a paper that was recently accepted for publication that has to do with chemotherapy induced myelodysplasia. 02:06

Q. Doctor, do you know who the peer reviewers were for the article that we're here for today, the Madison 2007?

A. No. 02:06

Q. Were you over told -- or did you ever correspond with the peer reviewers?

A. Well, no, you're not told that. In other words, you are given -- typically, the way the Journal operates is that you may recommend -- they typically ask you to recommend some people in the field; but then what happens is that you get a blank paragraph back from each of the reviewers or simply a letter saying the Journal isn't interested. And you don't know which reviewer wrote what, or if they used any of the people you suggested; but they simply ask you to suggest some names. 02:07

Q. Do you know if you worked on any benzene cases with Dr. Pyatt in 2007?

A. I think it's very doubtful.

Q. Okay. If you turn to a few pages where it says to review letter -- 02:07

MR. SCOTT: What's your exhibit number? I'm sorry, Eric, so we can keep track of what we're talking about --

MR. WILLIAMS: I apologize. All of this is in Exhibit F. I need to change that number. 02:08

MR. SCOTT: F.

(Exhibit F was marked.)

Q. (By Mr. Williams) Doctor, have you seen this page before? 02:08

A. No.
Q. Can you tell me what peer reviewer is identified on this sheet?
A. David Pyatt, M.D.
Q. Okay. And if you turn the page, were you -- to the highlighted section -- were you informed that David Pyatt viewed your article as acceptable with minor revisions and said that related issues and toxic tort litigation are on the rise and MDS is frequently at issue. Were you told that? 02:08 02:09
A. If I was given -- I certainly wouldn't be told who reviewed it. I might have been given this paragraph -- or a section of it, depending on what the editor supplied me with.
Q. And did you recommend David Pyatt as a reviewer of this article? 02:09
A. I probably did. I don't know that for a fact. I gave them several names, and his name could have been among them.
Q. Okay. Doctor, if you keep flipping until we get to your article -- 02:09
A. Yes.
Q. -- I believe you testified -- or you write in your article -- and it's at the end, Page 359 -- that there are certain forms of myelodysplastic syndrome that 02:09

you feel are caused by benzene exposure, the last paragraph of 359.

A. Yes, I said: Despite these caveats, based on considerable evidence presented here, benzene exposure cannot be considered of potential etiology for RARS although it remains a risk factor for certain forms of the myelodysplasia such as RAEB, an unclassified and/or hypocellular myelodysplasia syndromes, and for AML. 02:10

Q. Correct. And, Doctor, refractory anemia is a form of myelodysplastic syndrome; is that correct? 02:10

A. RARS is classified as a form of myelodysplasia, yes.

Q. No, just plain refractory anemia?

A. Oh, yes, you can have primary refractory anemia that is a form of myelodysplasia. 02:10

Q. And then when one develops ringed sideroblast, it would be RARS refractory with ringed sideroblastic?

A. Yes.

Q. And then when one develops RAEB, it would be refractory anemia with excess blast; is that correct? 02:11

A. Yes, but if you're talking about the same case, I don't think that you would see the transition from a primary refractory anemia into an RARS. You would see the progression from a primary refractory anemia into an RAEB. You would see the progression from an RARS into an 02:11

RAEB.

Q. And cases of RAEB, refractory anemia with excess blast would have excess amounts of ringed sideroblastic, too; is that correct?

A. If they started out as an RARS and the natural history of that illness is to, in some instances, move toward a Leukemia, as they increase blast, they become, by the classification system RAEB. They are the same illness, as far as I'm concerned; but they are classified as RAEB because they now have blast and they still have ringed sideroblast. 02:11 02:12

Q. Okay. Doctor, would that be the same for RAEB-T that you would have excessive blast and also possibly excessive ringed sideroblastic; is that correct?

MR. SCOTT: Object to the form. 02:12

A. Well, again, talking about the progression, if you had RARS-T, that's an illness which you are saying at diagnosis it's a myeloproliferative disease. It has excess ringed sideroblast. That disease may progress toward an acute myeloleukemia, too, and accumulate large numbers of blast and actually go into AML. 02:12

Q. (By Mr. Williams) Doctor, are there -- how much money have you made serving as an expert witness for various defendants in myelodysplastic syndrome cases?

MR. SCOTT: Object to the form. 02:12

A. I couldn't give you a number.
Q. (By Mr. Williams) And could you give us a number for how much money you have made in RARS cases?
A. I wouldn't have a guess. It looks like there were five, I think we saw, since 1982. I couldn't give a guess. 02:13
Q. Do you have an average of what it takes you to prepare a report and go through a deposition, average price, a range?
A. It depends on how long the deposition is in terms of how much that costs; and the preparation, my guess would be that it -- and this would be a guess, that it might be anywhere from six to ten hours, let's say, depending on the simplicity of the case in terms of reviewing the records. 02:13
Q. Okay. Have you ever treated a patient with myelodysplastic syndrome that was exposed to -- that was a chemist and was exposed to chemicals?
A. Yes.
Q. And was it your opinion that that chemist's exposures to benzene and other chemicals was the cause of his myelodysplastic syndrome? 02:14
A. I thought it was possible.
Q. Okay. Are there any studies, Doctor, in the world's literature that focus on the fact benzene, 02:14

besides your own, can't cause RARS?

A. Well, there are many articles that read on that point. In other words, there is the Dr. Ruiz article, which I think I cited, where he did bone marrows on 33 people with heavy exposure to benzene and pancitopenia 02:14 and he specifically tells us there were no ringed sideroblasts.

We have Dr. Irons article. He had two articles. One, I think, in 2005 and one recently where he's looked at a large number of people with heavy 02:14 benzene exposure and none have had ringed sideroblast.

We have Dr. Aksoy's work. And Dr. Aksoy was trained, in part, here in the United States with Dr. Damashek who was the world's expert on RARS. So, he certainly knew about that illness. And he did bone 02:15 marrows on a number of people he thought had benzene-related disease, and he makes no mention of ever finding RARS in their marrows.

And I would not think that could be missed by a person of his training. 02:15

We have the so-called Chinese benzene study, the Haze benzene studies in which Dr. Larsen and others reviewed slides, they claim, of seven people with myelodysplasia from that large cohort; and they make no description of seeing ringed sideroblasts. And all of 02:15

those people are very prominent hematologists and certainly would recognize ringed sideroblasts.

So that if we look through the literature in cohorts that have been studied by bone marrow analysis by prominent people, there is no mention of the occurrence of ringed sideroblast, and in many instances, mention that they are not evident, even after having been sought. 02:16

Q. Doctor, maybe you didn't understand my question. I asked you were there any other studies that are focused, the title or the objective is benzene exposure and refractory sideroblastic erythropoiesis. 02:16

MR. SCOTT: Object to the form.

A. I think I understand the question. Yes, that was the reason I wrote this article is because that was because early on, Wintrobe had asked that question and others had; and so, now, I was in the a position to review that question and try to answer that question. 02:16

Q. (By Mr. Williams) Basically, your study is one of a kind as to answering that question only? 02:16

A. Yes.

Q. Okay. Thank you.

A couple more questions, Doctor; and I think we're done.

Have you spoken with -- besides myself, 02:16

Mr. Scott, Bob Scott over there, regarding this deposition?

A. Yes, I've spoken with -- well, Mr. Asher called me right after you did; and I spoke with him. And then I spoke with Mr. Scott later on, several days later, I believe. And I also spoke with Stan Perry. That's the best I can remember. 02:17

Q. Okay. Start off telling us what you spoke with Mr. Asher about.

A. Well, what had happened is you called and said you wanted to depose me on my paper; and I specifically asked you whether this had to do with a specific case. And you told me, no, I just want to depose you about your article. And then I thought that was very peculiar. 02:17

And then shortly thereafter, I got a call from Mr. Asher saying you're going to be receiving a subpoena, if you haven't already; and it's about this Barry Wild case. 02:17

And I said, Well, I'm told I'm going to receive a subpoena but not that it's about a particular case. 02:18

And he said, Oh, yes, it is. It's about a particular case; and I'm going to send you a summary of the case, which he did. And that was the sum and substance of the conversation. 02:18

Q. And when you say "summary," are you referring to an expert report prepared by Defendant Fisher Scientific's expert, Gregory Sona?

A. Yes.

Q. And did you review that paper? 02:18

A. Yes, I did review the report.

Q. And when you say Ross Asher, you mean the gentleman to my right who represents Fisher Scientific. He is the one that contacted you?

A. Yes. 02:18

Q. Next you said Mr. Bob Scott contacted you. Tell me about that conversation.

A. Well, Mr. Scott said that -- I've forgotten what initiated the conversation because we had done other cases; but I mentioned this situation to him, and he 02:18 said, Well, that's very interesting because I'm involved in that Barrios case. And I didn't know that. Mr. Asher hadn't mentioned that to me.

And so, he said, When are you going to give this deposition? 02:19

And I told him and that was the -- in general, that was the substance of that case.

Q. And what cases have you worked on for Mr. Scott, what defendants was he representing?

A. I'm terrible on names, but we testified on a 02:19

case that was in -- was it -- New Mexico, I believe, that was a myelodysplasia case that comes to mind. I know there were probably several others, but I can't remember it by name.

Q. Was RARS an issue in any of the cases that you worked for with Mr. Scott? 02:19

A. I don't remember that. I think, yes, I think that case had to do with RARS.

Q. In New Mexico?

A. Yes, I believe so. That was an issue in that case. 02:19

Q. And did you testify at trial?

A. Yes.

MR. SCOTT: It was actually a Daubert hearing. I'm sure Dr. Natelson didn't understand the niceties of that. 02:20

Q. (By Mr. Williams) And have you served for Mr. Scott as an expert on several occasions?

A. I'm sure I have. I can't remember all of the cases. 02:20

Q. And then, I believe, you just told me that Stan Perry, that's the gentleman that's the national counsel for Shell Oil Company, called you?

A. Yes.

MR. SCOTT: Object to the form. 02:20

Q. (By Mr. Williams) What did Mr. Perry have to say?

A. I'm trying to recall what he specifically said. There was nothing -- he said, Well -- I asked him, I said, Isn't this a little bit peculiar to get subpoenaed about a case you're not involved in? 02:20

And he said, Well, it does sound a little peculiar; but I would just recommend you going ahead and giving the testimony, whatever you're asked. And he said, I don't have a clue why this has occurred. 02:20

Q. Do you know why Mr. Stan Perry, the national counsel for Shell Oil Company, contacted you when, in fact, Shell Oil is not a defendant in this case?

A. No, I was talking with him on another issue; and I brought it up. So, I said, How would you look at this issue? I said, isn't this somewhat peculiar? 02:21

And he said, Well, this does sound a little peculiar; but my advice is just go ahead and give the testimony.

MR. SCOTT: Object to the form of the last question. 02:21

Q. (By Mr. Williams) Did any of the attorneys that contacted you tell you to testify or lean one way or the other in this deposition?

A. No, none of them said, Don't Testify. All of 02:21

them said, theoretically -- I think, in fact, Mr. Asher said to me, he said, You know, you could really hire an attorney and try to get out of this?

And I said, Well, it just sounds like that would be more trouble than it would be worth. And so -- 02:21
but no one suggested I do that.

Q. Right. Besides Mr. Asher?

A. Well, he didn't suggest. He said I could.

Q. You could do that, right. Okay. Give me a second. That's it. 02:22

Do you have anything, Mr. Asher?

MR. SCOTT: Yeah, I definitely have some.

EXAMINATION

BY MR. SCOTT:

Q. Good afternoon, Dr. Natelson, and thank you for 02:22
being here.

You mentioned earlier that your first thoughts about benzene and any association with a disease known as refractory anemia with ringed sideroblast or RARS, as it's been called, came after reading something 02:22
that Wintrobe wrote.

Did I get that right?

A. Yes.

Q. Who is Wintrobe?

A. Well, Dr. Maxwell Wintrobe was the -- was a 02:22

hematologist, self-trained really, who was the chief of medicine in hematology in Salt Lake City at one time. He actually worked in Louisiana at one time and I believe he went to Rochester Medical School, but he became internationally known because he wrote the first major 02:23
textbook in hematology and was a very renowned and also very famous for having an enormous research -- reprint library. In the days prior to the Internet, if you wanted to have an article, you would write a letter or a postcard to an author and they would send you back a 02:23
signed copy; and Dr. Wintrobe had a massive research library where you could get all of your reprints there.

Q. This was before the Internet, I take it?

A. This is long before the Internet, yes.

Q. Is Dr. Wintrobe still with us? 02:23

A. No, he died a number of years ago.

Q. Does his hematology textbook continue to be with us, new editions from time to time?

A. Yes.

Q. And is it one of the hematology textbooks that 02:24
is used in medical schools, certainly in this country and perhaps around the world?

A. Yes.

Q. And exactly what is it that Dr. Wintrobe wrote or reported that piqued your interest with regard to 02:24

benzene and RARS?

A. Well, Dr. Wintrobe was aware of this illness. He was not the first discoverer of it. Some other doctors in the decade prior to when he wrote about it had made mention of this illness. And he decided that he 02:24
would study all the cases he had at Salt Lake City. I don't remember the numbers. They are in this article. Let's say, 19 cases or so that he had; and then I think he abstracted about 44 more cases from the world's literature. And he looked to see how you made this 02:24
diagnosis; how many ringed sideroblasts there were in the bone marrow; could there be known causes for this looking at drugs, looking at alcohol because it was known that alcohol could produce ringed sideroblasts.

And so, he looked to see if there was a 02:25
unifying feature in these patients that explained their illness. And he found what we really know today that a number of these people went on to develop acute Leukemia, that there was no particular relationship with alcohol, there was no relationship with lead poisoning which could 02:25
also give ringed sideroblasts. There was no association with benzole, as he put it, which he knew caused bone marrow depression. And so, he termed the illness idiopathic meaning that none of the known bone marrow toxins that he was aware of could produce this illness. 02:25

Q. You also mentioned an author, a Doctor named Aksoy.

A. Yes.

Q. And as I recall, he was a Turkish doctor; is that correct? 02:26

A. Yes.

Q. You indicated that he trained with Dr. Damashek. How do you know that?

A. Well, I happen to know that because Dr. Aksoy wrote many articles; and these were -- most of them were 02:26 written, I think, in the '70s, up until about 1982, I think, was his last article. And after he died, I have a review article by some of his colleagues that wrote about it. And they went in that article into his background and pointed out that he had studied with Dr. Damashek 02:26 doing a fellowship. And so, I learned a little bit more about his background. He was not -- I don't think his hematology training was in the United States but his fellowship was.

Q. And what is it that Dr. Aksoy wrote about that 02:26 was related, in your view, to the question of whether benzene is associated -- causally associated with the development of RARS?

A. Well, Dr. Aksoy studied a large number of patients. His patient base was about 29,000 people. And 02:26

I don't recall the exact number of how many had what he called pre-Leukemic syndromes and acute Leukemia, but let's say it was in the 30s to 40s of individuals that he personally studied. And I think in one of his articles he said he does bone marrows on 11 of them. And those were ones that he did, and I assume he looked at bone marrows that other people did on other cases. 02:27

In the era when he was writing those articles, the iron stain, the so-called Prussian blue stain, or pearls blue stain was a standard practice in hematology. And so, he would be familiar with looking at iron stains. 02:27

He also studied with Dr. Damashek who one of his favorite topics was sideroblastic anemia. So, certainly, it's reasonable to expect that a trained hematologist who studies with someone interested in this disease could recognize a ringed sideroblastic. 02:27

And in a normal bone marrow, one doesn't see a single ringed sideroblast. And in RARS, one may see 40, 50, 70 percent of the cells may be ringed sideroblast. I brought a cover here of a magazine to show how striking it is. 02:28

So, when Dr. Aksoy writes an article and he says, These are the abnormalities that I saw in benzene-related illnesses, he didn't have to tell me that 02:28

he looked for ringed sideroblasts. He had seen them, he would have commented that that was an abnormality.

In other words, it was just as though he doesn't say he didn't see malaria parasites or this or that. In other words, he said what he saw; and included in that was not ringed sideroblasts. 02:28

Q. You use the term "sideroblastic anemia." What relationship is sideroblastic anemia to refractory anemia with ringed sideroblasts or RARS?

A. Well, sideroblastic anemia is a general topic; and prior to the use of the term myelodysplasia and even subsequent to it, if you went to a hematology textbook, you would see a chapter on sideroblastic anemia. And that chapter would be divided into those that are hereditary, which there are some, and those that are acquired illness. 02:28 02:29

And then under the acquired illnesses, there would be broken down as to what the causes might be. For example, led poisoning gives you a sideroblastic anemia, very heavy arsenic poisoning can give you a sideroblastic anemia. Alcohol can give you a sideroblastic anemia. 02:29

Those all acquired sideroblastic anemias; but only, perhaps, in the arsenic related might they go on to a Leukemia. They are not a pre-Leukemia state. 02:29

But certain of the sideroblastic anemias for which there are no obvious causes, no drugs, no chemicals, they fall under the title Wintrobe called idiopathic sideroblastic anemia. And that was a group that he followed and he commented that they could live many years, and they often died of iron overload. They didn't always die of Leukemia. In fact, only occasionally did they die of Leukemia. Dr. Damashek thought about half of them would die of Leukemia, but Dr. Wintrobe realized that that was too big a number and it was much smaller than that that went on to develop Leukemia. 02:30

So, that would be what you would find in the textbook chapter. It would give you a discussion of all the different types of sideroblastic anemias. 02:30

Q. You say you have a cover that shows us a refractory anemia with ringed sideroblast or at least a ringed sideroblast?

A. Yes.

Q. Is that something that we can mark for this deposition and have it sent back to you? 02:30

A. Certainly.

(Exhibit No. G was marked.)

Q. (By Mr. Williams) And, Doctor, if you don't mind, would you hold that up for the camera; and we'll 02:31

see if he can zoom in on the cover here of Exhibit G.

A. This is a cover of a magazine called BLOOD, and Dr. Damashek was the founder of that magazine. He was the original editor.

Q. And is the journal BLOOD the JOURNAL OF THE AMERICAN SOCIETY OF HEMATOLOGY? 02:31

A. Yes, it is.

Q. Or SOCIETY OF HEMATOLOGY?

A. Yes.

Q. Now, can you point at -- it may be tough to do on the -- on the camera, I don't know, because you can't see the other side of it; but can you point out -- 02:31

A. I think I can.

Basically, when you prepare a slide to do an iron stain, what you like is to make a fairly thin film of the bone marrow; and that spreads out the mother cells that give rise to red cells. And they're counter stained with a slightly red stain. So, everything you see red is the nucleus of a cell that is going to be circulating a red blood cell. 02:31

Q. And that's sometimes called an erythroid cell; is that right?

A. These are called erythroid blasts in the bone marrow. And when you're staining them with the Prussian blue stain, any iron in the cytoplasm forms a blue 02:32

granule color. And in a normal bone marrow, all you should see is the red counter stain. There wouldn't be a single one of these cells with these multiple little blue dots around them. So, this smacks you in the face if you were looking at an iron stain on a bone narrow. 02:32

Q. This is not the kind of thing Dr. Aksoy would miss if he had seen it?

A. I'm confident Dr. Aksoy would recognize this, just as Dr. Damashek and many others have.

Q. I want to -- we've talked about Dr. Wintrobe and Dr. Aksoy. What other -- you have written a review article. What is a review article? You distinguish that between a review recall and a research. Can you describe for us what a review recall is and what the purpose of it is? 02:32 02:33

A. Well, a review article is to provide education for people in the medical community about a particular issue. And you take a subject and you try to review the literature intensively and find what you think are the pertinent articles to answer a particular question. And then you review those articles and mention why you're selecting them and why these articles help you come toward a conclusion. 02:33

In this particular case, we're talking about sideroblastic anemia and causation; and that's what 02:33

the purpose of this review was.

Q. And I take it that in preparing that article and writing that article, you did some sort of literature search to see what was available in the medical and scientific literature regarding benzene and refractory anemia with ringed sideroblast? 02:33

A. Yes.

Q. You've told us about Wintrobe and Aksoy. What other original work was in the literature that led you to your conclusions that benzene is not associated with the development of RARS? 02:34

A. Well, there were several articles; and some of these are referenced in the paper, and some of these are already discussed. One we didn't discuss, for example, is we discussed, let's say, the Ruiz study where he had people heavily exposed to benzene and he selected a group of 33 that he thought would be most reflective of that poisoning and he did bone marrows on them. And he tells us that none of them have ringed sideroblasts. 02:34

Q. Not a single one? 02:34

A. Not a single one.

Then you could look at that in reverse, and one of the articles I cited took a large collection of people with RARS, I think there were 84 of them. And they went back and interviewed those people and studied 02:34

their files to see how many of those 84 might have had it from benzene exposure. Did they have a chemical background that could have been causative? And in that article, they claim they found one person who alleged exposure to benzole; but that person had also received radiation therapy for a malignancy. And so, it did not appear that looking at a cohort of people with this illness that benzene stood out as a potential cause and effect. 02:35

Q. What was the article where they took the collection of people with RARS and went back to see if, in their history, they had benzene or solvent exposure? 02:35

A. Let me see if I can find that. Let's see where I reference that. I probably better find it from looking at my references. I believe it's reference 19, but let me see if that's correct. 02:36

Yes, it's my reference 19, which is called -- is by Garand, G-A-R-A-N-D.

Q. That was in the 1992, it looks like, from your reference list, correct? That was -- that article appeared in LEUKEMIA RESEARCH? 02:36

A. That article appeared in LEUKEMIA RESEARCH, Volume 16, Page 463 to 486, 1992.

Q. Are you familiar with a series of papers arising out of a study conducted by the National Cancer 02:36

Institute in conjunction with the Chinese Academy of preventative maintenance -- preventative medicine -- I've got a car problem. I keep saying "maintenance" instead of "medicine" -- of a large group of workers in China?

A. Yes. 02:36

Q. Does that article shed any light or provide any information that is helpful on the question of whether or not benzene has been associated with the development of RARS?

A. Yes, I think so. That was a very large cohort, 02:37 I believe, about 74,000 workers in China exposed to what are thought to be very large amounts of benzene in an occupational environment. And in that group, the -- there were seven cases identified as having forms of myelodysplasia. And according to the articles, those 02:37 cases were reviewed by hematopathologists. And they list the diagnosis of these seven, and none of them are RARS.

There is also a comment in one of the articles I cited about what the typical bone marrow looked like in these people, and there is no mention of 02:37 ringed sideroblast in that comment.

MR. SCOTT: What's our next exhibit?

THE COURT REPORTER: H.

(Exhibit No. H was marked.)

Q. (By Mr. Scott) Dr. Natelson, I'm going to hand 02:38

you what I've marked as -- actually, the court reporter has marked as Exhibit H, which is an Internet search form and then an article with a lead author Travis; and it was published in 1994.

Have you seen that article before? 02:38

A. Yes.

Q. Is that one of the papers out of this NCI CADM or Chinese Preventative Medicine Study?

A. Yes.

Q. On page -- the second page of that article which is numbered, I think, 92 -- and Lois Travis is the lead author; am I correct? 02:38

A. Yes.

Q. And in the right-hand column, there is a description in the first full paragraph that says: Evidence of dyserythropoiesis included the presence of -- and it lists a number of items, ringed sideroblasts, multinuclearity, nuclear fragmentation, megaloblastoid changes and so on. 02:39

What are those? What is dyserythropoiesis, and what are those items? 02:39

A. Well, dyserythropoiesis would be a general term meaning, in lay language, that the cell line looks abnormal; and it may be abnormal because it's too large. It may be abnormal because the cytoplasm is very 02:39

irregular on the cells. It may be abnormal because the colors -- the stain colors are abnormal. It may be abnormal because they are inclusions, like ringed sideroblasts, something that shouldn't be in there. It may be abnormal because the nucleus is splitting, that 02:39
you have two nuclei in a single red cell precursor, for example.

So, dyserythropoiesis is a general term means abnormal, morphology, funny-looking cells. And then they go on to say what some of those were, for 02:40
example, ringed sideroblasts we've discussed. Multinuclearity meaning there were multiple nuclei instead of a single one in the cell.

Karyorrhexis, what that means is the nucleus is fragmenting instead of being very well 02:40
defined.

Abnormal nuclear shape, I think I mentioned it should be like a bulls eye. It looks very round. It may be irregular.

Impaired hemoglobinization, what that means 02:40
is that as the cell matures, the cytoplasm becomes redder and redder as hemoglobin is manufactured. And so, impaired hemoglobinization means the cell looks very pale. It's not making it's complement of the hemoglobin.

Megaloblastoid changes meaning simulating 02:40

what we see with Vitamin B-12 deficiency where the cells are very large and abnormal looking.

And so, those are the things that they mention as would come under the heading of dyserythropoiesis. 02:41

Q. And part of the -- one of the items or things they were looking for as evidence of dyserythropoiesis is the existence or observation of ringed sideroblasts?

A. Yes.

Q. Can you turn to Table 5 of the Travis article, Exhibit H, which I think is on Page 97. Can you first confirm that Table 5 is a listing of the various -- among other things, the various items of dyserythropoiesis that the National Cancer Institute investigators had been looking for? 02:41

A. Yes.

Q. And under the cases of MDS, how many instances did they observe ringed sideroblasts?

A. None, according to this. They have looked for them, but they don't cite any cases as having them. 02:42

Q. And they do cite, if you can confirm, observation of megaloblastoid changes, abnormal nuclear change, impaired hemoglobinization and multinuclearity as you described for us earlier; correct?

A. Yes, that is correct. 02:42

Q. Is that the same thing as saying they look to see if there were ringed sideroblasts among their MDS cases and saw none?

A. Correct.

Q. And then finally the Irons article or articles, what do Dr. Irons and his group's articles in 2005 and I think it was titled something along the lines of benzene induces a unique form of dysplasia or something like that. And then in more recent 2009 article which we don't have marked -- do you have that article? 02:42 02:43

MR. WILLIAMS: It's right here.

A. Yes.

MR. SCOTT: Let's mark that as Exhibit I just so we have a sticker on it.

(Exhibit No. I was marked.) 02:43

Q. (By Mr. Scott) How did Dr. Irons' 2005 and 2009 articles or reports inform your view on whether benzene causes refractory anemia with ringed sideroblasts?

A. Well, in this particular article, he comments about how they looked at the bone marrows, that they did iron stains on the bone marrows. Let's see if I can find where he discusses that, but I know that he says that. 02:43

He says: Bone marrow aspirate and peripheral blood smears were prepared from fresh tissue 02:44

and evaluated using Wright-Giemsa stained preparations and special stains, including an iron stain.

So, he was doing an iron stain on all of this material.

And then he comments and I have to look to see what page this might be that -- here it is, Page 10 of the article. He says: There was no evidence of increased ringed sideroblasts. 02:44

Q. And was this among a group of people who had a myelodysplastic syndrome and had known and, in some cases, very high benzene exposure? 02:44

A. Yes, according to Dr. Irons, these were his signal cases, as he used that term, meaning that they had unequivocal enormous benzene exposure and abnormal bone marrows. 02:45

Q. Are there -- from your knowledge and review of the scientific literature -- and I want to turn away from RARS, at this point; but myelodysplastic syndromes, you have said that some myelodysplastic syndromes are associated with exposure to benzene? 02:45

A. Yes, I think that's true.

Q. Are there features, clinical features, morphologic features, cytogenetic features, type of features that, sort of thing, of the benzene-caused myelodysplastic syndromes? 02:45

(Mr. Trull enters the deposition room at this time.)

A. Well, I suppose the two best articles that would read on that would be the Ruiz article with his large number of cases, 33 cases that were studied and the Richard Irons article. And the results of those two articles are quite similar. They also are in line with the description that's in the cases seen in the Hayes of benzene study. 02:45

The description is that the bone marrows generally show reduced total cellularity or what we call hypocellularity, that they have abnormal morphology of the red cell precursors, that they have the presence of increased numbers of eosinophils, which are a cell that we see in inflammatory conditions, and that these eosinophils look peculiar. They are granules. They are very unusually colored and large, as we see in certain forms of acute Leukemia. 02:46

And the bone marrow also contains phagocytic cells, histiocytes that are prominent in these bone marrows. And the absence of ringed sideroblasts, for example, in these bone marrows. 02:46

Q. You say histiocytes or phagocytic cells, are those sometimes referred to as -- is that condition sometimes referred to as hemophagocytosis? 02:47

A. Yes.

Q. And the abnormal eosinophils, increased eosinophils and peculiar appearance, morphologic appearance, are those in the peripheral blood or in the bone marrow? 02:47

A. Well, in the case of Leukemias, they can be both in the peripheral blood and bone marrow in certain forms of Leukemia.

In the case of benzene bone marrows that are described, they are confined to the bone marrow. 02:47

Q. And are these sometimes called precursors because they are in the bone marrow?

A. Well, a general statement would be that most of the cells that you see in the bone marrow are precursors to cells that eventually come out and circulate in the 02:48 peripheral blood.

Q. In normal MDS, myelodysplastic syndrome case, is the bone marrow hypercellular, that is, greater cellularity or more cells in the marrow or hypocellular?

A. I think in general, you might find the figure 02:48 that looking at all types of myelodysplasia, perhaps 20 percent are very hypocellular, sometimes referred to as hypocellular myelodysplasia. Many have a normal cellularity, and many have increased cellularity.

Q. Are you familiar with a disorder known as -- or 02:48

referred to as myelodysplastic syndrome/myeloproliferative disorder or sometimes myeloproliferative neoplasm?

A. Yes.

Q. What is that disorder or disorders? 02:49

A. That classification is a relatively new classification by the World Health Organization, and this really came about because what the World Health Organization has been trying to do is to become as specific as it can about a particular diagnosis. For 02:49 example, we had the illness chronic myeloid Leukemia, which, for many years, we considered most of them to have a positive Philadelphia chromosome but also some of them to be missing that chromosome, but we still called them chronic myeloid Leukemia. 02:49

Well, the World Health Organization took the position that only chronic myeloid Leukemia with a Philadelphia chromosome is the real thing and we've got to do something else with these cases of chronic myeloid Leukemia that lack the Philadelphia chromosome. And 02:49 there is another illness called chronic myelomonocytic Leukemia, which is another myeloproliferative disease, which the cause is unknown. And the question was, where are we going to place that.

So, they came up with a category called 02:50

myeloproliferative myelodysplastic syndromes. And the best known in this category to be chronic myelomonocytic Leukemia, what's called atypical CML -- that is CML lacking the Philadelphia chromosome, an unusual illness called juvenile myeloid Leukemia. And eosinophilic Leukemia would be another in this category. 02:50

And a provisional member of this is once called RARS-T. These are illnesses for which they are all myeloproliferative illnesses. They are not myelodysplasia. They are all myeloproliferative diseases. However, they can have funny-looking cells. So, they can have some degree of myelodysplasia; but they are quite different from the illnesses we classify as myelodysplasia. And those illnesses are all thought to be of unknown cause at this time. So, the articles on that subject tell us that the diseases in that category of myelodysplasia, myeloproliferative disease are all of unknown cause. 02:50 02:51

Q. I want to hand you -- I'm going to hand you two things here, one a very poor color print that I have made. 02:51

(Exhibit No. J was marked.)

Q. (By Mr. Williams) Dr. Natelson, I've marked as Exhibit J, two pages out of what I will represent to you as the World Health Organization's 2008 classification of 02:51

tumors of hematopoetic and lymphoid issues. And I'm going to turn to the book -- mine is sort of messed up here so that we can copy it, but can you just confirm that, one, this is, in fact, the 2008 World Health Organization classification book; and second, that the pages I've handed you are, albeit poor, but copies of Pages 85 and 86 from that book? 02:52

A. Yes, I'm glad you're not checking books out of my library. Yes, that's what these are from.

Q. And what is this particular -- what disease or disease entities do these pages deal with, Exhibit J, that I've handed you? 02:52

A. What you've handed me are Pages 85 and 86; and they are referred to as myelodysplastic/myeloproliferative neoplasm, unclassifiable. 02:52

Q. Now, is that the disease entity that -- or entities that you were describing for us a moment ago before I handed you that document?

A. Yes. 02:52

Q. Now, is MDS/MPN, I think WHO calls it, is that a myelodysplastic syndrome?

A. All of these diseases in this category are myeloproliferative disease or neoplasms, whichever term you like; but they may have myelodysplastic features. 02:53

Q. What is the difference for a layperson between MDS or myelodysplastic features and myeloproliferative features?

A. Well, the easiest way to think about it is this way. Myelodysplasia is characterized by what we call ineffective myelopoiesis. What that means is -- a simple example is, if I take a person and inject them with radioactive iron, within about 30 minutes or so, that iron disappears from the circulation. It's gone. It goes right into the bone marrow. 02:53

Now, if I sample the blood over the course of a week, by the time you get out to seven to ten days, all of that iron has reappeared out into the circulating blood; but now it's inside the red cells in the hemoglobin. 02:54

In other words, the bone marrow took that iron, built it into new red blood cells and all of that radioactive label came out circulating. That's effective erythropoiesis.

Now, if I do that same experiment on someone with RARS, I inject them with the same amount of radioactive iron. In the same sort of period of time, it will go right into the bone marrow. Now, if I look to see where that iron is at seven to ten days, sometimes as little as 5 percent of it will be back out and 02:54 02:54

circulating red cells.

What's happening is the iron gets into the red cell precursors and it churns in the bone marrow and the cells are made and die and made and die in the bone marrow and it's ineffective. The production is -- the machinery looks like it's there, but it's not efficient. The cells aren't coming out. That's ineffective erythropoiesis. The same would be true if you're looking at white cells or platelets. The general term is ineffective myelopoiesis. That's a very strong characteristic of all myelodysplastic disorders. 02:54 02:55

When you look at myeloproliferative disorders, like atypical chronic myeloid Leukemia, for example, or chronic myelomonocytic Leukemia, the bone marrow is very efficient. You look in the bone marrow, it's full of white cells. They are coming right out and circulating. So, they don't have this problem. They have -- they have a very proliferative disease. 02:55

So, in myelodysplasia, typically, everything is low. We have what we call cytopenias -- low red cells in the peripheral blood, low numbers of white cells, low numbers of platelets. 02:55

On the other hand, in the myeloproliferative diseases, you may have white counts of 300,000 because the bone marrow is quite efficient. It's 02:55

making these cells, and they are coming out and circulating. And so, that's a major difference between those two illnesses.

Q. We have talked about your opinions and views on whether benzene is causally associated or causes RARS -- refractory anemia ringed sideroblast. What is the evidence as to whether benzene causes myeloproliferative disorders? 02:55

A. Well, to my knowledge, there is none. In other words, this has been looked at by a number of people, particularly in illnesses like chronic myeloid Leukemia and myelomonocytic Leukemia, chronic myelomonocytic Leukemia; and there isn't evidence that those myeloproliferative diseases can be caused by excessive benzene exposure. 02:56

So, the general dogma in hematology would be that myelodysplasia, that category, certain types can be caused by excessive benzene exposure. In fact, the World Health Organization booklet says that.

Myeloproliferative diseases, on the other hand, there isn't evidence that benzene can cause those. 02:56

Q. The same question for this MDS/MPN myelodysplastic syndrome/myeloproliferative disorder or neoplasm, what is the evidence that benzene causes those disorders? 02:57

A. Well, there is none. And, in fact, the reviewers on that, the latest reviews that are perhaps a year or so old tell us the cause of all of those illnesses in that category, the etiology is unknown.

MR. SCOTT: Doctor, that's all I have. Thank you very much. 02:57

EXAMINATION

BY MR. ASHER:

Q. Dr. Doctor, my name is Ross Asher.

Did I hear you correctly earlier to say that myelodysplastic syndrome or myelodysplasia is a term for a classification of a group of diseases? 02:57

A. Yes, it's a classification system that was first proposed around 1982.

Q. So, if someone is diagnosed with myelodysplastic syndrome or myelodysplastic disorder, is that a general diagnosis; or is that a diagnosis of some specific disease? 02:57

A. Well, it's a little of both. It's a general term. It might be, like, akin to saying hepatitis; but there are many forms of hepatitis. It's a general category of bone marrow failure; but there are many, many different forms of myelodysplasia. 02:58

Q. I want to go back and ask just a couple of questions about -- pardon me -- the article that you were 02:58

asked about earlier, Benzene Exposure Refractory Sideroblastic Erythropoiesis: Is There an Association, that article, I believe, was published in the AMERICAN JOURNAL OF MEDICAL SCIENCE?

A. Yes. 02:58

Q. Is the AMERICAN JOURNAL OF MEDICAL SCIENCE a peer-reviewed publication?

A. Yes.

Q. And can you explain for the ladies and gentlemen of the jury what it means for an article to undergo peer review? 02:58

A. Yes, well, this particular journal is one of the oldest journals in the country, medical journals; and what happens is that when you send an article into a journal, they have an internal editorial board. And their people review the article and see if they feel that it has merit. And many times when you send an article into a journal, it will never get out of the journal. In other words, the internal review board turns it down flat. They say it's not of interest to the general public. It's poorly written. We're not even going to bother to send this out to a reviewer not connected with our journal. 02:59 02:59

And ultimately, if they decide it has potential, they will send it out, typically, to three 02:59

reviewers. And, for example, I, just a few weeks ago got an e-mail from a journal called HEMATOLOGICA.

And they said, Would you be willing to review an article for us?

And I said, okay. 03:00

And so, they sent me that article, all electronically.

And what happens is they then gather the comments of the reviewers they send it out to; and if there is a disagreement, they may send it out to a few more reviewers. And then they come to some decision and will send a letter back to you saying what they feel you should do with your article. 03:00

Q. And what's the purpose, generally, of peer review before publication? 03:00

A. Well, it's multiple eyes. In other words, they are sending it out to people who don't necessarily think alike, have different expertise and might find something that's incorrect that another reviewer might gloss over. And so, you're looking for several people to look at a study and see if you feel it has merit. 03:00

Q. And the article we're talking about here that you've written on benzene exposure, that was peer reviewed; is that right?

A. Yes. 03:00

Q. And it was published by that -- by the AMERICAN JOURNAL OF MEDICAL SCIENCE after being peer reviewed; is that right?

A. Yes.

Q. I wasn't quite certain, did you say that when you spoke to Mr. Williams, he told you that your deposition today wasn't for use in any specific case? 03:01

A. Yes, as I recall, the conversation was something; and, of course, I don't have a recording.

But he said that you're going to receive a subpoena, and I want to question you about your article. 03:01

And I said, About my article?

He said, yes.

I said, Well, are we talking about a particular case or -- he said, No, no, I want to question you about your article. 03:01

And I said, Okay. I hadn't received the subpoena at that point, but I said that sounds all right. I'll be willing to do that.

Q. Have you come to find out that you are here today because of a specific case that's going on? 03:01

A. Well, you informed me of that when you called me.

Q. And I want to make sure we clear up one thing that you mentioned earlier. 03:02

Did I ever suggest to you in a telephone call that you should try to avoid this deposition today?

A. Absolutely not.

Q. And did I inform you that I represented a party to the case and we had not designated you as an expert witness and, therefore, I couldn't represent you? 03:02

A. Correct, you said that.

Q. Sir, I think that's all the questions I have for you right now.

FURTHER EXAMINATION 03:02

BY MR. WILLIAMS:

Q. When we originally talked, I informed you that this deposition didn't involve a case that you were an expert in; is that correct?

A. I can't recall the exact language. You said something to the effect -- when I asked you, Is this regarding a case? 03:02

You said something, as best I can say, This is no case -- this has nothing to do with any case you've ever had anything to do with, or something to that effect. 03:02

Q. Fair enough.

Doctor, do you recall one other thing you told me on the phone when I explained that I wanted to discuss your 2007 article dealing with RARS, do you 03:02

recall what you told me?

A. I don't recall.

Q. Do you recall what you told me about -- that you couldn't call it a RARS case without looking at the slide? 03:03

MR. SCOTT: Object to the form.

A. Oh, yes, I said -- I don't remember how we got on that; but I said, if it's a particular case, I said, I would have to look at the marrow slides to be convinced that that was a diagnosis. 03:03

Q. (By Mr. Williams) Doctor, what percentage of ringed sideroblasts do you need to have a RARS diagnosis?

A. Well, that's an interesting question. The typical number given by bodies such as the WHO is 15 percent of all of the red cell precursors of the bone marrow should be ringed sideroblasts. 03:03

Hematologists traditionally don't count cells. We look at it. And many of these cases, there are 60 and 70 percent ringed sideroblasts. It's obvious what they have. It's like looking at an old friend. And I think you would find very few hematologists who would laboriously count whether it's 15 percent, 16 or 17 percent. Some pathologists might; but not too many of them, either. 03:03

So, it's usually a visual diagnosis; but, 03:04

technically, the number is supposed to be 15 percent or greater.

Q. And if there aren't 15 percent ringed sideroblasts present, you couldn't make a diagnosis of RARS; is that correct? 03:04

A. It does not meet the standard of care that this diagnosis requires.

Q. And, Doctor, one final question: Did you receive any type of compensation whatsoever for the writing and drafting and publishing of your 2007 benzene RARS article? 03:04

A. No. In fact, it cost me a few dollars, as I gave you the receipt.

Q. As a matter of fact, this is your invoice --

A. That is my invoice. 03:04

Q. -- that you paid to get a published copy of the book?

A. Yes, most journals will give you a charge per page and a very large charge if you have color prints; and so, it can be very expensive to publish an article these days. 03:04

MR. WILLIAMS: We'd like to mark his invoice. I don't have any further questions. Thank you, Doctor.

(Exhibit No. K was marked.) 03:05

FURTHER EXAMINATION

BY MR. SCOTT:

Q. Dr. Natelson, on this issue of counting ringed sideroblasts, is this one of those issues where practicing clinicians and hematologists, such as yourself, basically don't need a weatherman to know which way the wind blows? 03:05

A. Well, when considered that way, I think in my career, I've probably, personally, looked at at least 7,000 bone marrows more. And so, usually, if I'm looking at a bone marrow, it doesn't take more than a few milliseconds to give me a general idea of what the bone marrow is going to show. 03:05

Now, I will study it for much longer than that, particularly if I'm photographing it to find a good feel to illustrate a point. But usually, to an experienced hematologist, just a short time under the microscope tells you what you need to know. 03:05

Q. And that's an interesting point. Is it accurate to say that even if one were to count sideroblasts, the counting must be done in representative fields from the bone marrow pathology? 03:06

A. Certainly, it's not only the representative fields; but also is the slide preparation proper? There is an art, as well as a science to making a good iron 03:06

stain of a bone marrow. It needs to be a relatively thin film, and it needs to be incubated with the two reagents that you use -- cyanide reagent and a hydrochloric acid reagent, and it needs to be properly incubated and then it needs to be properly counterstained because if you over counterstain it, you may obscure a lot of things there. And if you don't incubate it long enough, you don't get the good blue color. 03:06

So, there is a bit of a science and an art to making this; and I've seen many bone marrow slides which are very thick. And you really can't tell whether there is ringed sideroblasts there or not, and you may have to repeat a stain. 03:07

Q. If staining is done in a way that the stain was negative as a processing artifact, can that affect the count, if you will, of ringed sideroblasts when you observe the slides under the microscope? 03:07

A. Yes, because what happens is you flood the slide with a stain; and sometimes, if there is a little grease on the slide or it's not properly fixed with alcohol, you will get uneven staining. Some areas will be very densely stained. Other areas not well sustained at all. So, you have to look sometimes at multiple slides and you'll find a, quote, good area that looks well sustained with good colors; and that's what you -- 03:07

if I were going to photograph something, that's what I would seek.

Q. Did you bring a copy of your CV today?

A. I didn't. It wasn't asked for. So, I didn't bring it. 03:08

Q. I understand. I neglected to do that myself.

Do you diagnose and treat patients with Leukemia lymphoma, myelodysplastic syndromes essentially every workday of your life?

A. Yes. 03:08

Q. How long have you been doing that?

A. I've been seeing hematology patients exclusively since around 1969.

Q. Do you teach medical students and hematology specifically to medical students? 03:08

A. Yes.

Q. And for how long have you been doing that?

A. Well, I've been in medical education my entire career; and that might involve interns and residents. And I'm a director of one of our residency programs, and 03:08 it might be students of various types.

MR. SCOTT: I believe that's everything I have. Thank you, Doctor.

MR. WILLIAMS: Thank you, Doctor.

MR. ASHER: Whoa. 03:08

FURTHER EXAMINATION

BY MR. ASHER:

Q. Doctor, with regard to this question of 15 percent ringed sideroblasts in order to have a diagnosis of RARS -- 03:09

A. Yes.

Q. -- does that 15 percent count have to come in any particular time? For example, if you have two bone marrow samples taken at different times, an earlier bone marrow sample doesn't show 15 percent but a later one 03:09 shows greater than 15 percent, is there any particular time that 15 percent number has to appear?

A. No. And, of course, an earlier one might have been a poor stain; but, in other words, you would have to look at the case in total. But, typically, 15 percent or 03:09 greater makes a diagnosis along with the other features of the illness.

MR. ASHER: Thank you, sir.

FURTHER EXAMINATION

BY MR. SCOTT: 03:09

Q. Since Ross has asked, now I have to. Do repeated blood transfusions cause the development or observation of ringed sideroblasts?

A. No.

MR. SCOTT: That's all I have. Thank you, 03:09

sir.

THE VIDEOGRAPHER: Going off the record. The time now is 3:09.

(Signature requested.)

CHANGE AND SIGNATURE

PAGE	LINE	CHANGE	REASON
28	7	blast	to Blast Numbers
28	20	myeloleukemia	to myeloid leukemia
30	5	pancitopenia	to pancytopenia
30	22	Haze	to Hayes
32	18	Barry Wild	to Barnes
41	19	led	to lead
53	16	ahe	to have
56	12	myelodysplasia	to morphologic dysplasia
68	16	feel	to field
5	14	BARRY	to BERRY
40	10	pearls	to Pearl's

I, ETHAN A. NATELSON, M.D., have read the foregoing deposition and hereby affix my signature that same is true and correct, except as noted above.

ETHAN A. NATELSON, M.D.

THE STATE OF TEXAS
COUNTY OF Harris

Before me, Marie C. Wyeth, on this day personally appeared ETHAN A. NATELSON, M.D., known to me (or provided to me under oath or through _____) to be the person whose name is subscribed to the foregoing instrument and acknowledged to me that they executed the same for the purposes and consideration therein expressed.

Given under my hand and seal of office this 16th day of Februaray, 2010.

Marie C Wyeth
NOTARY PUBLIC IN AND FOR
THE STATE OF Texas

MARIE C. WYETH
Notary Public, State of Texas
My Commission Expires
January 15, 2012

STATE OF TEXAS:

REPORTER'S CERTIFICATION

ORAL DEPOSITION OF ETHAN A. NATELSON, M.D.

TAKEN ON FEBRUARY 10, 2010

I, Minnie Cadena, Certified Shorthand Reporter in and for the State of Texas, do hereby certify that this deposition transcript is a true record of the testimony given by the witness, ETHAN A. NATELSON, M.D., after said witness was duly sworn by me.

The witness x was / ___ was not requested to review the deposition.

I further certify that I am neither attorney nor counsel for, related to, nor employed by any of the parties to the action in which this testimony was taken. Further, I am not a relative or employee of any attorney of record in this cause, nor do I have a financial interest in the action.

GIVEN under my hand and seal of office on this the 15th day of February, 2010.

Digital Certificate of Authenticity Attached

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