UNITED STATES
COURT OF FEDERAL CLAIMS

THERESA CEDILLO AND MICHAEL CEDILLO, AS PARENTS AND NATURAL GUARDIANS OF MICHELLE CEDILLO,	)	
Petitioners,	)	
v.	)	Docket No.: 98-916V
SECRETARY OF HEALTH AND HUMAN SERVICES,	)	
Respondent.	)	

Pages: 2278 through 2495

Place: Washington, D.C.

Date: June 22, 2007

HERITAGE REPORTING CORPORATION

Official Reporters
1220 L Street, N.W., Suite 600
Washington, D.C. 20005-4018
(202) 628-4888
hrc@concentric.net

IN THE UNITED STATES COURT OF FEDERAL CLAIMS

THERESA CEDILLO AND MICHAEL CEDILLO, AS PARENTS AND NATURAL GUARDIANS OF MICHELLE CEDILLO,	)	
Petitioners,	)	
v.	)	Docket No.: 98-916V
SECRETARY OF HEALTH AND HUMAN SERVICES,	)	
Respondent.	)	

Ceremonial Courtroom
National Courts Building
717 Madison Place NW
Washington, D.C.

Friday,
June 22, 2007

The parties met, pursuant to notice of the Court, at 9:00 a.m.

BEFORE: HONORABLE GEORGE L. HASTINGS, JR.
HONORABLE PATRICIA CAMPBELL-SMITH
HONORABLE DENISE VOWELL
Special Masters

APPEARANCES:

For the Petitioners:

SYLVIA CHIN-CAPLAN, Esquire
KEVIN CONWAY, Esquire
Conway, Homer & Chin-Caplan, P.C.
16 Shawmut Street
Boston, Massachusetts 02116
(617) 695-1990

APPEARANCES: (Cont'd.)

Also for the Petitioners:

CLIFFORD J. SHOEMAKER, Esquire
Shoemaker & Associates
9711 Meadowlark Road
Vienna, Virginia 22812
(703) 281-6395

For the Respondent:

VINCENT J. MATANOSKI, Esquire
TRACI R. PATTON, Esquire
LINDA S. RENZI, Esquire
U.S. Department of Justice
Civil Division
Torts Branch
P.O. Box 146
Ben Franklin Station
Washington, D.C. 20044-0146
(202) 616-4122

C O N T E N T S

P R O C E E D I N G S

(9:00 a.m.)

SPECIAL MASTER HASTINGS: Good morning to all in the courtroom and if there are any of you listening in at home.

We had a technical breakthrough in the last few hours, and we were able to work the system so that we can be on phone conferencing this morning for the testimony of the witness coming in by telephone from England, Dr. Chadwick.

I apologize for the information I gave out yesterday that the phone conferencing wouldn't be available, but I'm glad that it is for those who are able to listen.

With that, we've got Dr. Chadwick on the line. Dr. Chadwick, can you hear me? Dr. Chadwick, can you hear me?

DR. CHADWICK: I can, yes.

SPECIAL MASTER HASTINGS: Yes. This is Special Master Hastings.

DR. CHADWICK: Hi.

SPECIAL MASTER HASTINGS: Hello. Good morning to you.

DR. CHADWICK: Good morning.

SPECIAL MASTER HASTINGS: Or afternoon

perhaps where you are.

DR. CHADWICK: Yes.

SPECIAL MASTER HASTINGS: I'm going to ask you, please. We're going to give you the oath for testifying here. I'm going to ask you to raise your right hand.

Whereupon,

NICHOLAS C. CHADWICK

having been duly sworn, was called as a witness and was examined and testified as follows:

SPECIAL MASTER HASTINGS: All right. Who will be doing the questioning?

MS. PATTON: I will be.

SPECIAL MASTER HASTINGS: Ms. Patton will be doing the initial questioning.

DIRECT EXAMINATION

BY MS. PATTON:

Q Good afternoon, Dr. Chadwick.

A Hi.

Q Can you please state your name for the record?

A Yes. Nicholas Chadwick. Nicholas Charles Chadwick.

Q And do you recall writing a declaration for this case, which is signed on May 23, 2007?

A Yes, I do.

MS. PATTON: For the record, we'll be referring to Respondent's Exhibit QQ, which was filed on May 25, 2007.

BY MS. PATTON:

Q Dr. Chadwick, do you swear under penalty of perjury that the contents in that declaration are true to the best of your knowledge?

A Yes, I do.

Q We're not going to go through the entirety of your declaration, but I'm going to ask you a couple questions about several portions of that declaration that we'd like the Court to pay particular attention to.

A Okay.

Q You stated in there that you began working in Dr. Wakefield's lab at the Royal Free in 1994. Is that right?

A Yes, that's right.

Q And the lab started focusing on samples and testing from autistic patients in 1996?

A Yes. Yes.

Q In your affidavit you state that you were present in the operating room -- I think the operating theater is what it's called over there -- during

collection of gut biopsy material and cerebral spinal fluid. Is that right?

A Yes, that's right. It was an endoscopy suite rather than an operating theater.

Q And what was your role in the collection of the material?

A My role was to take the material, bring it to the lab and process it by extract RNA and then look for evidence of measles RNA.

Q Okay. Did you personally test the gut biopsy samples for measles RNA?

A Yes.

Q What tests did you perform?

A A PCR test, a polymerase chain reaction.

Q What results did you receive from the gut biopsy materials for measles RNA?

A They were all negative.

Q They were always negative?

A Yes. There were a few cases of false positive results, which I used a method to see whether they were real positive results or false positive, and in every case they turned out to be false positive results. Essentially all the samples tested were negative.

Q So when you say you got a positive and it

ends up being a false positive, what further testing or what did you do to determine that those positives were actually false positives?

A Well, we sequenced the products of the PCR reaction and could find out whereabouts the virus came from, and in every case it was a lab strain virus based on the sequence and didn't match up with any known wild-type or vaccine strains.

Q You sequenced wild-type that's in the lab for control or to make sure your testing worked?

A Yes, that's right. It was just to validate any positive samples. If we had a positive sample we would have to sequence it to make sure it was a real positive rather than a false positive.

Q Did you personally test CSF samples from autistic children in the lab?

A Yes, I did. Again, they were all negative. I can't recall how many I tested, but they were definitely negative, the ones I did test.

Q Did you personally test peripheral blood mononuclear cells, the PBMCs?

A Yes, that's right. I tested PBMC samples from the blood of the autistic patients and also cultured some of those blood cells in the lab to enable any measles virus present to replicate and

become detectible, but in every case again the samples proved to be negative.

Q So you personally tested while you were in Dr. Wakefield's lab gut biopsy material, CSF and PBMCs?

A Yes, that's right.

Q And all the results were either negative, or if they were positive it always turned out that they were false positives?

A Yes, that's correct.

Q Did you inform Dr. Wakefield of the negative results?

A Yes. Yes.

Q You state in your affidavit that you sent samples of RNA to Dr. Kawashima.

A Yes, that's right. Dr. Kawashima had been working on the detection of measles virus in a different disease, and Dr. Wakefield thought it would be a good idea to use his methodology to see if any of our samples proved positive using his methods.

Q Dr. Chadwick, what was your role in sending the samples to Dr. Kawashima?

A My role was just to put the samples in test tubes and randomize them, code them and randomize them so that only we would know which samples were which

and Dr. Kawashima wouldn't know which samples he was testing.

Q What were the results of Dr. Kawashima's testing?

A Well, some of the samples we sent over as duplicate samples so if one of them was to come up positive then we would expect the other sample to come up positive as well. In every case where he did have a positive result then the duplicate didn't match that, which led us to question his results or led me to question his results.

When he told us that he had some positive results he sent us the sequencing data back, but the sequencing data matched up with the positive control samples that we sent out to him, which indicated to me that he had contaminated his samples and they were false positive samples.

Q Based on the coding that you had done beforehand, you knew that all of the positives that he was reporting were false positives?

A Yes, that's right. I was pretty sure based on, you know, how I'd coded the samples.

Q Did you tell Dr. Wakefield about the problems with Dr. Kawashima's results?

A Yes, I did.

Q You state in the affidavit that during your time on your Ph.D. research in Dr. Wakefield's lab you only obtained nine positive PCR results for measles. Every time you did that you sequenced them?

A That's correct, yes. We sent it off to a sequencing lab to be sequenced, and the data that came back showed that they were all false positive results.

Q Every positive result you got was a false positive?

A Yes. Yes, apart from the case of the positive control samples which we had, which were a measles infection, a brain disease. We were able to detect measles virus in those cases, so I was confident that the methods were working fine.

Q Towards the end of your affidavit you state that you had reservations about the immunohistochemistry done to detect measles virus, specifically the use of an antibody from Porton Down?

A Yes, that's right. The antibody seemed to cross-react.

Experiments we did in the lab seemed to show that the antibody cross-reacted with bacterial proteins, which I think is an artifact of how the antibody was made, and that led us or led me to think that it may have been cross-reacting with bacteria in

the gut of patients rather than measles virus.

Q Now, that would lead to contamination?

A Well, it would lead to a false positive result. Say for instance if the antibody was binding to something in the guts of these patients, it may well have been a bacteria rather than the measles virus.

Q Okay. Producing the false positives in those?

A Yes, that's correct.

Q You also state in your affidavit that you believe Dr. Wakefield was aware of all of your negative results when he submitted his paper, "Ileal Lymphonodular Hyperplasia, Nonspecific Colitis and Pervasive Developmental Disorder," which was published in 1998 to the *Lancet*.

A Yes, that's correct.

Q You were working at the lab at that time, and you had actually published some articles with Dr. Wakefield on other subjects, hadn't you?

A Yes. Yes.

Q Why isn't your name on the paper I just referenced?

A Well, my name isn't on that because none of my data went into that paper.

There was a manuscript which did use some PCR data I think from Dr. Kawashima's lab, and I asked for my name to be taken off anything that was related to PCR data because I wasn't comfortable with the quality of the data.

Q You specifically asked that your name not be on that paper because of your reservations about the data?

A Yes, that's right.

MS. PATTON: Thank you, Dr. Chadwick. I have no further questions.

THE WITNESS: Thank you.

SPECIAL MASTER HASTINGS: Ms. Chin-Caplan, any questions?

MS. CHIN-CAPLAN: Just a few.

SPECIAL MASTER HASTINGS: Please go ahead.

MS. CHIN-CAPLAN: Thank you.

CROSS-EXAMINATION

BY MS. CHIN-CAPLAN:

Q Good morning, Dr. Chadwick. My name is Sylvia Chin-Caplan, and I represent the Petitioner, Michelle Cedillo, in this case.

A Hi.

Q Hi. You're aware that Dr. Wakefield is not a witness in this case, are you not?

A I'm not aware of that.

Q Are you aware that the Kawashima Lab is also not the lab in question here?

A Well, I don't know the details of the case, to be honest.

Q When you were approached to testify in this matter, what were you asked to do?

A I was asked to provide a statement regarding the work I did for Dr. Wakefield relating to the autistic patients.

Q And did you ask why?

A Sorry. I couldn't hear that last question.

Q Did you ask why?

A Did I ask why? Because it was a case regarding the safety of the vaccine.

Q Now, you testified that you worked with in-situ PCR. Is that it?

A Yes. This was used before any of the autistic work was being undertaken. I did a few months of working on this methodology.

Q In-situ PCR?

A Yes. I did a few months at the beginning of my project with Dr. Wakefield, and I did a few months at the very end as well on in-situ PCR.

Q So this was all on in-situ PCR? Is that

correct?

A The work that was in my thesis relating to autistic patients was using normal PCR, not in-situ PCR. The in-situ PCR work I performed was never written up.

Q I see. So the in-situ PCR is more specific than the regular PCR, isn't it?

A No, that's not the case.

Q It's not?

A No, it's not specific. Because of the methodology it's actually less specific so there's less way of being certain about what is being detected.

Q Okay. Doctor, did you at any time use TaqMan PCR?

A No. TaqMan PCR wasn't really available while I was doing the Ph.D. It was something which came afterwards.

Q I see. Are you aware that the case that we're dealing with involves TaqMan PCR?

A I'm not aware, no. No.

Q Are you aware that the lab that we're dealing with involves the O'Leary Lab in Dublin, Ireland?

A Okay. I've heard of that lab, but I didn't

know that that was the lab that you were using in this case.

Q And you've had no relationship with the Dublin lab, have you?

A No.

Q You have no knowledge of their procedures or the testing that was done there, do you?

A No. I mean, I'm aware of TaqMan PCR, but that's all I know about the O'Leary Lab.

Q And as of the date that you left Dr. Wakefield's lab, you had not utilized TaqMan PCR in an experiment, had you?

A No.

Q Doctor, is there anybody with you?

A No.

Q No? You're by yourself?

A Yes.

MS. CHIN-CAPLAN: Okay. I have no further questions.

SPECIAL MASTER HASTINGS: Any redirect?

MS. PATTON: No, sir.

SPECIAL MASTER HASTINGS: Dr. Chadwick, again this is Special Master Hastings with the Court in Washington. I want to thank you again for taking the time to be with us. You're excused at this time.

THE WITNESS: Okay. Thanks so much.

SPECIAL MASTER HASTINGS: Thank you, sir.

(Witness excused.)

SPECIAL MASTER HASTINGS: So, Mr. Matanoski, we'll be taking Dr. Brent's testimony next?

MR. MATANOSKI: That's correct, sir.

SPECIAL MASTER HASTINGS: All right. Maybe while we're getting the phone out of the way Dr. Brent could take the witness stand.

DR. BRENT: Yes, sir.

(Pause.)

MS. RENZI: Special Master, may I?

SPECIAL MASTER HASTINGS: Yes, please. We have now Dr. Brent in the witness chair, and Ms. Renzi will be doing the examination for the government.

Dr. Brent, I'm going to ask you to raise your right hand.

Whereupon,

JEFFREY BRENT

having been duly sworn, was called as a witness and was examined and testified as follows:

SPECIAL MASTER HASTINGS: All right. Ms. Renzi, when you're ready go ahead.

//

//

DIRECT EXAMINATION

BY MS. RENZI:

Q Good morning, Dr. Brent.

A Good morning, Ms. Renzi.

Q Could you please state your name for the Court?

A Sure. It is Jeffrey Brent, B-R-E-N-T, M.D.

Q And what are your professional titles?

SPECIAL MASTER HASTINGS: Please speak up.

MS. RENZI: Okay. I will speak up.

BY MS. RENZI:

Q What are your professional titles?

A I am presently a full clinical Professor of Pediatrics and Internal Medicine at the University of Colorado Health Sciences Center in Denver.

Q And do you also maintain a private practice?

A Yes. I have a private practice which is a group practice. It's a single specialty practice that deals solely with issues related to medical toxicology. The name of the practice is called Toxicology Associates.

Q And could you briefly go through your education and training?

A Okay. How far back do you want me to go?

Q Start with your undergraduate degree.

A Okay. You may have listened to me long enough to realize my undergraduate was obtained in New York where I went to college and subsequent to that did a Master's and subsequently a Ph.D. in Biochemistry at the Mount Sinai School of Medicine in New York.

Following that I went to Columbia University College of Physicians and Surgeons as a postdoctoral fellow there. After completion of my postdoctoral fellowship I attended medical school at the State University of New York School of Medicine at Buffalo, New York, and then went to Harvard where I served as an intern and subsequently ended up completing my primary residency at Emory University School of Medicine in Atlanta.

Once I graduated from that I moved to Colorado to pursue a subspecialty fellowship in medical toxicology. That was a two-year fellowship. I did that fellowship from 1987 to 1989, and upon completion of the fellowship I got offered a faculty appointment to stay on.

It was a very attractive offer and I stayed on, and I've remained basically in Denver on faculty and in practice ever since.

Q Could you briefly list some of the honors

you have received?

A I could. I mean, you know, they're listed on my curriculum vitae. I assume everybody has a copy. I can give you one or two examples without going into any detail.

It's interesting when you think of honors. There are ones that are the most prestigious and there are the ones that are the most important to you, and they're not always the same.

For example, the one that to me is the most important to me was when I was given the Excellence in Teaching Award from the second year medical students. Not a big thing in the world, but I was touched by that.

Probably the most prestigious was last year I received what's called the Louis Roche Award from the European Association of Poison Control Centers and Clinical Toxicologists. I guess it's the year before last now.

They award the Louis Roche Award to one person each year as an acknowledgement of their contributions in the field, and associated with that I had to go and give what they call a Louis Roche lecture, which is a big lecture that is at a meeting. That was in Berlin.

Q Have you had occasion to deliver to professional groups lectures on toxicology?

A Quite often, yes. That is something that I do quite a bit. I get invited to lecture not infrequently both in the United States and abroad.

I've given multiple lectures -- I think most of them are listed in my curriculum vitae -- on various aspects of toxicology, including mercury toxicity.

Q And what professional organizations and honorary societies are you a member of?

A A whole group of them. The American Academy of Clinical Toxicology, the American College of Medical Toxicology, the American Medical Association, the American College of Occupational Environmental Medicine, European associations. I think that's most of them. There might be one or two others.

Q And do you currently serve as a peer reviewer for any medical journals?

A Yes. Oh, yes.

Q Could you list a few?

A Sure. I end up spending a lot of time being a peer reviewer. I'm senior editor of one journal, so I obviously peer review quite a bit for that, and that's for the journal called *Clinical Toxicology*.

Clinical Toxicology is the largest circulation peer reviewed journal in the world devoted to clinical toxicology.

I also routinely peer review for a number of other toxicology journals plus general medical journals. I review quite a bit for *New England Journal of Medicine*, *Journal of the American Medical Association*, some occupational medicine journals, environmental medicine journals.

Q And you have published over 200 peer reviewed articles relating to toxicology? Is that correct?

A Well, my publication lists over 200 publications. That includes peer reviewed articles, books, book chapters, letters, abstracts and so on, reviews of various kinds.

Q Have you ever received funding from a pharmaceutical company for a speaking engagement?

A I recall back it was in the vicinity -- don't hold me to this year, but I think it was maybe in the vicinity of 1991. It was shortly after I finished my fellowship.

I gave a lecture for which a pharmaceutical company paid me with an honorarium for giving that lecture. I don't recall any subsequent to that.

Q And have you ever received money from a pharmaceutical company for research?

A Back once again in the early 1990s I had some grants when I was a fellow. I had just passed my fellowship. I had a very, very small grant from a pharmaceutical company, which I had a couple of other grants from pharmaceutical companies.

I have not taken a grant -- I have not taken pharmaceutical company research money -- probably in 15 years. However, I was an investigator on an FDA grant. The money came from the FDA for a clinical trial of a new antidote. A pharmaceutical company was sort of my partner in that grant. I was the principal investigator, but they were on the grant as well.

Q And other than your testimony today, have you ever testified as an expert witness in a legal case?

A Yes, I have.

Q Approximately how many times?

A Oh, boy. I don't know. Since graduating from my fellowship in 1989, several dozen times usually.

Q Have you ever testified as an expert witness on behalf of a pharmaceutical company?

A I have.

Q Can you recall the circumstances?

A I probably have over the years at least a half a dozen times. One on behalf of Pfizer Pharmaceuticals with regard to a medication that caused hepatotoxicity and has subsequently been taken off the market called Rezulin.

I gave testimony once on behalf of Merck Pharmaceuticals. Another example, I think probably the most relevant example, is I gave testimony once in a case where the allegation was autism induced by thimerosal.

Q And do you recall the name of that case?

A Yes. That was the Easter case.

Q And were you an expert for the pharmaceutical company or the defendant? For the defendant pharmaceutical company?

A For the defendant, GlaxoSmithKline, yes.

Q And did you testify at a trial in that case?

A No. I testified at deposition in that case. There was ultimately no trial because the case was dismissed on the basis of a Daubert motion.

Q Have you ever testified as a legal expert on behalf of a medical device company?

A Yes, I have.

Q Could you describe that, please?

A Sure. In the early 1990s I was chair of a national panel which was assessing the issues of potential health effects in terms of systemic disease related to silicone breast implants.

There was a lot of concern about it at the time, and we had concluded that the data was very anecdotal and didn't support systemic effects. I think subsequently everybody has come to that same conclusion.

However, during that time period of the 1990s there was a good deal of litigation going on regarding silicone breast implants, and manufacturers came to me and said would you testify regarding your work that you did on silicone breast implants. I said I would, time permitting, and I testified in a number of those trials over the 1990s.

Q I'd like to move on now to your experience. Could you describe your position as a clinical professor at the University of Colorado Health Sciences Center?

A Right. My duties at the University of Colorado Health Sciences Center involve three things. It involves some patient care, it involves teaching, and it involves maintaining my academic activities. Those academic activities are reviewed annually.

The teaching is both my direct teaching in the medical school by way of lectures and other similar forms of teaching and bedside teaching. We have a service which is called the clinical pharmacology and toxicology consultation service where we do consultations regarding adverse effects, toxicology consultations regarding adverse effects of drugs or chemicals, adverse drug reactions, whatever, on people in the hospital.

Those consultations, because it's a teaching hospital, are generally primarily done by the group on the toxicology service, which generally involves probably about five or six people, including a medical toxicology fellow in training, maybe one or two residents, a couple of medical students.

They do the initial assessment and then I round with the patients at the bedside with them and go over their assessment, go over their examination and see how it concurs with my examination, go over the laboratories, and then we discuss a plan of what to do next, what our impressions are, and then the house staff usually writes up a consultation note, which I generally co-sign.

Q And could you describe the nature of your private practice?

A My private practice is Toxicology Associates, and at Toxicology Associates we have three major missions and that is patient care, teaching and research in the area of medical toxicology.

Our patient care component, we actually have two components to the patient care component, an inpatient and an outpatient one. Our inpatient component involves admitting patients directly to our hospital. They're generally admitted directly to us. Most often our hospitalized patients are intensive care unit patients. I do a good deal of intensive care medicine.

These are patients who have been acutely poisoned for one reason or another. It could be a drug overdose. It could be a child with an accidental poisoning. In Denver at this time of the year we treat a lot of rattlesnake bites. A couple of months from now it starts getting a little cooler. We start treating a lot of black widow spider bites. In the winter we treat a lot of carbon monoxide poisoning from heating systems.

We have patients who have adverse drug reactions that can make them very sick, so there's a number of ways that patients can end up coming to our toxicology service and being admitted to our inpatient

service.

We also have an outpatient service, a clinic, and in the clinic we see patients who have concerns about occupational or environmental exposures.

We will sometimes follow up patients that we've seen in the hospital, and we also do a good deal of following workers who are exposed to hazardous material in their work where OSHA mandates that these workers get followed periodically and evaluated, so we do a lot of that as well.

Q Have you ever treated a patient with mercury toxicity?

A Quite a number of times. Yes, I have.

Q Could you describe some of the circumstances in which you've treated a patient?

A Sure. Absolutely.

SPECIAL MASTER HASTINGS: Before we go into that question, let me interrupt.

Just for the benefit of those who may just be coming on line within the last few minutes to listen in on the phone conferencing, I wanted to let you know that right now we have the testimony of Dr. Brent, an expert witness for the Respondent, a toxicologist from the University of Colorado. We have

just gone through his credentials and background.

I wanted to let the folks know that we finished with the testimony of Dr. Chadwick earlier. I told you yesterday the best information we had at that point was we would not be able to put Dr. Chadwick's testimony -- Dr. Chadwick was the witness who was going to be coming in by telephone. We wouldn't be able to put him on the phone conferencing.

It turned out at a last minute breakthrough here we were able to put Dr. Chadwick's testimony on this morning. I apologize to anyone who tuned in after that. He gave very brief testimony, about 15 to 20 minutes. That testimony will be available by downloading the audio from our website or by viewing the transcript on our website.

I apologize to those who missed that testimony, but now we've got Dr. Brent testifying for the government with Ms. Renzi questioning him.

Mr. Renzi, why don't you ask that last question again?

BY MS. RENZI:

Q Could you describe some of the patients you've treated with mercury toxicity?

A Well, mercury toxicity is distinctly unusual to see, so most of the time when we see it it's a very

unusual circumstance.

I've seen some workers who were overexposed to mercury. I have had a patient not too long ago who was a dentist and bought a dental practice from another dentist who was apparently rather sloppy and had spilled mercury from fillings on the floor. It was a rug floor, and apparently there was mercury in the rug.

Now, what this dentist who was my patient did -- it was a woman -- is she not only ran the practice, but she would also clean it. She used the vacuum cleaner on the rug. Never use a vacuum cleaner on a mercury contaminated rug because it vaporizes all the mercury. She developed a neurological syndrome and was found to have very high levels of mercury. We ended up chelating her.

I had a patient who we believe her husband tried to kill her by putting large amounts of liquid mercury in her study in an area where it wouldn't be seen and allowing it to vaporize in the air.

Probably my most colorful patient was a gentleman we took care of -- we actually published the case -- about a year or so ago who had a form of Munchausen syndrome where they like to make themselves sick and get medical care. He injected mercury

intravenously, liquid mercury intravenously, and then came to my hospital.

Q Have you ever treated or examined a child diagnosed with autism?

A Oh, yes.

Q Under what circumstances?

SPECIAL MASTER HASTINGS: Do speak up, Ms. Renzi.

THE WITNESS: Well, under a number of circumstances. One is that autistic children, just like any other child, can end up accidentally overdosing, and in fact it's a little bit more common in autism because they have a tendency towards pica. They have a tendency to put lots of stuff in their mouth.

So we have had patients on our service who were autistic who had overdose on various things. It happens occasionally. It's unusual, but we do see it from time to time.

When all this stuff about mercury toxicity and autism spectrum disorder found its way into the blogosphere and websites we started to get a number of calls from mothers primarily asking about and wanting to know if their child should be chelated with a mercury toxic. We've seen a number of those as well.

BY MS. RENZI:

Q I want to move on to your opinions today. Do you have an opinion whether Michelle Cedillo's autism is causally related to the receipt of thimerosal-containing vaccines in conjunction with an MMR vaccine?

A Yes, I do have an opinion about that.

Q What is that?

A Well, I've looked at the medical records quite extensively. I've reviewed the literature in a great deal of detail, and I think it's clear there's no relationship between thimerosal administration and the development of autism or ASD.

Q And do you have an opinion whether it is more likely than not that the thimerosal-containing vaccines that Michelle Cedillo received caused an immune suppression that was ongoing at the time she received her MMR vaccine?

A There's absolutely no evidence that I saw that would suggest that thimerosal in the doses administered in vaccines would cause immunosuppression.

Q Doctor, you discussed in your credentials that you're a medical toxicologist. Could you just describe medical toxicology and how that differs from

toxicology?

A Sure, I would be glad to.

SPECIAL MASTER HASTINGS: Now, we just got a slide on the screen so let me interrupt again.

It looks like we've got a set of slides that Dr. Brent is going to be showing, and we have a paper copy of those slides so let's mark that paper copy as Respondent's Trial Exhibit No. 17.

We've just put on the screen page 1 of that presentation, so go ahead, Dr. Brent.

THE WITNESS: Sure. Well, it's important before I tell you what a medical toxicologist is, it's important to understand what a toxicologist is.

Toxicology is simply the science of the adverse effects of chemical substances on living systems. There's no formal requirement to being called a toxicologist. Anybody can tell you I've studied the stuff and therefore, you know, I'm a toxicologist.

In contrast, the use of the term medical toxicology is a specific term that has attached to it a whole series of very formal and official requirements, and that comes from the fact that in medicine we have a number of specialties -- you know, we have pediatrics, internal medicine, surgery, so on,

radiology -- and a number of subspecialties under those specialties, and all of those, all of the recognized specialties and subspecialties, are under the purview of what's called the American Board of Medical Specialties.

Medical toxicology is a subspecialty. It's a recognized subspecialty by the American Board of Medical Specialties, and therefore to call yourself a medical toxicologist you have to complete their requirements and get certified as a medical toxicologist, much like if you were going to call yourself a cardiologist or if you were going to call yourself a thoracic surgeon. You know, you'd have specific requirements you'd have to meet under ABMS.

For medical toxicology you have to complete a primary residency in a clinical field. Following that you do a two-year full-time medical toxicology subspecialty fellowship in an accredited program after which you are then eligible to take the medical toxicology certifying examination, and if you successfully complete that certifying examination then you are certified as a subspecialty, a board certified medical toxicologist.

BY MS. RENZI:

Q And you are one of approximately 250 board

certified medical toxicologists in the United States?

A Yes. It's fascinating. You know, as interesting as this field is, there's a very small number of us that are actually medical toxicologists. About 250 I think, 260 certified ones in the United States today.

Q Dr. Brent, is it your understanding of this case that the receipt of thimerosal-containing vaccines by Michelle Cedillo caused an immunosuppression that was ongoing at the time she received her MMR vaccine?

A No. I think there's no evidence to support that.

Q Okay. We'll move on to Slide 2. What is thimerosal?

A Thimerosal is a preservative. It was a preservative that was in vaccines and still is in some vaccines and other medications that are given to patients. It's been widely used as a pharmaceutical since the 1920s.

In 1931, Powell and Jamieson published a major study, which for its time was a state-of-the-art safety study, which established its safety based on current standards, and it continued to be used.

Actually its use blossomed incredibly during

World War II because what happened during World War II is the military surgeons learned that where there is penetrating trauma associated with blood loss, i.e., gunshot wounds, that there would be a significant beneficial effect on outcome, saved lives, if the blood volume that was lost from bleeding was aggressively replaced with blood plasma.

The blood plasma was preserved with thimerosal, a great deal of use of very, very large quantities of thimerosal during that period, with clearly an excellent safety profile.

Q And how is thimerosal different from ethyl mercury?

A There's a very important difference between thimerosal and ethyl mercury.

Q And we're on Slide 3 now.

A What you can see, if I may just switch around here for a minute. I'll try to bring the mic over. What you can see here on the screen is the thimerosal molecule. Thimerosal is chemically ethyl mercury thiosalicylate.

Now, here you see this Hg atom. That's a mercury atom. You see it's right here in the middle of the molecule. This part of the molecule to the left is the thiosalicylate part of the molecule, and

this part to the right is the ethyl mercury part of the molecule.

As soon as this gets into the body, this bond, which is a relatively weak bond, breaks and hence you end up simply with ethyl mercury as opposed to the whole thimerosal molecule, so thimerosal becomes ethyl mercury plus thiosalicylate.

There's probably even some disassociation of this bond in the vial before it even gets to the body, so clearly ethyl mercury is a very different molecule from thimerosal.

Q Doctor, on page 3 of Dr. Aposhian's report, and that's Petitioners' Exhibit 55, he states that it is an enigma that thimerosal was included in childhood vaccines, and I'll quote, "because there is no bona fide evidence for either thimerosal's presumed bacteria static activity or presumed safety."

Have you read that?

A Yes. Yes, I have read that.

Q There's also a footnote cited by Dr. Aposhian that relies on two government rulings for that statement, and I'd like to show those.

A Right.

Q The first one is a 1982 FDA ruling that's 47 Federal Register 436. Have you read this ruling?

A Well, actually, Ms. Renzi, it wasn't a ruling. It was a notice of proposed rulemaking and request for comments, and I have read it, yes.

MS. RENZI: And I also have passed out a copy to the Court and to Petitioners' counsel of the actual rulings cited by Dr. Aposhian.

SPECIAL MASTER HASTINGS: Right.

MS. RENZI: I think that would be Exhibit 18.

SPECIAL MASTER HASTINGS: Let's make that Respondent's Trial Exhibit 18.

BY MS. RENZI:

Q I'm sorry, Dr. Brent. Please continue.

A Yes, I have read it, and what it was was an assessment by an FDA panel of the use of a series of mercurial compounds as over-the-counter sort of disinfectants.

We probably all remember growing up that we've had merthiolate put on our wounds. Thimerosal. There were a whole series of these organic mercurial disinfectants, and the panel that was assessing the safety and efficacy of those disinfectants had expressed three areas of concern.

One is that if you in an unregulated fashion just pour all the stuff directly on a wound -- you

know, you buy it over the counter. You just pour it on the wound. You can get a very high concentration on the wound, and therefore you can get a concentration that could be potentially tissue toxic.

The second concern was that wounds have associated with them some blood and pus and so on, and they cited data that shows that thimerosal loses its efficacy as a bacteria static agent when it comes in contact with pus and therefore may not be a good thing to use on a wound.

The third concern they expressed was one of potential allergy.

Q Is this proposed rule in any way relevant to demonstrate the doses of thimerosal contained in thimerosal-containing vaccines are unsafe?

A No. No. It just dealt with that unique circumstance of putting it on. You're buying it over-the-counter and just pouring it on wounds.

It had nothing to do with its potential use as a preservative in vaccines where these various concerns wouldn't apply.

Q And is it relevant to demonstrate that the doses of thimerosal contained in thimerosal-containing vaccines cause immunosuppression?

A No. There's nothing about that.

MS. RENZI: The second ruling that Dr. Aposhian refers to us 21 C.F.R. 310.545. We can pull that up on the screen as Slide 4, and I've also passed out the actual ruling to the Court and Petitioners' counsel

SPECIAL MASTER HASTINGS: So let's mark that as Respondent's Trial Exhibit No. 19.

BY MS. RENZI:

Q And are you familiar with this ruling?

A I am.

Q Could you describe it, please?

A Sure. Thimerosal, like so many substances that have been sort of used for many, many, many years since the FDA evolved, ended up being sort of grandfathered in and was used, did not go through the typical new drug application process which right now is a very, very complex process that the FDA requires of new drugs to certify that they're appropriately safe and effective for use.

What they did is they listed here approximately 700 substances that had been used medicinally over the years and had just sort of ended up going through this grandfather process of being used without the FDA doing a formal assessment of their safety.

Yes, thimerosal was on that list. A number of interesting substances were on that list if you look. For example, aspirin is on that list; lidocaine, which you might get if you go to a dentist and get an injection to numb your gums; honey in cough syrup, in cough drops is on that list. I was very disappointed to see caffeine was on the list. I maybe wonder if I should give up Starbucks.

The calcium salts which we give now to women particularly who have bone loss to prevent that from happening; the iron salts that we give to treat iron deficiency anemia, or pregnant women very often need iron salt; codeine. Almost all the vitamins in your daily vitamin pill are on that list.

We could go on quite a bit with what's on that list. You'll find wheat germ on that list, garlic and thimerosal.

Q Is this regulation in any way relevant to demonstrate that the doses of thimerosal and thimerosal-containing vaccine are unsafe?

A There's nothing in this regulation that says that.

Q Or that they cause autism?

A No. There's nothing that says that.

Q As a medical toxicologist, how do you

determine whether a person's exposure to a certain chemical has caused a particular outcome?

A Well, in medical toxicology we have a very formal set of criteria that we go through to determine when we see a patient whether a chemical to which the patient was exposed may have caused the condition that we're treating or that that patient has.

Although it's rather a complicated formalism, it can be really boiled down to three very basic and simple steps.

SPECIAL MASTER HASTINGS: We've got Slide 5 on the screen now?

MS. RENZI: Yes.

SPECIAL MASTER HASTINGS: Go ahead.

THE WITNESS: We just ask three simple questions, and the first and very important one is what was the patient exposed to. I have to know what chemicals the patient was exposed to to know whether that chemical caused the adverse effects. To what was the patient exposed?

Then we ask the question can that exposure to that chemical under any circumstance cause that patient's disease. I put there, and I hope I've got this right. I believe that's your legal concept of general causation.

If the answer is no, that this chemical is not associated with that disease, then we really don't have to look any further. If the answer is yes, however, then the next question becomes did that chemical in this particular patient under these circumstances cause this disease.

In other words, did the patient get a sufficient dose of the chemical under the right circumstances that's been shown to be associated with that disease, and I think you call that -- correct me if I'm wrong -- specific causation.

We always tell students all you have to remember is three words: what, can, did. That embodies this formalism, which if you apply it it can be a quite complex exercise, but this is essentially the formalism that you have to go through to reach conclusions about whether a chemical can cause a disease in general and whether it may happen in a particular patient.

BY MS. RENZI:

Q I'd like to move on now to in vitro studies. Doctor, what is an in vitro study? We're going to pull up Slide No. 6.

A We talk about two different kinds of studies, and they are referred in the scientific

literature to in vitro studies and in vivo studies. An in vivo study or an in life study is a study that is done in an intact animal or an intact human being.

On the other hand, many scientific studies are done in the laboratory where we might work with just cells that are taken from an animal or cells that are taken from a human being, grown typically in what's called a petri dish, and treated in some way under experimental conditions. That's an in vitro study. That's an in vitro study.

Q And if a chemical causes an adverse reaction in vitro can you extrapolate that the same results will occur in a human? We'll turn to Slide 7.

A Absolutely not. I'd like to make a couple of points. Actually, if we could go back to Slide 6 for a minute?

It's important to realize that when you have some cells growing, and I'll show you some pictures of this in a bit. When you have some cells growing in a petri dish in the laboratory they are in such a dramatically different environment than when they are in a whole animal or a whole human that they become highly susceptible to all kinds of perturbations and to all kinds of insults that would really never happen when all the defenses that are present in the intact

animal or the intact human are there.

Now we can go to the next slide. Let's take, for example, so we don't get too abstract, let's take mercurial compounds like ethyl mercury. If you were to do an experiment where you just take some cells from an animal and grow them in a petri dish and then put ethyl mercury on them, that is completely different from administering ethyl mercury to an intact animal.

Because when the cells are in an intact animal there are all kinds of protective systems that the body has against foreign substances. In the case of mercury compounds, for example, there's a protein called metallothionein which binds and inactivates mercury. There's glutathione which inactivates mercury. There's cysteine which inactivates mercury. There's a variety of other proteins to which mercury binds and is inactivated.

If you look at the mercury, organic mercury like ethyl mercury in the blood which is going out to the tissues, almost all of it is in red blood cells. Those red blood cells aren't present when you just put the ethyl mercury on the cells.

So for that reason the cells become so vulnerable and things that could kill cells in vitro

at very low levels are harmless in vivo. Water. If you put too much water on the cells you will kill them.

The in vitro environment is a highly vulnerable environment. Cells are very susceptible in ways that they would not be in vivo, so you can never make the assumption that affects you see in vitro occur in vivo.

I was here actually when Dr. Aposhian testified about that, and he himself said if you just show in vitro results nobody will believe that it occurs unless you can show it in an intact animal.

Q And has the IOM commented on the use of in vitro studies?

A As a matter of fact they have specifically even in this context. We see here the 2004 IOM report about thimerosal and vaccines, and it discusses the various in vitro studies.

As you can see, they say, "Demonstration of an adverse effect of mercury in vitro does not readily translate into a physiologic argument." I think this is a well accepted concept in science.

MS. RENZI: And that's Respondent's Exhibit JJ at page 140.

SPECIAL MASTER HASTINGS: Thank you.

BY MS. RENZI:

Q Are in vitro studies ever useful?

A Oh, yes. They're used all the time.

Q When are they useful?

A Well, they're useful in a number of circumstances. Number one, they're useful for what we call hypothesis generation.

If I want to know if a compound causes some potential effect before I go to the very large expense of an animal study, for example, I might want to see what happens in vitro. If it doesn't do anything in vitro it's not going to happen in the animal.

If I know there is an effect in a human, let's say, or in an animal and I want to study what happens on the subcellular level I can do that by studying the cells in vitro, but you can never say that's exactly what's happening in the animal, in the animal or the human, until you test the animal or the human.

Q Both Drs. Aposhian and Byers rely on in vitro studies to form their opinions that thimerosal-containing vaccines cause immune suppression.

Specifically they rely on two studies that I'd like to discuss with you now. One is the Goth study, which is Petitioners' Exhibit 55 at Q, and the

other one is the Agrawal study, which is Petitioners' Exhibit 55 at Tab A.

In your opinion, is it reliable science to extrapolate the results of these studies to conclude that immunosuppression will occur in humans following the receipt of thimerosal-containing vaccines?

A I think there's no reasonable way anybody could conclude from the Goth and Agrawal studies that the thimerosal from the vaccine would cause immunosuppression.

Q We have the Goth study up on the screen as Slide 8. Could you summarize the Goth study, please?

A Sure. It's an in vitro study, and it studied a rare cell type in mice called the dendritic cell. The dendritic cell plays a role in the immunological response. They presented some data with ethyl mercury and some data with thimerosal, but really most of the meat of their experiments were done with thimerosal.

Now, I'm not exactly sure why they did it with thimerosal because if you'll recall cells in the body are not exposed to thimerosal. They're exposed to ethyl mercury following a thimerosal injection. Thimerosal disassociates very quickly into ethyl mercury.

So they were looking at effects of thimerosal, and we don't know to what extent, if any, any of this translates into what would happen with ethyl mercury. What they primarily studied were some calcium influxes, which are part of the physiology of these dendritic cells.

Q Dr. Aposhian testified that he found this study compelling because the concentrations of thimerosal that were used in this experiment was almost equal to the concentration of thimerosal used in thimerosal-containing vaccines. Is that correct?

A No. That is absolutely wrong.

Q Is the 100 nanomolars of thimerosal used in the Goth study equivalent to the amount of thimerosal that these cells would have been exposed to following the administration of the thimerosal-containing vaccine?

A Well, first of all you have to back up and realize that following the administration of a thimerosal-containing vaccine these cells would not be exposed to any thimerosal at all. They would be exposed to ethyl mercury, a different compound.

But let's put that part aside for a minute. You know, we have to look at what the cells would actually experience following the administration of

the vaccine, the dose that they would get.

Now, the Goth study reported effects of about 100 nanomolars when thimerosal was in the medium in which the cells were incubated. Forgetting for a minute that in the blood there is no thimerosal, let's just put that aside. That amount, however, would be equivalent to a mercury concentration of about 20 micrograms per liter. We convert 100 nanomolars over to 20 micrograms per liter.

Now, it's critically important to realize that we're talking about here's an example of how dramatically different an in vitro and an in vivo study can be. In the body when the cells are exposed to mercury for a cell to be exposed to mercury the mercury has to be free and available to interact with that cell.

Now let me show you. We go to the next slide, the little diagram.

Q And this is Slide 10.

A Here we have an example. Here we have a picture of how cells experience substances that are in the blood, and what you can see is that we have the blood vessel and the blood is in the blood vessel. The blood contains two things. It contains plasma and cells. So we have the plasma, and we're not showing

here red blood cells.

Now, here is the tissue. Tissues lie outside of the blood vessels. So material from the blood diffuses in and out of the tissues through these little pores in the blood vessels, and if they're small enough to get through these pores it will go through and interact with the cells. This is, for example, how cells would experience ethyl mercury if they were exposed to ethyl mercury, if there's ethyl mercury in the blood.

Now let's look at what happens when there's ethyl mercury in the blood. We know --

SPECIAL MASTER HASTINGS: Now we've gone to Slide No. 11.

THE WITNESS: We know that for organomercurials, greater than 90 percent of the organomercurial is actually in the red blood cell. We see here we have most of the mercury here in the red blood cells. Ten percent would be in the plasma.

A lot of that 10 percent, by the way, and I'm going to put this aside for a minute, but a lot of that 10 percent would be bound to these proteins we talked about, so the amount that's free and that can get through these pores is probably a much smaller percentage.

Let's just use that 10 percent figure worst case scenario. So what we see of the total mercury in the blood, only this fraction of less than 10 percent is actually free to interact with the cells.

Thus, when the Goth study has a mercury concentration of 20 micrograms per liter from the thimerosal in the medium and so the cells were directly exposed to 20 micrograms per liter, that's equivalent to 20 micrograms per liter in the plasma.

In order to get 20 micrograms per liter in the plasma, we need a whole blood level of 200 micrograms per liter because 90 percent of it is in the red cells. Two hundred micrograms per liter is an incredibly high blood level. Most people in this country are walking around with blood mercury levels less than five micrograms per liter.

If you look at the Vacikero data after vaccination, total blood levels are one to 1.6 micrograms per liter, and here we have an exposure essentially equivalent to 200 micrograms per liter.

BY MS. RENZI:

Q Is this study scientifically reliable to determine what will happen in humans following the receipt of the thimerosal-containing vaccine?

A No. No, of course not. First of all --

Q And we're on Slide 12 now.

A First of all, they used thimerosal, and these cells aren't even exposed to thimerosal in the body. As we just saw, the concentrations that they used were unrealistically high. You never get these kinds of concentrations from vaccines.

It's also important to remember that let's just put all that aside. Let's just put all that aside and say yes, they used ethyl mercury. They used reasonable doses. Let's even say that. This study still says nothing about the duration of effect.

You would expect that any effects they saw would happen while the ethyl mercury was there and then would go away once the ethyl mercury was gone. I mean, you wouldn't expect anything they reported to be a long-lasting or clinically significant effect.

Now, I looked at Michelle Cedillo's medical records. Just as an example of the case here, her last thimerosal exposure was approximately nine months prior to receiving her MMR. Now, thimerosal in the blood has about a eight day half-life, so that thimerosal within about a month is essentially gone or five weeks essentially gone.

So this thimerosal could not possibly have been exerting any kind of effect nine months hence

when she got her MMR vaccination.

Q Drs. Byers and Aposhian also rely on the Agrawal study, and I'd like to go over that as well.

A Sure.

Q That's Slide No. 13. Could you describe the Agrawal study?

A The Agrawal study was in many ways similar to the Goth study. It also studied dendritic cells in vitro, but these were human dendritic cells. They too, like Goth, studied thimerosal, but not ethyl mercury.

They found that at 50 nanomolars thimerosal there was a shift in dendritic cell function towards what we call a TH2 or a pro antibody production and anti-inflammatory posture of the immune system. They saw this at 50 nanomolars. They did not see this when they went down to 10 nanomolars thimerosal.

Q And like with the Goth study, is the 50 nanomolars of thimerosal that was used in Agrawal equivalent to the amount of thimerosal that these types of cells would have been exposed to following the administration of a thimerosal-containing vaccine?

A No. It's exactly the same thing. First of all, they used thimerosal, and these cells would never be exposed to thimerosal, but let's just put that

matter aside for a minute.

The simple math tells us that 50 nanomolars of thimerosal is equivalent to a blood mercury level of 10 micrograms per liter. Now, once again this is not whole blood. There's no red cells, so it's all pure 10 micrograms per liter in the medium, just like 10 micrograms per liter in the plasma.

In order to get the 10 micrograms per liter in the plasma you'd have to get a whole blood mercury level of 100 micrograms per liter or actually probably more for any interaction at this level in the cells, so clearly these cells were overdosed with thimerosal.

Q And is this study scientifically reliable to extrapolate what will happen in humans following receipt of a thimerosal-containing vaccine?

A No. That would be a tremendous leap of faith. First of all, it's an in vitro study so you can never conclude that this is what is going to happen in humans for all the reasons that we talked about.

Secondly, once again they exposed these cells to ethyl mercury. That's not even the right substance.

Q Do you mean thimerosal?

A Yes, to thimerosal. That's not even the

right substance. Thank you.

You know, additionally they studied dendritic cells from normal individuals, not ones with ASD. They did not study anything about the response of these cells to measles virus. They did not study anything, for that matter, about ASD.

Like the Goth study, there's no implications in this study about any long-lasting effect so here, for example, once again to take us back down to reality to the case that we're discussing here, there's no reason to think even if these results applied that they would possibly be applicable at the time that Michelle Cedillo received her MMR vaccine.

Q Are in vitro animal studies scientifically appropriate to extrapolate what will happen in humans?

A No. You can never conclude from an animal study that exactly the same thing will happen with humans. You could never get a drug approved through the FDA just on the basis of animal studies because if you want to know what happens in humans you have to study humans.

Animal studies once again are very good for hypothesis generation to see what happens and to ask the question does it happen in humans, but the scientific landscape is too replete with examples

where results in animals, even primates, don't translate into what happens in humans.

I put a couple of examples here, the famous saccharin example that caused a great deal of stir a number of years ago where rats were getting bladder cancer from saccharin and there was great concern because that was all the diabetics had to avoid sugar at the time. It turns out that doesn't happen in humans. There's no relationship.

You know, everybody here I'm sure in this courtroom takes Tylenol from time to time. It's a very safe drug. Just a very tiny dose of Tylenol, a subtherapeutic dose of Tylenol, is actually lethal to cats.

I could just go on forever about these various examples, but I won't. The bottom line is you can never infer human causation only by animal studies.

Q And is there any evidence that thimerosal in the doses contained in thimerosal-containing vaccines adversely affect immunological function in humans?

A There's not a single study. I believe there's already been testimony here from Dr. Aposhian that there's not a single study that would suggest or that demonstrates that the dose of thimerosal in

vaccine causes adverse effects on the immune system in humans.

Q And is there any evidence that Michelle Cedillo's immune system was adversely affected by receipt of thimerosal-containing vaccines?

A No. If we go back to looking at the timing of her vaccination, between the time of her last thimerosal-containing vaccine before the MMR, the time she received her MMR, that was the time period of about nine months between March of 1995 when she got vaccinated with a thimerosal-containing vaccine to December when she got her MMR.

There's nothing in the medical records that suggests that she was immunosuppressed, that she had increased infections, doctor visits for infections during that time period. There's no indication that she was immunosuppressed, nor would you expect her to be.

Q Doctor, I'd like to move on to dose.

A Okay.

Q As a medical toxicologist, is it possible to assess the toxicity of a substance without considering dose?

A No, absolutely not. Dose is the most fundamental concept that we deal with as a medical

toxicologist.

I know there's been discussion about dose here earlier. I was here for some of that discussion. I think there may have been some confusion about the importance of dose so I'd like to just say a couple of words about this.

You know, this concept really goes back to Paracelsus and the famous saying, "Poison is everything. Nothing is without poison." The dosage makes it either a poison or a remedy. He was actually talking about mercury compound at the time.

SPECIAL MASTER HASTINGS: We're on Slide 19 now. Go ahead.

THE WITNESS: And as you see here on Slide 20, the bottom line we take from Paracelsus and is still quoted in every toxicology textbook today as a fundamental principle is that there is no such thing as a poisonous substance. There are only poisonous doses.

There is no substance that at low enough doses will not hurt you, and there is no substance that at high enough doses can be toxic. Water. I've had patients die from water, from drinking too much water. Psychogenic polydipsia it's called.

Almost any medication which can be very

beneficial at certain doses, if you get the high doses obviously as a medical toxicologist I can tell you can cause significant adverse effects.

We think of things like cyanide as being a pretty dangerous molecule, but in fact the bad news is that as we're sitting here today we are breathing in a couple molecules of cyanide with every breath we take, but it's such low doses that it absolutely can't hurt you. The same is true of mercury or virtually any other substance.

BY MS. RENZI:

Q And this principle is accepted by the scientific community? Is that correct?

A This principle is accepted as the most fundamental principle of toxicology by the scientific community.

Here you have a book called *Casarett & Doull*. This was a book, by the way, that was endorsed by Dr. Aposhian. It's probably the most widely used basic scientific text in the world, and if you just go to one of the first chapters, Principles of Toxicology, you see here that they point this out very clearly.

"One could define a poison as any agent capable of producing a deleterious response in a

biological system, seriously injuring function or producing death. This is not, however, a useful working definition for the very simple reason that virtually every known chemical has the potential to produce injury or death if it is present in a sufficient amount.

"Paracelsus phrased this when he noted, 'What is there that is not a poison? All things are poison, and nothing is without poison.' Solely the dose determines that the thing is not a poison."

If you go further in that chapter, Principles of Toxicology, you see once again this is emphasized. "The characteristics of exposure and the spectrum of effects come together in a correlative relationship customarily referred to as the dose/response relationship. This relationship is the most fundamental and pervasive concept in toxicology. Indeed, an understanding of this relationship is essential to the study of toxic materials."

Now, I know there's been testimony here that dose is an outmoded concept, but I think that testimony is probably incorrect in terms of the mainstream thinking in toxicology.

SPECIAL MASTER HASTINGS: Now, for the record here I note that Dr. Brent has just read a

couple excerpts from the toxicology textbook that he mentioned in his slides and in his testimony.

You've given us a copy, a paper copy, of those excerpts. Let's mark that as Respondent's Trial Exhibit No. 20.

Go ahead, Ms. Renzi.

BY MS. RENZI:

Q Doctor, I know you have one more example of the fundamental concept.

A Yes. Let me show you one more very important example, and you'll see why it's an important example in a minute.

This is a well respected text on toxicology by Sullivan and Krieger, and I want to draw your attention to the chapter called Principles of Toxicology.

SPECIAL MASTER HASTINGS: So now this is going to be page 3 of our Trial Exhibit No. 20.

THE WITNESS: And the senior author of that chapter, as you notice there, is Dr. Glen Sipes. Let me just point out what Dr. Sipes has to say about dose.

"One of the most important concepts in toxicology is the dose/response relationship. The underlying premise is that any compound can be toxic

if it is encountered in large enough doses. No matter what the compound's potency or how little compound is necessary to produce an effect, its respected toxic dose threshold must be surpassed to produce toxicity."

Now, that chapter was written, as you saw, by Glen Sipes. Glen Sipes is Professor of Medicine in the Department of Pharmacology at the University of Arizona, which is Dr. Aposhian's institution, and is actually head of Pharmacology and Toxicology there.

And, as a matter of fact, if you look at the Sullivan book, John Sullivan, the senior editor of the book, is a dean at the University of Arizona.

BY MS. RENZI:

Q To discuss more about those, Dr. Aposhian's report contained several examples of mercury toxicity in humans, and I'd like to pull up Slide 24. We have a comparison chart.

Can any comparison be drawn from these case reports about the toxicity of low doses of ethyl mercury in thimerosal-containing vaccines?

A No. No, clearly not. It's a very profound chart that I think makes the point clearly. These are the cases that were cited by Dr. Aposhian in his report where there was information about dose or exposure. It's basically three papers, Opitz,

Nierenberg and Fagan.

The Opitz paper, that was a totally different kind of mercury. It dealt with elemental mercury vapor, and, yes, there was toxicity. The calculated blood level that this person has from that exposure was almost 500,000 micrograms per liter.

Now, a typical blood level we see in the United States is one, two, three, maybe five micrograms per liter depending on how much seafood you eat. It could be 10 if you're a big sushi eater. This is almost 500,000 micrograms per liter, and it's elemental mercury vapor. Clearly this has nothing to do with very low dose exposures to thimerosal or ethyl mercury.

The Nierenberg paper is a case report about the chemistry professor at Dartmouth, which I think everybody here has heard about. She was using a very scary form of mercury that has nothing to do with anything in this case called dimethyl mercury, and her dose was over a million micrograms of mercury. A million micrograms. Look at her blood level. Almost 150,000 micrograms per liter.

The next one that Dr. Aposhian cited was the Fagan report where thimerosal at high concentrations was repeatedly applied to an individual's what's

called amphalocele, part of the remnant of the umbilical cord. We don't know the dose, but we know the blood level, which gives an assessment of those, and here too -- look at this -- over 1,000 micrograms per liter.

Now, by contrast -- by contrast -- if we look at the Vacikero data on vaccination where individuals got up to 62.5 micrograms of mercury, this gives blood levels in the one to 1.6 micrograms per liter range.

Clearly here we're seeing that the dosage to cause these adverse effects are overwhelmingly higher than anything that can possibly occur related to vaccination.

Q Dr. Brent, what are the different species of mercury?

A There are certainly different species of mercury. There are many different kinds of mercury, and it's important to remember that they are all toxicologically different.

Here we have another quote from that *Casarett & Doull* book. It says, "No other metals better illustrate the diversity of effect caused by different chemical species than does mercury." That is true. The different forms of mercury have very,

very different chemicals.

In fact, I think there's already been testimony by Dr. Aposhian in that regard as well. I believe he agreed with that.

Q And which type of mercury exposure has been the most extensively studied by scientists?

A It depends on the timeframe that you're talking about. In the past it was probably mercury vapor and organic mercury because of industrial exposures. More recently it's probably been methyl mercury.

Q And why is that?

A The reason for that is because of the fact that we all get significant exposures to methyl mercury via our diet through seafood. As physicians we're always telling our patients back off on the red meat, eat more seafood, and yet seafood is the source of methyl mercury.

So it's important to remember that when we talk about mercury compounds they're all different. There is the organic. We divide them into two major categories, the organic and the inorganic. The inorganic can be mercury vapor or mercury salts.

There are a number of different organic mercuries. One of them is methyl mercury, which is

the kind that you'd find in seafood, and I think there has been some discussion here about Minamata disease where the fish in Minamata Bay in Japan became highly contaminated because of industrial release, became highly contaminated with methyl mercury.

The individuals that were eating off those fish -- there were lots of fishermen families -- got very, very high doses of methyl mercury, and that caused the condition called Minamata's disease. It primarily affected individuals who were in utero at the time of the exposure. That's methyl mercury.

It's very important to remember that methyl mercury is a different compound from ethyl mercury, and here you see an example of the significance of the difference between methyl mercury and ethyl mercury.

Why is methyl mercury called methyl mercury? Let me point this out. Here you see the structure of methyl mercury, and it is a carbon and three hydrogens, and that is what we refer to chemically as a methyl group, so it is a methyl group attached to a mercury atom, so it is methyl mercury.

On the other hand, where we have a carbon and three hydrogens and then a carbon and two hydrogens, that's what we call an ethyl group. So we have an ethyl group attached to a mercury atom. That

is what we call ethyl mercury. This can have unbelievable consequences in terms of the differences in the properties of the compound.

Let me show you an example that is virtually identical. Here we see a methyl group, just like a methyl mercury. A methyl group attached to an oxygen hydrogen group. An oxygen hydrogen group is an alcohol group, so this is methyl alcohol.

Here we see an ethyl group attached to an alcohol group, so this is ethyl alcohol. Ethyl alcohol is what is in spirits. Ethyl alcohol is what is in beer or wine. Ethyl alcohol is probably what everybody is going to go drink at the end of the day today.

Methyl alcohol, on the other hand, instead of having an ethyl group and just having a methyl group, it is also referred to as methanol or wood alcohol, which is one of the more dangerous substances known to mankind. Just small sips of methanol can kill you, and for those people who survive the serious illness that you get from methanol, they will almost uniformly end up blind.

You can see here that there is a huge difference between a methyl group and an ethyl group when it's attached to a molecule.

SPECIAL MASTER HASTINGS: And he was just looking at Slide No. 27. Go ahead.

BY MS. RENZI:

Q So is it scientifically valid then to use the toxicological properties of methyl mercury exposure to determine what the effects of ethyl mercury exposure will be?

A Of course not.

Q I'd like to turn now to reference dose. Up on the screen we're going to show Dr. Aposhian's slide that showed how the doses of mercury that Michelle Cedillo received through her thimerosal-containing vaccines relate to the Environmental Protection Agency's reference dose for methyl mercury.

SPECIAL MASTER HASTINGS: Was that Slide 39?

MS. RENZI: No. Actually it's not a slide.

SPECIAL MASTER HASTINGS: Okay. No?

MS. RENZI: It's Petitioners' Trial Exhibit 1, page 39. It's Dr. Aposhian's slide presentation at page 39.

SPECIAL MASTER HASTINGS: Okay.

BY MS. RENZI:

Q What is a reference dose?

A Okay. A reference dose is, if you'd go to the next slide --

Q Let's go to Slide 28.

A Yes. A reference dose is a concept used by the Environmental Protection Agency, the U.S. EPA, and what it is is a designation for that dose of a substance when averaged over a lifetime of use would not be expected to cause an adverse effect, would be safe.

Now, it's important to remember that there is no reference dose for thimerosal, and there is no reference dose for ethyl mercury. What we just saw shown on Dr. Aposhian's slide, which he took the reference to those from methyl mercury and applied it to ethyl mercury. That can't be done. They are different compounds.

There's no scientific basis for applying one reference dose for one compound to a dose of a different compound, although I should point out that even if we accept the reference dose -- remember, the reference dose, it's not a dose you can't ever exceed on any given day. I mean, we could easily exceed it every time we have a seafood meal. It is just over a lifetime. It's just an average dose over a lifetime.

If you were to figure out Michelle Cedillo's mercury exposure, unless she had some other unusual exposures from other sources she would be under the

reference dose even at this point in her life.

Q A reference dose is not a threshold amount above which toxicity will occur. Is that correct?

A No, it is clearly not a threshold amount above which toxicity occurs. There is a big difference between the reference dose and the dose in which toxicity will occur, as I'll show you in a minute.

It's also important to remember that Dr. Aposhian, when you talk about the EPA reference dose for methyl mercury, there are other agencies that have reference dose like the FDA and the Centers for Disease Control, and really those don't get exceeded by vaccinations. It's very rare for that to happen.

But, it's important to remember that you cannot apply the reference dose as a daily limit. It is an average over a lifetime. You have expected exceedences over the course of days.

Q What was the basis for the EPA's reference dose regarding methyl mercury? We're on Slide 30.

A The EPA's reference dose for methyl mercury is based on events that happened initially in Iraq a number of years ago when there was methyl mercury contamination of grain that people ate.

And then there was data from the Faroe

Islands which more updated our database with regard to methyl mercury and was used in the reference dose analysis. It dealt with prenatal exposure. It was based on prenatal exposure to methyl mercury and effects that were found related to prenatal exposure.

Now, it's important to remember. Reference dose has nothing to do with risk of autism or ASD or immunosuppression. None of that is implicit in the reference dose.

What the reference dose is based on, and now they use the Faroe Islands study. What the reference dose is based on is looking at prenatal exposure and then as you follow children out in time they are clinically normal children, but if you do sensitive testing on them you can find subtle subclinical deficits based in learning memory and language in children who are otherwise clinically normal. That's the basis for the reference dose.

Now, it's important to remember. You had asked the question, Mr. Renzi, about whether exceeding the reference dose means there's a threshold for toxicity. It's important to remember it's clearly not because the technique used by the EPA to determine this reference dose is called benchmark method.

What they do is they look at the population.

They look at the effects of the population and through the benchmark method come to a conclusion about dose that is very, very unlikely to affect anybody in that population.

They take that dose, and then they take just a safety back just to be on the safe side. Of course, that's EPA's job. Just to be on the safe side we'll drop it down another tenfold below that, and that's where the reference dose comes in, so there's a big safety margin implicit in the reference dose.

Q So if we go back to Dr. Aposhian's chart, and I think you've already said this. Would the amount of mercury contained in Michelle Cedillo's thimerosal-containing vaccines cause her to exceed the EPA reference dose?

A Well, as you can see on individual days, yes, she has exceeded the reference dose. In fact, over the period of time that she was being vaccinated she exceeded the reference dose.

If you go out, however -- remember, this is something you average over a lifetime. If you go out over a period of time you find that, no, she would no longer be over the reference dose.

Once again, remember the reference dose isn't even about the ethyl mercury or the thimerosal

from vaccines. It's about methyl mercury, so it's not even applicable. It's not even applicable in this instance.

Q Dr. Aposhian stated in his testimony that autistic children have a mercury efflux disorder. Are you familiar with the term mercury efflux?

A I've heard the term.

Q What is it? We'll look at Slide 31.

A Well, it's this hypothetical disorder that is based on the belief that children with ASD somehow cannot properly excrete mercury and hence become mercury toxic. They have adverse effects of mercury.

This efflux disorder hypothesis is really based on two studies. It's based on a study of Amy Holmes, and it's based on a study of Bradstreet and the Geiers.

This study I know was discussed here. It's important to note that much better studies from other investigators could not replicate the results of either the Holmes study or the Bradstreet/Geier study.

Q Could we go over the Holmes study, please? We'll start with Slide 32.

A Okay.

Q If you could describe that study, please?

A What the Holmes study purported to do was to

measure hair levels of mercury in autistics and compare them to normal controls.

Here you see the data summarized. If you look at the autistics, the hair levels were reported out at about 0.47 parts per million. If you look at the normal control, the hair levels averaged about 3.6 parts per million.

They therefore saw this difference and concluded, and this is the conclusion of their paper, hair excretion patterns among autistic infants were significantly reduced relative to control.

Now, if you look at this data you're immediately struck by the fact that something must be very, very wrong here because there's a very excellent, huge study, a United States Government funded study called the NHANES study, National Health and Nutrition Exposure Survey, and what the NHANES study did was went out and surveyed randomly many people in the U.S. population, and among things that they looked at were hair levels of mercury.

If you look at what you expect from the NHANES study of hair levels of mercury in the U.S. population in children, you see that the average is about 0.22 parts per million, remarkably close to what was reported in the Holmes study for the autistics.

But if you look at the normal control, they have very, very, very elevated hair levels. This suggests that there is something clearly wrong with this data in that their controls are so highly nonrepresentative of the general population in the United States, and that's what you would think the controls would be.

Q Does this study provide a reliable scientific basis to conclude that autistic children are not able to excrete mercury?

A No, it doesn't for a number of reasons. Number one, the data doesn't make any sense. The data clearly had a problem that has not been addressed in the study: Why the autistics have normal hair levels and the controls have so very elevated hair levels.

Number two, this study studies hair. Hair is not a significant excretory organ for mercury. We don't get rid of our mercury through our hair. There is some mercury that goes out in the hair, but that's an insignificant mode of excretion.

Q And what is hair a measure of? If you were to measure the mercury in hair, what is it a measure of?

A It's a reflection of blood levels. So this suggests if this data were true, which obviously

there's an unaddressed problem with this data, that the autistics have lower blood levels than the controls, but then again the controls have such numbers you really can't reach any conclusions about that.

Q You stated earlier that this Holmes study has never been replicated. Is that correct?

A Well, people have tried.

Q And we're now on Slide 33.

A There have been two subsequent studies that have shown no difference in hair mercury levels between autistics and controls. Actually there's been three, but one of them has not been published yet.

Kern studied a number of cases of autism or ASD with controls and found that there was no significant difference in the hair levels between the two.

Ip from Taiwan did a similar study with 82 cases and 55 controls and once again demonstrated that there was no significant difference.

So it appears that the Holmes study, probably because of the very unusual data that it had in it, cannot be replicated.

Q Dr. Aposhian also relied in his testimony on an MIT study, which I believe is the Hu study, H-U.

A Yes.

Q We filed this as Respondent's Exhibit L, Tab 27, and we'll discuss it at Slide 34. Could you describe the Hu study?

A Sure. I was sitting here as this was described as the study that verifies that the Holmes study was right. Basically it was a study from MIT from an analytical laboratory where they reported hair mercury concentrations in three people that had autistic spectrum disorder.

Now, two of those individuals were undergoing what they called having been "under treatment for heavy metal detoxification." That usually means no seafood, probably a chelating agent. Lo and behold, these two individuals had low mercury levels.

There was a third individual, an autistic individual, who was not undergoing detoxification, and his hair mercury concentration was 0.4 parts per million, exactly what you'd expect from the general population.

Q So this study is not a reliable scientific basis to conclude that autistics cannot excrete mercury?

A No, of course not.

Q In addition to the hair studies, Dr. Aposhian relies on a chelation study published by Drs. Bradstreet, Geier, et al., in the *Journal of American Physicians and Surgeons*, and that's Petitioners' Exhibit 55 at Tab E. Have you read this article?

A Yes, I have.

Q We're now on Slide 35. Could you describe the Bradstreet/Geier study?

A Sure. What that study involved was taking a number of individuals who were diagnosed with either autism or pervasive developmental disorder and comparing them with controls, and they gave them a mercury chelator succimer, also known as DMSA, and they measured their urine mercury output.

Now, the control in this study were individuals who were brought to Dr. Bradstreet's clinic because of concern about mercury toxicity, and what you can see here is that following the administration of the succimer when they measured the urine mercury levels there was higher mercury concentrations in the urine in the autism and PDD group than in the control group.

Q On page 77 of that Bradstreet article there's a chart that I want to pull up for you to look at. It's on the left-hand side.

A Right. This chart basically gives the whole population they studied. They did it in two parts. They studied the whole population, and then they studied a group where the autistics were matched by age and sex to the controls.

This is the whole population study, and, as you can see, looking at this whole population you had the higher mercury excretion in the cases than in the controls, but if you look one of the things that is striking about this result is that their ranges are so huge from zero to 60 micrograms of creatinine in the urine, zero to six in the control, with standard deviations, which is a measure of the variance of the result, how different the results are from individual to individual.

There are standard deviations here that exceed the actual values that they were looking at. This is a huge amount of variance in the study.

Q What are some of the other reliability problems with the Bradstreet study? We'll go to Slide 36.

A Oh, there's a number of them. There is the fact that the study clearly had some confounding by diet. The authors themselves acknowledge it, but didn't do anything about it.

Remember, the individuals who made up the control group were people that were brought to this clinic because of a concern about mercury toxicity. I can tell you, this is a population that avoids seafood like crazy and so it's very likely that the control population had relatively low urine mercury because they were avoiding seafood. They did not control for that fact. They could have controlled for it, but they didn't.

As we saw, the ranges and the standard deviations were huge. There was a large amount of overlap between the values in the autistics and the control population.

Another thing. I looked at those numbers, and I said, you know, with those standard deviations I'm surprised the result was statistically significant. I spent a lot of time with their statistical methodology, as did other people in my office, and based on the statistical methodology that they describe in their paper I could not come up with a statistically significant result which they said that they had.

Further, there was no assessment of compliance with the chelation treatments. We don't know if the control were taking the chelation

treatment as much as the autistics were. It's possible that they weren't because they might have been less motivated to take it.

Q We'll go on to Slide 38.

A If you look at the urine excretion of the autistics of the PDD population, it's really not terribly different than what you would expect to see in the general population under conditions of chelation.

It's also important to realize, remember, what they did is they gave the chelating agent, and they measured the urine after that. They came to the conclusion that yes, the chelating agent mobilized all this amount of mercury.

Well, they don't know that. I think Dr. Aposhian was very clear about this in his testimony. He's done a lot of chelation research. What you have to do in any chelation study is you measure the unchelated urine, you give the chelator, and then you measure the chelated urine to know if the chelator is mobilizing any mercury.

For some reason, and I don't know what that is, they didn't get a nonchelated urine. All they did is they gave the chelator and they measured the urine. That is a major flaw in this study. They also did not

exclude people who had prior chelation, and there was a high likelihood that some of these people had prior chelation.

The other thing is the question is what does it tell you anyway? It's important to remember that chelation challenges don't really tell you anything about body burden of mercury. Most mercury is stored in the kidney, and when you give a chelating agent basically what it does is it mostly removes the mercury that's in the kidney, so it's a good reflection of kidney mercury, but it doesn't really tell you about body mercury.

This study was published in the *Journal of American Physicians and Surgeons*, which is very much of a fringe journal with lots of alternative agendas, and it's not even indexed by the National Library of Medicine.

I should point out that this study was attempted to be replicated by a better study that was published in a legitimate journal, and that study could not replicate the results of the Bradstreet study.

Q And that's the Soden, et al. clinical study?

A That's the Soden study where they gave DMSA to children with autism and to normal controls that

were also coming to their clinic, and they found no difference in the excretion of metals, including mercury, following DMSA.

The conclusion of their paper, and they were talking about that there was this hypothesis about a novel mode of heavy metal toxicity in autistics based on the Bradstreet paper, and they were saying in the absence of a proven novel model of heavy metal toxicity the proportion of autistic participants in this study with DMSA provoked excretion results demonstrate an excess chelatable body burden of arsenic, cadmium, lead or mercury is zero. The proportion is zero that had an excess chelatable body burden.

SPECIAL MASTER HASTINGS: And that was on Slide 39. Go ahead.

BY MS. RENZI:

Q Is mercury efflux a recognized diagnosis in the medical community?

A No.

Q We're on Slide 40.

A Yes. I have yet to find any standard medical textbook that describes this condition.

You know, for all research that we do in toxicology and research, that we do in medicine and

billing and virtually everything we do in medicine, we communicate, is done on the basis of what we call ICD codes, International Classification of Diseases.

Everything we do, every diagnosis we give, has to be given in the form of an ICD code. This is done internationally. If you look, there is no ICD code for a mercury efflux disorder. It doesn't exist. It's not recognized. There is fundamentally no scientific support for the hypothesis that the kinetics of ethyl mercury are any different in patients with ASD than anybody else suggesting an efflux disorder.

I heard testimony when I was here where Dr. Aposhian said well, yes, the problem with the Vacikero study is that they didn't study autistic children, and had they studied autistic children they would have gotten very different results.

Well, in fact there's not one shred of scientific evidence that suggests that autistic children have any different kinetics of ethyl mercury than anybody else.

Q Dr. Aposhian presented the hypothesis regarding mercury efflux to the IOM in 2004. Are you aware of that?

A Yes, I am.

Q And that's Respondent's Exhibit L at Tab 4. What did the IOM conclude?

A The IOM basically rejected the efflux hypothesis by concluding that they were rejecting the entire concept of an association between thimerosal and the development of autism or ASD.

In fact, when you look at the body contradicting the Holmes and Bradstreet studies, which are highly questionable studies, I think it makes the efflux disorder hypothesis completely implausible.

Q I want to turn now to Dr. Aposhian's hypothesis that there is a genetically susceptible subpopulation to mercury in autistic spectrum disorder. To your knowledge, is there any evidence that supports this hypothesis?

A I have found none.

Q We're on Slide 42 now.

A I know the ASD population. I follow it on the internet. It's a subject of interest to me. It's intensively scrutinized. There has never been a susceptible subpopulation to thimerosal in the ASD population identified.

Now, what's interesting about this is that in instances where there is a genetic component to cause a susceptible population to a chemical -- for

example, Wilson's disease where people are very sensitive to copper -- with relatively little looking the gene was easily identified. There are many examples in toxicology where specific genes are identified with specific kinds of susceptibility.

The ASD population has been studied more intensively than almost any other population I can think of with regard to genetic susceptibility to a chemical substance, and not a single one has been identified.

It's also important to realize if this hypothetical genetic susceptibility hypothesis were true there certainly has been no evidence presented that Michelle Cedillo has whatever genetic susceptibility.

Q I want to go to the next slide, which is a bell curve representing dose amount necessary to cause a toxic response. Could you explain this curve?

A Yes. It's important to understand what the normal bell curve is when you want to talk about a genetic susceptibility or a susceptible population.

If we take any toxicologic response -- let's say the amount of alcohol that's required to render somebody unconscious -- it's not going to be exactly the same for everybody. There's going to be a good

deal of variation.

If you look over the scope of the entire population you find that it generally falls into sort of a bell-shaped curve. Most people are going to be kind of in this range, some people significantly less, some people significantly more. You normally expect to see that kind of variation within the general population.

On the other hand, if you have a hypersusceptible population to a substance and you look at what happens then what you see is that you get the bell-shaped curve for most of the population, but then you can identify another population here where you have this susceptible population.

This kind of demonstration has never been done with regard to thimerosal or ethyl mercury and autism.

Q Dr. Aposhian used the example of acrodynia, Pink's disease, to demonstrate that there is a genetic susceptibility to mercury toxicity, but he did so without knowing the dose or mercury blood levels. Is his reasoning valid?

A No, clearly not.

Q I want to turn to the next slide. If you could just describe what Pink's disease is?

A Sure. Here on Slide 45 we have some of the clinical characteristics of so-called Pink's disease or acrodynia, which has a lot of clinical features. There's bright reddening of the skin, photophobia, intense discomfort, multiple other manifestations. I didn't want to list all the manifestations.

The manifestations, by the way, of acrodynia are extremely similar -- almost identical -- to the manifestations that you see from an acute high dose exposure to inorganic mercury.

By the way, it is not autism or ASD. It has nothing to do with it. It was linked to the fact that when there was an outbreak of this children were using calomel, which is mercurous chloride, as a teething powder and hence were getting overexposed to mercury.

Q And what do we know about the blood levels in acrodynia cases?

A Well, it's important to remember that in the acrodynia cases they were almost all due to inorganic mercury.

I could only find one case in the English language literature and peer reviewed studies that has suggested a possibility of acrodynia from thimerosal in one individual who got massive amounts of thimerosal, so it's really all mercurous chloride.

Mercurous chloride can be assays as what comes out in the urine to measure urine levels and so one of the things we know, and actually there is a very interesting paper which I guess has recently come up in this litigation. I hadn't seen this paper in a while, but when it came up in this litigation I went back and re-read it. It's truly a fascinating paper.

It demonstrates unambiguously that urine mercury concentrations tend to be very high, exceedingly high, in acrodynia, suggesting that acrodynia is due to very high exposures to mercury, to mercurous chloride.

Q And we'll bring up that article that you're referring to.

A Right. This is basically reviewed.

Q Is this article the Court's exhibit that we're referring to? It was given to me by the Court.

SPECIAL MASTER HASTINGS: It was given us by what?

MS. RENZI: It was the article that was given to Respondent by the Court.

SPECIAL MASTER HASTINGS: Go ahead.

THE WITNESS: This article was pointing out that conventional wisdom had been some children get acrodynia, and many do not, when using this teething

powder.

You know, the conventional wisdom, which has really been carried on in a lot of the literature, is that therefore it must represent some sort of an idiosyncratic reaction. Some get it. Some don't. But, as a matter of fact, it's probably due to the fact that the ones who got it had very high exposures.

In this article, this Warkany article, they're reviewing studies, and they point out when they're talking about this study of Holzel and James of 94 children with active acrodynia, in 61, or 65 percent, there are increased amounts of mercury ranging from 200 to 2,500 micrograms per liter found. Now, they're talking about urine here. Normal urine mercury is maybe one or two micrograms per liter, so this is a very, very high mercury level.

These authors state that no abnormal mercury secretion was detected in 33, or 35 percent, of the patients, but it is not clear how many excreted significant amounts under 200 micrograms per liter, and that's because the techniques that were in play at the time when this was done could not get below about 200 micrograms per liter, so there could be individuals in there with 100, 150, 180, huge mercury levels, that make up the rest of that group.

BY MS. RENZI:

Q And finally, Doctor, has any agency or scientific body ever concluded that there is a relationship between the ethyl mercury contained in thimerosal-containing vaccines and autism spectrum disorder?

A No. You know, there are a number of governmental agencies and mainstream nongovernmental agencies who have taken the position that there is no relationship.

That includes obviously the National Academy of Sciences, the Institute of Medicine Panel, which has rejected -- taken the unusual step of rejecting -- the possibility of a relationship. The American College of Medical Toxicology has taken the position there's no relationship. The American Academy of Pediatrics has said there's no demonstrable relationship.

The World Health Organization has said there's no demonstrable relationship. The U.S. CDC has said there's no demonstrable relationship. The European Medicines Agency, which oversees pharmaceuticals in the European Union, has said there's no relationship.

To answer your question, not a single such

organization has taken the position that there is a relationship.

MS. RENZI: Thank you. I have no further questions.

THE WITNESS: Thank you.

SPECIAL MASTER HASTINGS: And that was looking at Slide 47.

MS. RENZI: Slide 47.

MR. MATANOSKI: Before we take a break, I'd just like to clarify for the record.

The Warkany article, the 1953 article, I believe that that was provided by one of the Court's clerks to both parties approximately two or three days ago.

SPECIAL MASTER HASTINGS: All right. Thank you for clarifying that.

MR. MATANOSKI: Certainly.

SPECIAL MASTER HASTINGS: Let's take our 15 minute break at this point.

(Whereupon, a short recess was taken.)

SPECIAL MASTER HASTINGS: All right. We're back from our morning break.

We have Dr. Brent back in the witness chair. Ms. Chin-Caplan will have some questions for him.

Before we do that I just want to note

something very briefly for the record to clarify. There was a reference during Dr. Brent's testimony to an article called "Acrodynia and Mercury" by Dr. Warkany and Dr. Hubbard. Ms. Renzi called this a Court exhibit.

I just wanted to clarify for the record the history on that. This article is about the relationship between Pink's disease and mercury, a topic that was raised in a number of the expert reports filed in this case, particularly Dr. Aposhian and Dr. Brent.

After Dr. Aposhian's testimony, he in his testimony cited to a figure that one in 500 people was considered to be susceptible to Pink's disease. We had a question of where that came from.

We noticed in the Clarkson 2002 article, which was filed both by the Petitioner as Exhibit 55, Tab G, and by the Respondent as Exhibit L, Tab 13, in that Clarkson article it made reference to this Warkany article as the source of that number, so we had our law clerk give copies of this article to both sides and simply stated that there was interest in this article and there might be a question about it later in the proceeding.

We hadn't made it a Court exhibit, but we

will. We are going to at this time and file it into the record so this article becomes a part of the record in the case.

With that clarification, Ms. Chin-Caplan, please go ahead.

MS. CHIN-CAPLAN: Thank you, Special Master.

CROSS-EXAMINATION

BY MS. CHIN-CAPLAN:

Q Dr. Brent, you indicated that you are currently a clinical professor at Colorado Sciences Health Center. Is that it?

A University of Colorado. Is this on? Can everybody hear me? University of Colorado Health Sciences Center, yes.

Q And you indicated that as a clinical professor your duties and responsibilities are divided into three areas. One was patient care, the second was teaching, and I didn't catch the third one.

A Academic activities.

Q Academic activities. And when you say academic activities, does that mean sitting on committees and things like that for the hospital and medical school?

A No. It means more scholarly activities -- publications, research, a role in professional

organizations.

Q Okay. Now, approximately how much of that time is spent in patient care?

A Are you talking about in my entire practice, my private practice and the university?

Q Well, you said that you were a clinical professor at University of Colorado.

A Yes.

Q I'm asking you how much of your time as a clinical professor is spent in patient care?

A At the university?

Q Yes.

A Well, in my clinical professor role we see patients at university and at Children's Hospital, which are both part of the University of Colorado system.

It depends on the year. It varies over time. Right now I cover that service about two days a month at the University of Colorado Health Sciences Center, and I have about six days a month where I cover the service at the Children's Hospital.

Q That's approximately eight days in the month that you work as a clinical professor for the University of Colorado?

A That I have responsibilities regarding

patient care consistent with my faculty appointment, yes.

Q And would your teaching responsibilities be included within that eight-day period?

A No. Well, I shouldn't say that. My bedside teaching responsibilities are, yes, where we have patients on the service that we round on and see as a group and I supervise the care. But, no, I have other teaching responsibilities beyond that.

Q And what are those other teaching responsibilities?

A Well, you know, they vary quite a bit from time to time. They are anything from months when it can be one or two hours, or I've had months where I have no hours of formal teaching responsibility other than bedside teaching responsibilities, to I have had months not long ago when I had six hours of formal teaching responsibility. That includes, for example, giving lectures to the medical school class.

There's been a little bit of a revolution in the way medical education is carried out in the United States right now. Traditionally it's been large lecture hall classes.

It's making a transition now, which every faculty member sets up, to a lot of small group

teaching and so, you know, we do spend a lot more time now doing small group teaching. We'll have on some subjects six or eight individuals that we'd be teaching on a topic for a while.

Q So your teaching responsibilities can range anywhere from zero to six hours a month?

A Yes. I can't remember a month where it's been more than six hours. You know, once again including bedside teaching.

Q And would that be primarily to medical school students?

A Medical students, interns, residents and fellows in training.

Q Okay. The clinical people -- the interns, the residents and the fellows -- would those be the people at the bedside?

A They would be both the people at the bedside and in my formal lectures.

Q Okay. You indicated that your academic activities take up part of your responsibilities. How much time do you spend in academic activities at the medical school?

A Well, my primary office is at my private practice, so in terms of the actual academic activities that I participate in -- for example,

teaching. Excuse me. For example, writing, editing is done either in my medical office or in my home study.

Q Private practice?

A Either in my medical private practice office, or I do a great deal of my academic work, just because of space considerations, in my home study. I mean, I do a lot of my writing there, for example.

Q Okay. So where is your research done?

A It varies, depending upon the particular project that I'm doing.

For example, right now my research involves pesticide residues that are transmitted to individuals through tobacco smoke, pesticides that are used to grow the tobacco plant. We're doing that in conjunction with people at the Colorado School of Mines who have a very good assay system for these pesticides.

Q The Colorado?

A School of Mines.

Q School of Mines. Is that an academic institution?

A Oh, yes. It's a primarily Ph.D. granting institution.

Q Okay. So your research is done at other

areas outside of the university?

A It depends on the project. It depends on the project. I mean, I've done many projects within the university. I've done many projects within my private practice.

The work on these pesticide residues in tobacco smoke is done in the lab that has the greatest expertise to do these kinds of assays.

Q So you have no research laboratory at the University of Colorado?

A I don't have my own research laboratory, no.

Q Okay. And you're working right now on studying pesticide residues at the Colorado Safety & Mines program?

A The School of Mines. The Colorado School of Mines. It's a very, very internationally known institution in scientific research. It is done in conjunction with several hospitals and coroner's offices.

Q So would it be fair to say that you're a consultant with them?

A No. I'm an investigator.

Q You're an investigator?

A Yes.

Q Now, you also discussed your private

practice, and I believe it's called Toxicology Associates?

A That's exactly right.

Q Doctor, how do you get patients referred to you?

A Well, we do it in a number of ways. It's a very interesting thing. Our practice is pretty well known, and there aren't many toxicology practices around so I think anybody from the Rocky Mountain area who needs to refer somebody to a medical toxicologist most likely will refer them to our practice.

We get patients coming down from Wyoming, from Montana, from Utah, from New Mexico, from Arizona, from Canada, from Nebraska. What happens is we probably get half a dozen calls a day into our office, and probably more, from people who call us and they say I think I've been poisoned. We want to see a toxicologist.

We have found that most of those kinds of patients tend not really to benefit from seeing us because they tend not to end up actually being poisoned and there are other issues, so we have taken the position, as in most specialty practices these days, that for a patient to come to us they have to be referred in from another physician so that some

initial screening is done to be sure it's appropriate to send to a medical toxicologist. So our patients basically come -- or a lot of our patients anyway come -- through referrals from other physicians.

In addition, we have some various workers that we follow in our worker surveillance program, and of course our patients in the hospital, many of them come to us directly through the emergency department or get transferred in from other hospitals or sometimes are in the hospital for another reason on somebody else's service and ends up either it becoming clear to them that they had an unrecognized toxicologic problem and therefore were admitted directly to us and then it became clear it was and we get involved or that they've had a very bad adverse drug reaction that requires consultation.

Q So with reference to your patient care, would it be fair to state that it overlaps with your hospital responsibilities?

A Oh, yes. The hospital responsibilities are a very big part of patient care.

Q Okay. So that's in your private practice?

A Private practice and at the university.

Q And you get approximately half a dozen phone calls, but most of your practice entails referrals

from other physicians?

A Yes. Yes. Right. We don't tend to see patients on the basis of cold calls.

Q So in your private practice how much time is spent on patient care?

A Oh, it varies. I would say, you know, between the hospital work and the outpatient work I'd say it's 30 or 40 percent of my time.

Q Now, you also indicated that you did teaching in your private practice.

A Most of my teaching is associated with my university work, although sometimes physically I'll be giving lectures in my conference room to students and so on.

Q So the students from the medical school would come to your private practice office for lectures?

A That's correct. It was on the toxicology service, the specific toxicology service of which I'm one of the attending physicians overseeing the service. We give them a lot of lectures, the individuals on that service. They rotate.

Sometimes we'll give them lectures at the university hospital, the medical center. Sometimes they'll come over to my office for lectures.

Sometimes they see patients with me in my office.

Q Since your teaching responsibilities at the university are approximately zero to six hours per month, does your private practice teaching encompass that? Is it encompassed within that zero to six hours?

A It is.

Q You indicated that you do research on medical toxicology. You don't have a private laboratory you indicated. Where do you get the topics to research on?

A Well, a lot of it depends. You know, it varies over the years. I spent many years doing laboratory research. I published many papers on laboratory research.

My interest is more clinical. I'm more of a clinician. I like being around patients. I like taking care of patients and so my research evolved into a clinical trial research. That was that FDA-sponsored research that I discussed before.

For a number of years recently we worked on a number of major clinical trials. Ultimately we published them in the *New England Journal of Medicine*. They ended up getting some new antidotes approved through the FDA, and now I am doing this tobacco work.

Q I'm sorry? I missed that.
A And now I'm doing the tobacco work.
Q You indicated you're running a clinical trial with FDA currently?
A No. I did.
Q You did?
A We're done with that now. We published it. The drug is approved. We're done.
Q What was the drug?
A It's called Fomepizole.
Q And what is that for?
A Fomepizole is a drug. It's very interesting. It's very interesting that you asked that because as you'll recall, this morning we were talking about methanol and how bad methanol was, methyl alcohol.

Well, what's interesting about methanol is that many people actually drink it, and we get a lot of people come to the hospital that drink it. They also drink a related substance called ethylene glycol, which is an antifreeze.

These are potentially lethal things to drink, and we developed a new antidote for the treatment of methanol poisoning and for ethylene glycol poisoning. The drugs's name is Fomepizole.

It's marketed under the name Antizol. That's the trade name.

We did clinical trials in both methanol poisoning and in ethylene glycol poisoning that resulted in the FDA approving the drug for both indications.

Q Doctor, was that published in the *Internet Journal of Medical Toxicology*?

A No. Both of those clinical trials were published in the *New England Journal of Medicine*.

Q And was it also published in the *Internet Journal of Medical Toxicology*?

A The clinical trials? No.

Q There's an article called, "Antidotes and Alcohol: Has Fomepizole Made Ethanol an Obsolete Therapy?" Is that the same topic that you speak of for your clinical trial?

A That article relates to the clinical trials. It's not the publication of the clinical trials. You won't find the clinical trial data in that article.

Q And, Doctor, in that publication you indicated that you received research support from is it Orphan Medical?

A That's correct.

Q What is Orphan Medical?

A Orphan Medical was my partner in the FDA grant. It actually doesn't exist anymore, but it is a company that specializes in the development of what is called orphan drugs.

An orphan drug is a drug that is intended for only a very limited use audience, and therefore because of the small volume of people that intend to use the drug major pharmaceutical companies generally are not interested in developing these orphan drugs.

Orphan Medical's mission was to develop these small, limited niche type of drugs that other companies would not develop. Certainly this antidote is an example of a drug, of a limited niche type of drug, so they were very interested in developing that.

Q And what was their relationship to the Fomepizole?

A Orphan and I had the FDA grant to develop the drug, which is called an orphan drug grant. The FDA has this program because once again it's important to develop these orphan drugs, and since major pharmaceutical companies don't have a big interest in developing them the funds have to come from someplace.

The FDA developed this granting process and so they were the company that was interested in developing and subsequently marketing the drug.

Q So did they provide the financial support for this research?

A The support came through the FDA grant, and it ran through Orphan.

Q It ran through Orphan?

A Right.

Q FDA granted fundings to a drug manufacturer to fund research?

A Absolutely. This was the Orphan Drug Development Grant Program, and it was specifically intended to encourage the development of these important orphan drugs.

Q But Fomepizole wasn't an orphan drug, was it?

A Yes, it was.

Q Well, the title says "Has Fomepizole Made Ethanol an Obsolete Therapy?"

A Right.

Q So ethanol was an existing therapy, correct?

A Yes.

Q So Fomepizole is not an orphan drug, is it?

A Well, there's two things about that. Ethanol was used. It was never FDA approved for that purpose, so it was not an approved drug for the treatment of ethylene glycol and methanol poisoning.

Although it was used for that purpose, it did not have FDA approval for it.

The second thing is there is nothing in the orphan drug context that says if there is a therapy for one of these sort of low niche diseases, low population niche diseases, that you can't develop a better therapy, and this is certainly a much better therapy than ethanol therapy was.

Q But most of the orphan drugs don't have any other therapies. Isn't that true?

A Well, I don't know about the other ones, but I know that at least in this area where I was doing research that although we did have a drug, ethanol, Fomepizole was potentially and it turned out in fact to be a very great improvement over ethanol, and the FDA felt that they wanted to support the development of Fomepizole through an orphan grant to us.

Q So that was your prior clinical trial. Where were the clinical trials run?

A Where were the clinical trials? It was a multicenter trial in a number of centers across the country. I was the primary investigator that coordinated the whole trial.

Q Okay. And how did they find you?

A Well, because I had an interest in the area

and in these particular poisonings. I had an interest in the area of the poisonings. I had a very busy clinical service where we saw a number of these poisonings.

There was an investigator in Norway by the name of Dr. Jacobsson who had done a lot of the basic work in the development of the drug Fomepizole, and I often contacted him just as a consultant to get some information about how to proceed with the idea of developing this drug.

Dr. Jacobsson could not be the primary investigator. He was in Norway. He suggested that they come and talk to me because I was very knowledgeable in the area and I had a lot of experience with these poisonings and I was a clinical investigator.

Orphan called me and asked if I would be interested in developing a clinical trial in this area or two clinical trials actually.

Q So the individual whose research this really was is in Norway and wanted to operate clinical trials in the United States, and they needed a principal investigator from the United States to coordinate matters. Is that it?

A Well, no. Dr. Jacobsson had done a lot of

the basic preclinical research, had not done really any studies on or had not done very much work on individuals who were truly poisoned, but had done some of what we call the preclinical research, done the volunteers, showed it was safe, did some mechanistic studies.

So the natural thing now would be to put the drug actually in clinical trials. Clinical trials had to be done in the United States because the FDA does not like to accept drugs based on international data. They really put strong pressure to do studies in the United States.

Therefore, there was I think no question the trial had to be done in the United States. I'm not sure if it was even a requirement in our FDA grant that it be done in the United States. It might have been.

In talking to Dr. Jacobsson, they felt that I was somebody for them to go to to discuss developing this FDA grant and if we got it to develop the drug.

Q Do you know how it got from Dr. Jacobsson to FDA?

A It didn't go from Dr. Jacobsson to FDA.

Q Then how did FDA become involved in this grants process?

A Orphan Medical was interested in the drug, and they contacted Dr. Jacobsson in Norway to act as kind of a consultant to help them make an assessment about whether this would be a good drug to pursue, whether this would be an improvement over existing therapy.

Dr. Jacobsson I think encouraged them to go through with the drug, felt very strongly that this drug would be an improvement and ultimately recommended that they contact me to do the clinical trial.

Q But where does FDA fit into this?

A Orphan and I then went to the FDA and solicited an orphan medical grant from the FDA to do the trial.

Q So you went to FDA with the drug company to solicit a grant from the drug company to do the research?

A No. From the FDA to do the research.

Q But the FDA grant was funded by the drug company?

A No. The FDA grant was funded by the FDA.

Q And Orphan had nothing to do with the grant process? They didn't pay for any of this research?

A I think it all came from the FDA grant.

Q Okay. Now, Doctor, we have your research, this one piece of research that you discussed. What else are you researching other than the research that you're working with with the Colorado Mines?

A That's primarily it. I am very busy right now. I'd like to be doing some additional research projects, but in addition to the tobacco research that we're doing I'm very busy right now with two other issues.

One is my editorial responsibilities, and the second is about three years ago we published a major textbook in medical toxicology, and this was an extremely time consuming, labor intensive activity. It almost ruined my marriage. It ended up being a very good book, and now we are getting prepared to go into the second edition.

So I sort of have the next couple years of my life scheduled in addition to various other academic activities and professional society activities and my research to doing the second edition of the book, because it's about five years since the first edition.

Q Do you have an active consulting practice?

A Consulting in what sense? We do lots of different kinds of consulting.

Q Do you consult to industry?
A We do from time to time, yes.
Q Do you consult to the drug companies?
A Occasionally.
Q Are you currently consulting with drug companies?
A I'm not consulting with any drug companies regarding any research areas of anything of that nature. There are one or two medical/legal cases -- I can think of one -- where I am looking at a case on behalf of a drug company.
Q And what case is that?
A It's a case that involves an infant death and any possible relationship to a diphenhydramine-containing skin cream that was put on.
Q A what? I'm sorry.
A A skin cream that contained a medication called diphenhydramine.
Q And you testified that you worked in the Easter case, correct?
A I did work in the Easter case, yes.
Q And that was on behalf of the defendants. Is that true?
A That's correct.
Q And the defendants were drug manufacturers?

A GlaxoSmithKline. I think there were some others as well.

Q I missed that.

A GlaxoSmithKline was the company I was working with most closely. I believe there were some other defendants as well.

Q That was one of the drug manufacturers?

A That's correct.

Q How much did you get paid on that, Doctor?

A On the Easter case?

Q Yes.

A Oh, boy. I don't know the exact figure. I had to go through all the records. It was a substantial amount. I had to go through all the records, actually went to Texas to participate in the evaluation of the child, and then I had to prepare a report, and I had a deposition in the case.

That was the end of the case. As I mentioned, the case was dismissed on what's called a Daubert motion, I believe. I'd be guessing, but it could have been $40,000, $50,000.

Q Are you currently consulting on any other thimerosal cases?

A No. I should say I have been sent on occasion from pharmaceutical companies, to give a

complete answer, occasional thimerosal cases, but I don't have any active ones going on, no.

Q Okay. And so in your medical/legal work does it involve working solely for the defendants?

A No.

Q And in these cases that you've just described to me have they involved working solely for the defendants?

A The ones you've asked about where I've worked as a consultant for the pharmaceutical industry, yes, those have been for defendants.

Q Okay. Do you consult to Third World countries at all?

A I have done some. It depends on what you call a Third World country.

I don't have a lot of opportunity to do that. I have done some things for emerging nations through the U.S. State Department.

Q And what have you done for them?

A Well, one thing is really a fascinating thing. It's a really fascinating thing. These really weren't Third World countries, but they were sort of emerging into mainstream countries, into mainstream activities. One was China. One was Russia.

A number of years ago China invited a

delegation of medical toxicologists to come to China to meet with their medical toxicology community, and I was invited to lead that delegation. I was the delegation leader and went there.

Then a really fascinating, an extraordinary story in Russia.

Q Did you say in Russia? I'm sorry.

A In Russia.

Q What did you do in China?

A The delegation traveled and met with many of their toxicologists or individuals who were interested in toxicology, and we exchanged ideas and so on and saw some patients together.

Q Okay. And you were moving on to Russia?

A Yes. It's a fascinating story, a fascinating story.

I work with the United States Centers for Disease Control in the rather scary area of chemical weapons.

Q I'm sorry. I missed that. In the area of what?

A Of chemical weapons because there's great concern about what if there is a chemical weapons attack, a terrorist attack.

They have harvested together a group of

about 12 medical toxicologists from around the country to have a high level of expertise working on these, being knowledgeable about them and to be able to respond and take on leadership positions in case of an actual event to get the knowledgeable people there on the ground very quickly. I have a secret security clearance with doing that.

Now, this is a very fascinating story. One of the issues that came up was that the Soviet Union used to have a very active chemical weapons program, and with the dissolving of the Soviet Union there was concern about what are all the chemical weapons scientists doing.

The United States Government had a great interest in, number one, finding out what they were doing and, number two, figuring out ways to engage them and so they send a number of medical toxicologists to Russia to meet with the Soviet weapons experts and to establish a dialogue and to engage them and mostly to find out sort of what they were doing in general.

We didn't interrogate them with what are you doing, but just what they were doing in general and what they wanted to be doing, the idea being that if we could figure out what they wanted to do we might be

able to arrange funding for them to do it and to prevent them from doing things that we didn't want them to be doing.

That was a fascinating -- we did this two or three years ago -- experience with the State Department.

Q So this wasn't then at the invitation of Russia?

A You know, I don't know exactly who instigated it. I know what the agenda was from the United States point of view, but I don't know who instigated it.

Q Any other consulting to emerging countries?

A That's about all I can think of for now.

Q So there's nothing to Third World countries?

A No. No.

Q Any medical research in mercury?

A I published a number of papers on mercury and have done academic assessments of the area. I haven't done any primary research on mercury. I've published a case or two on some treatment issues on mercury.

Q Okay. So primarily on treatment issues?

A Yes.

Q So no primary research, but you have

published a few articles on how to treat mercury toxicity. Is that it?

A Articles, book chapters. I've lectured nationally and internationally on mercury toxicity and a couple of publications regarding treatment.

Q Now, you indicated that you've actually treated three mercury cases, correct?

A No. I've treated many, many more than three mercury cases. I gave three examples.

Q Okay. One of the examples that you gave were two workers who were overexposed to mercury on the jobsite. Am I wrong?

A Today?

Q Yes.

A I remember giving the example of the dentist.

Q The dentist.

A I remember giving the example of the woman whose --

Q Munchausen.

A -- husband was trying to kill her.

Q Right.

A Let me think. And the individual who intravenously injected the mercury.

Q Who was the second one that you just

mentioned, the woman?

A Yes, who she thought her husband was trying to kill her from the mercury.

Q Oh.

A I just chose off the board three colorful examples, not the more mundane mercury cases.

Q So there was no situation where you were consulted where two workers who were exposed to mercury on the worksite?

A Oh, yes. I've seen a number of cases of workers exposed to mercury on the worksite. I didn't mention those examples today. They're not nearly as colorful as the ones I mentioned.

I can't catalog every case of mercury exposure that I've seen. I don't even think I remember all the cases of mercury exposure that I've seen.

Q So what are the industries that are still using mercury on the worksite?

A That is a good question. You know, I don't necessarily even know what the job processes are because that's not necessarily part of my -- I strictly do medical assessments of exposure and medical condition.

But, I do know that in some industrial

thermometers they're still using a good deal of mercury. Fluorescent bulb manufacturers are using mercury. I'm sure there are others.

Q And have your cases come from those two industries?

A I don't recall. Do you mean worker exposure?

Q Yes.

A I don't recall specifically.

Q Now, I think you also mentioned that part of your clinical responsibility is surveillance of workers. Could you just describe what that involves?

A Oh, sure. I'd be glad to. OSHA has a requirement that if workers are working in the area of hazardous materials that they have to be in a medical surveillance program, and that typically involves a baseline evaluation before they start working and an evaluation -- it can vary a little bit -- typically once a year to assess them to assure that they are not having any adverse effects from being exposed to whatever the particular substances are.

Very often that often involves an assessment of their ability to use an appropriate respirator as personal protective equipment to prevent them from inhaling material.

There are a lot of workers that need to be in these programs. We see a good number of them and do their baseline evaluations. You know, if a worker is going to go in working on a lead project they come in and get their baseline evaluation just so we can compare that with after they're finished working on it or any other material. We see them annually.

We see them if they feel they've been exposed, if something happened on the jobsite and they feel they've been exposed. Sometimes if they really are exposed we take care of them in the hospital, and then often we'll see them at the termination of their employment.

Q And how many programs are you currently surveying?

A I don't know the number.

Q You don't remember?

A I have no idea.

Q Is it more than one?

A Oh, yes.

Q Is it more than 20?

A Probably, but I don't know. I can't tell you for sure.

Q Do any of them involve mercury?

A I'm sorry?

Q Any of them involve mercury?

A You know, it's possible because I know that on some of the workers we've seen we've gotten mercury levels, and usually what happens is our office -- not me personally, but somebody in our office -- determines in advance, because we have to let the employers know how much it's going to cost, what tests we're going to get and so the first thing that we ask is what are the exposures, and then they can get the appropriate tests.

I know I've seen a number of workers come through where we have gotten mercury levels, so they probably at least had the potential for being exposed to mercury.

Q So when you order a screening do you order a screening such as a heavy metal screening? Is that it?

A No. Usually what we do is we order a very specific test, not just a general heavy metal screening, and it can vary depending upon the circumstances.

For example, for mercury we can get either a blood mercury level or a urine mercury level, depending upon the circumstances.

Q So you would have to know ahead of time that

the person had already been exposed?

A Yes.

Q Now, Doctor, we discussed very briefly the *Federal Register*, which you very kindly provided to us. It's currently marked as Respondent's Trial Exhibit 18. Doctor, this was proposed on January 5, 1982, is that correct?

A That is correct.

Q And the title of it is, "Mercury Containing Drug Products for Topical Antimicrobial Over-the-Counter Human Use: Establishment of a Monograph," correct?

A That is correct.

Q And it was a proposed rule?

A That is correct.

Q The summary says, "The Food and Drug Administration, FDA, is issuing an advance notice of a proposed rulemaking that would classify over-the-counter or OTC mercury-containing drug products for topical antimicrobial use as not generally recognized as safe and effective and as being misbranded."

Have I read that correctly?

A You have.

Q So, Doctor, as you indicated, thimerosal had never been evaluated by FDA for safety and

efficaciousness, correct?

A That's right. It had been used for such a long time with a good safety record that it just continued to be being used without, to my knowledge, an actual application for use, as was very common for medications that had been around for a long time.

Q And it was grandfathered in, as you stated, right?

A I believe that's the right term, yes.

Q Right. And there was a period of notice and comment? Is that true?

A That's correct.

Q How long did it take for this law to become effective?

A The rulemaking?

Q Yes. When did this law become effective?

A I don't know when it became effective. I think it was a number of years later.

Q So the proposed rulemaking was first issued on January 5, 1982, and the period of notice and comment lasted until April 11, 2007, according to what you handed out to us, correct, on Respondent's Trial Exhibit No. 7?

A Let me take a look. What page? Written comments by April 5, 1982. Reply by May 5, 1982.

Where are you talking about 2007?

Q Well, the effective date. It says April 11, 2007, doesn't it?

A What page are you looking on?

Q Respondent's Trial Exhibit No. 7, page 1.

MR. MATANOSKI: Just to clarify, I think you're actually now looking at 21 C.F.R. § 310.545.

SPECIAL MASTER HASTINGS: That's Respondent's Trial Exhibit 19.

MS. CHIN-CAPLAN: Is it 19? Okay. Exhibit 19. Sorry.

MR. MATANOSKI: And the notice of proposed rulemaking is 47 Federal Register 436.

BY MS. CHIN-CAPLAN:

Q So, Doctor, the effective date was April 11, 2007? Am I correct?

A I think you may have changed years. I just want to be sure I follow what's going on.

You had originally asked me about the proposed rulemaking, and now we're not talking about that anymore, but we're talking about --

Q The rule. We're talking about the actual rule.

A No, no, no. This rule did not derive from his proposed rulemaking. These are two totally

separate areas.

Q They are?

A Yes.

Q And what is your knowledge about that?

A Well, the proposed rulemaking dealt with the propriety of using mercury-containing over-the-counter compounds in an unregulated way as an antiseptic for skin, and that's what these comments were about, strictly mercury-containing over-the-counter compounds in an antiseptic for skin.

The 21 C.F.R. 310.545 was a list of about 700 compounds, substances -- not just mercury compounds, but everything; everything from wheat germ to vitamins -- that had been used by the FDA through sort of this grandfather policy and had never gone through the approval process that they were pointing out. Thimerosal was one of those substances.

That's a totally different issue than this proposed rulemaking on mercury-containing compounds on skin.

Q So your belief is that 47 Federal Register 436 dealt solely with a topical --

A Yes.

Q And, Doctor, 21 C.F.R. 310.545, which became effective on April 11, 2007, involved thimerosal,

correct?

A Yes.

Q So FDA actually broadened the category of mercury-containing products, didn't they?

A No. Actually I think you're mistaken. If you look at this proposed rulemaking for topical, there is a long list of mercury-containing products.

If you look at 21 C.F.R. 310.545, that has a couple of mercury-containing products in it -- in fact, I think much fewer than the proposed rulemaking -- but is about 700 different pharmaceuticals completely unrelated to mercury. Honey and wheat germ and vitamins don't have anything to do with mercury.

Q You're absolutely right, Doctor, but the proposed rulemaking that you have testified about you indicate involved merthiolate, correct?

A Yes.

Q Which is a topical antiseptic applied to the skin, correct?

A That is correct.

Q And the final rulemaking contained at 21 C.F.R. 310.545 involves all over-the-counter thimerosal-containing products, doesn't it?

A It contains thimerosal, yes. Yes. It includes thimerosal, over-the-counter or not over-the-

counter.

Q Correct. So hasn't FDA broadened their category of mercury-containing products and there was more than merthiolate that was being regulated in 21 C.F.R. 310.545?

A If you look at the proposed rulemaking, there's a large list of mercury-containing products here, more than merthiolate, in the original proposed rulemaking.

Some of those products were carried on to this other document, but most of the things on this other document had nothing to do with mercury.

Q That's correct, Doctor. However, merthiolate was just one kind of over-the-counter product that contained mercury, wasn't it?

A That's correct.

Q And the final rule banned all thimerosal-containing products over-the-counter, didn't it?

A Well, thimerosal is a merthiolate.

Q Yes.

A Yes.

Q But all of them. Anything that contained thimerosal over-the-counter was banned, not just merthiolate, wasn't it?

A Well, thimerosal was. This rule I don't

think is a banning rule. I mean, they didn't ban aspirin. They didn't ban vitamins. They didn't ban wheat germ. It just listed those products that hadn't gone through the approval process.

Q So let's look at this law then, Doctor. Under (a) it says, "A number of active ingredients..."

SPECIAL MASTER HASTINGS: Now you're looking at page 1 of Trial Exhibit 19?

MS. CHIN-CAPLAN: Page 1.

SPECIAL MASTER HASTINGS: Okay.

BY MS. CHIN-CAPLAN:

Q Under (a) it says, "A number of active ingredients have been present in OTC drug products for various uses as described below. However, based on evidence currently available there are inadequate data to establish general recognition of the safety and effectiveness of these ingredients for the specified uses."

Thimerosal is listed as one of those ingredients. Isn't that true?

A I think it's on this list. I can find it. Let's see.

SPECIAL MASTER HASTINGS: Ms. Chin-Caplan, it's a long list.

MS. CHIN-CAPLAN: Yes. I'm trying to find

the page for him.

SPECIAL MASTER VOWELL: It's on page 39, I believe.

MS. CHIN-CAPLAN: Page 39?

SPECIAL MASTER VOWELL: Page 39.

MS. CHIN-CAPLAN: Thank you, Special Master.

SPECIAL MASTER VOWELL: At the bottom of the page. Towards the bottom.

BY MS. CHIN-CAPLAN:

Q Page 39, Doctor.

A Okay. Now, on 39 are we still in (a)(1)?

Q Yes, we are.

A Okay. Actually, we're not. Page 17 becomes (b). They go into bulk laxatives.

Q (a)(1).

A And then on page 18 they go into stimulant laxatives, and then on page 19 they go into oral health care products. We could go on and on, so I think we're past that initial section by the time we get to page 39.

Q Okay. Perhaps what we could do is get the proper citation for the Court, so let's go through this list here, Doctor, okay?

SPECIAL MASTER VOWELL: Ms. Chin-Caplan, in the interest of time I believe rather than (a) it is

(i), but that may be indented so it means something else. We're talking about first aid, antiseptic drug products.

MS. CHIN-CAPLAN: Yes.

SPECIAL MASTER VOWELL: That is where thimerosal is located.

MS. CHIN-CAPLAN: Thank you. Thank you, Special Master.

BY MS. CHIN-CAPLAN:

Q So, Doctor, if you look immediately above it on that page it looks like it is 27(i), and it starts listing a number of mercury-containing products.

A Okay. So now we're going to page 39. Is that correct?

Q Page 39.

A Okay. So here they are listing first aid antiseptic drug products?

Q Right.

A Okay.

Q And they list a number of mercury-containing products, correct?

A That is correct.

Q And underneath it there is mercury, correct?

A Correct.

Q And there is thimerosal?

A That's correct.

Q And merthiolate would be included within this group of mercury-containing products, correct?

A That is correct.

Q But there is more than one mercury-containing product here listed, isn't there?

A That's correct.

Q So hasn't FDA broadened its application of the federal rule that they initially proposed in 1982 to include these other mercury-containing products?

A No. I think you missed the point. If you look at the federal rule, there's a long list.

This proposed rulemaking, there's a long list of mercury-containing products in here, a bigger list than this, so I wouldn't describe it as broadening.

Q Okay. Doctor, if we go to page 40, and the citation there I believe would be 21 C.F.R. 310.545(b). Do you see where I am on page 40?

A I've got that. I'm looking for the (b). Oh, the (b) on the bottom?

Q Yes.

A Yes.

Q It says, "Any over-the-counter drug product that is labeled, represented or promoted for the uses

specified and containing any active ingredients as specified in paragraph (a) of this section is regarded as a new drug within the meaning of § 210(p) of the Federal Food, Drug and Cosmetic Act for which an approved new drug application under § 505 of the Act and Part 314 of this chapter is required for marketing. In the absence of an approved new drug application, such product is also misbranded under § 502 of the Act."

I've read that correctly, haven't I?

A You have.

Q And, Doctor, while this was not an outright ban, wasn't the practical effect of it a ban?

A You know, I don't know. You're asking me a legal question, and you've certainly exceeded my legal ability. I can tell you thimerosal is still used in FDA approved pharmaceuticals.

Q That's right, in vaccines.

A And other stuff.

Q So, Doctor, in your report, and if I'm wrong please tell me, you acknowledge that methyl mercury has caused problems and Minamata Bay would be one of those instances. Wouldn't that be true?

A That is correct.

Q And do you acknowledge, also, that methyl

mercury has caused problems in the Iraqi grain contamination cases?

A It has.

Q And there were a number of those, correct?

A Yes.

Q And the Faroe Islands, that also looked at methyl mercury, correct?

A Faroe Islands listed methyl mercury. Faroe Islands' data is a little complicated because of the coingestion of polychlorinated biphenyl in high concentrations that happens. We don't see those polychlorinated biphenyls in the Seychelles Islands and they don't see the same effects really in the Seychelles Islands, so we don't know what to make of the Faroe versus Seychelles dilemma. It's still an unresolved question.

Q So are you aware of any literature that has actually looked at the PCBs that were involved in Faroe Islands and made a determination that it did not affect the outcome of the study?

A They have attempted to control the PCBs and concluded that they could not find evidence that the PCBs were the cause of the difference. That has not ruled out the PCBs certainly, but they could not find evidence that the PCBs were causing the problem.

Q You mentioned the Seychelles Islands. The Seychelles Islands was also a seafood population people, group?

A Seafood eating population, yes.

Q And to be perfectly clear the Faroe Islands involved the ingestion of pilot whale, didn't it?

A That's correct, and that's where the PCBs came from.

Q Right. And it was not a steady state of ingestion, correct?

A That's correct.

Q And the Seychelles Islands involved a steady state, correct?

A That's correct.

Q Now, you were present in the Court when Dr. Aposhian testified, weren't you?

A I was here, yes.

Q Did you hear him say that when the White House conference was convened of which he was a member they were there to try and resolve this issue of the Seychelles Islands with their steady state exposure and the Faroe Islands with their bolus type of exposures, correct?

A Yes.

Q Did you also hear what Dr. Aposhian

indicated occurred at that meeting?

A You'd have to tell me what specific aspect of his testimony you're referring to.

Q Do you recall him saying that the recommendation of this White House conference on mercury was that the Seychelles Islands should utilize the same tests as those utilized by the Faroe Islands?

A Well, yeah. There was definitely the issue, and this has been well written about in the literature, that there was not exactly the same testing protocol between the Faroe Islands and the Seychelles group. There was concern that may be why they see effects in the Faroes and they don't see it in the Seychelles. The suggestion had been made, well, let's just do exactly the same test on both groups.

The fact is that if you look at the testing protocols they tested pretty much the same domains, the same aspects of neuropsychological function and neurocognitive function, they just used slightly different tests to do it.

So there was certainly a question of well, that may be the source of the discrepancy, but I think there is considerable doubt in peoples' minds that it's simply a result of the testing protocol given the

fact that the domains that they look at are so overlapping between the two studies.

Q Do you recall Dr. Aposhian saying that when they did utilize the same tests as the Faroe Islands that they obtained the same results?

A I think you have to look very closely at that. The adverse effects in the Seychelles that they ultimately found were on a test called the grooved pegboard, and that was one test on a large testing battery.

It's unclear whether that one result on that one test, and it was primarily seen with the nondominant hand, which is strange, so it was questionable whether that actually -- and the literature reflects this.

It's not in my opinion, it's well-written in the literature. The literature reflects that nobody really knows what the significance is. I mean, you know, it tested a little bit more abnormally on the grooved pegboard test. They then did subsequent analyses because -- and I don't want to get too complicated about this, and stop me if I get too complicated -- all these tests had been done using a so-called linear model.

In other words, looking for a dose response

whereby, you know, you double the dose you expect to see double the effect or some proportionate effect to dose, and they couldn't find any effect on the grooved pegboard on the dominant hand. They then went back and they said well, let's try a different model, and so they used what they call a nonlinear model.

We're saying well, let's assume it's not a discognitive dose response group, let's assume it gets flat, flat, flat, flat, flat and you reach a threshold and it goes up. Using the nonlinear model they were able to say, well, maybe there's an effect here on the dominant hand. That's a lot of data dredging, and as reflected in the publications nobody really knows what the significance is.

Nobody knows whether you're supposed to use a linear or a nonlinear model. So, yes, they found a test, one test, where there was an abnormality in the Seychelles that they saw in the Faroe Islands at an older age group with lots of other confounding factors. What that ultimately means in the long run, I think the dust has to settle on that.

Q There was also a New Zealand study done as well, wasn't there?

A Well, there was. There was a study by a guy by the name of Karrollstan, with a *K*, in New Zealand,

and they did some analysis, too. That study has never been published in the peer-reviewed literature, but there was a study, which actually, as best as we can tell given the study has never been published has reported results similar to the Faroes.

Q Now, Doctor, the Iraqi grain cases contained contamination with thimerosal as well, too, didn't they?

A No.

Q Or ethyl mercury?

A Well, no.

Q There haven't been?

A There have been Iraqi grain cases where there's miscontamination with ethyl mercury, paratoluene sulfonates, if that's what you're referring to.

Q Yes.

A EMPTS. EMPTS is not ethyl mercury, although it's got a ethyl mercury in the name. It is a significantly more complicated molecule than ethyl mercury.

Q So it's your testimony that none of the Iraqi grain contamination cases involved ethyl mercury?

A I don't recall. I know there has been

methyl mercury, I know there's been EMPTS. I don't recall if there was another one with ethyl mercury.

Q Okay. Now, Doctor, in addition to the grain contamination cases there have been a number of ethyl mercury poisonings, haven't there?

A Yes, there have.

Q And you actually listed quite a few of them in your report, didn't you?

A Yes. In my report?

Q Yes.

A Yes, I mentioned some. Yes.

Q Before we move on to that area, Doctor, do you recall Dr. Aposhian saying that at the end of this White House conference of which he was a member that the FDA agreed to lower their standard to meet that of EPA?

A He might have said that. I don't recall.

Q Okay. Now, on page 15 of your report you say there is reliable scientific evidence that thimerosal is not toxic to humans including infants and children at doses delivered either individually or cumulative by thimerosal containing vaccine, and on page 16 you list a number of cases. I'd like to go through those cases with you. The first one that I see was the Stajich article.

A Uh-huh.

Q Stajich is contained at Respondent's Exhibit L, Tab 54. Do you have that, Doctor?

A I don't have that article. I might have it here on my computer. You have a hard copy of it? Okay.

Q Okay. This involved mercury exposure after hepatitis B vaccination in preterm infants, correct?

A I believe it was term and preterm infants.

Q Okay. They compared pre and postvaccination mercury levels. Is that true?

A Yes.

Q And they indicated in the abstract that it showed a significant increase in both preterm and term infants after vaccination, correct?

A Sure.

Q Then they said that additionally postvaccination mercury levels were significantly higher in preterm infants as compared to term infants, yes?

A Sure.

Q Then it says because mercury is known to be a potential neurotoxin to infants further study of its pharmacodynamics is warranted. I've read that correctly?

A Yes.

Q You don't disagree with that, though, do you?

A Well, once again, you know, I spent a lot of time this morning talking about dose. Yes, there's no question in my mind that at a high enough dose that mercury is a neurotoxin to infants and to adults. I think what we're showing here is if you look at these levels that these levels are certainly not anything close to what you would expect to be associated with any toxic effects.

Q Doctor, I'd like you to take a look at the Haeney report, which is contained at Respondent's Exhibit L, Tab 23. Could you just tell the Court what this case involved?

A Sure. I just want to see if I have it on my computer. I'll take a look at it here in a second for you. Okay. This one I believe is the study where they gave long-term administration of infants who had a condition known as hypogammaglobulinoemia, they had decreased immunoglobulin levels, and so they infused them with immunoglobulins.

Q I'm sorry. Did you say infants?

A Patients. I'm sorry. Patients.

Q And what were their ages?

A Let's see what their ages were.

Q It's at the top of page 13.

A Let's see. Twenty-six patients, four to 67.

Q Yes.

A And so they infused them with immunoglobulin containing thimerosal and fundamentally these people obviously developed elevations in their blood mercury level because of the thimerosal, but it was basically well-tolerated. Mercury levels went much, much higher than anything you would see with vaccinations.

Q Doctor, on page 14, the very last sentence, doesn't it say hence, most patients with hypogammaglobulinoemia are theoretically at risk for mercury exposure, and although no clinical evidence of toxicity is yet apparent physicians responsible for each patient must be alert to the need for continued long-term detailed clinical examination to detect any subtle disturbances that may occur? I've read that correctly, right?

A You've read that correctly. Basically, what they're saying here is look, we have given this immunoglobulin to all these people, and we have driven mercury levels up very high, very high, and yet we do not see clinical toxicity. They haven't driven it up high enough to get clinical toxicity, but they're huge

compared to what you'd get from a vaccine.

So, yeah, I think they're saying look, we don't see any toxicity, but bear in mind these mercury levels are pretty high, so it's probably a prudent thing to keep an eye on these people and make sure they're not getting mercury toxin.

Q And they should do that, Doctor, because the medical profession knows that there's a long latency period between mercury exposure and injury, correct?

A Well, I don't think that was the crux of what they were saying. I think what they were saying is look, these levels are pretty high, and so when you expose somebody to high levels of something even though you don't see any sign of toxicity it is good, particularly when you expose them, to keep an eye on them.

I didn't see anything in here about raising particular concern about latency because these people were treated over a period of time, so that would have included, you know, any latency for effect to occur.

Q But prolonged latency is known to medical professionals, and you know it, correct?

A There is a latency period, yes.

Q And it's quite long from time of exposure to the time when injury can occur, correct?

A Well, it depends on the dose, it depends on the circumstances of the exposure. Could be months.

Q Could be months.

A Yeah.

Q In fact, for the Iraqi grain contamination cases it was months, wasn't it?

A Yeah, months.

Q Months at the very high dose, correct?

A Could be months, yes.

Q So, if we go to the next article that you speak of, Axton, which is contained at *L*, Tab 7, now, in Axton you spoke of one six week old infant, but this report actually involved six cases of poisoning after a parental organic mercurial compound, and they called it merthiolate, correct?

A Right.

Q Doctor, would you just generally describe these cases to the Court?

A Sure. As I recall without stopping too fast to read the whole article --

Q Sure. Take your time.

A -- and I may have to stop to look up certain points, but I recall that there were six cases here with deaths. Five of them died. If you look at the survivor, it's actually the youngest one of the whole

group that survived, and that individual received about 13,000 micrograms of mercury and maybe as much as 220,000 micrograms of mercury.

Do you have any other questions about this article?

Q Yes. Let's just go over this. The first one, these cases all involve chloramphenicol, an antibiotic, correct?

A Yes.

Q And the antibiotic had been preserved with thimerosal?

A Right, and I believe they had used too much thimerosal in the reconstitution of the antibiotic. It wasn't the standard amount. Yes.

Q Correct. Yes. Rather than grams they put in kilograms.

A They used a lot of thimerosal.

Q They used a lot. Yes.

A Yes.

Q Doctor, in Case No. 1 a seven year old child was administered the chloramphenicol IM, correct?

A Seven year old child, da, da, da, IM chloramphenicol. Yes.

Q Yes. That means by injection, yes?

A Correct. Intramuscular injection.

Q Yes. Then four days after administration his right buttock was noted to be swollen and very tender.

A Right.

Q Ten days after admission the skin over his right buttock appeared necrotic.

A Right.

Q What does necrotic mean?

A It means the cells were dying.

Q Right. A similar area appeared on the anterior aspect of the left thigh, both areas were intramuscular chloramphenicol had been given. Is that true?

A Correct.

Q Yes. And he died on the 21st day after admission?

A Right.

Q And when they did a biopsy, Doctor, what did they find on biopsy?

A Are you talking about biopsy or autopsy?

Q I'm sorry, autopsy.

A Okay. You want me to go over all the autopsy findings?

Q Well, just let's go to this one.

A Go back to all the autopsy findings in this

child?

Q Yes.

A Oh, okay. Fine. Well, it says here he had an ulcer covered by a black *S* scar, which is basically dead skin, over the right side there.

Q How large was the ulcer?

A Ten centimeters.

Q And in inches?

A Five.

Q Five inches. A five-inch ulcer from being injected with thimerosal?

A Right. It says the edge was undermined and indurated, and the underlying muscles were brown and necrotic. There was no free pus, and the changes extended almost to the pelvic bone. A five centimeter abscess containing thin brown material was found in the left thigh. Muscle necrosis in this area was also extensive. Areas of consolidation were found in both lungs. The spleen was moderately enlarged.

The kidney was enlarged and pale. When they did a histological examination, in other words stained sections under the microscope, there were thrombi or blood clots in blood vessels, there was an area of the lungs which had infarcted or died, there was tiny what's called petechial hemorrhages in the brain.

Then it talks about necrosis at the injection site.

In the kidneys microscopically there was degeneration and necrosis in the tubules and blooming of the proximal tubular cells, flattening of the tubular epithelium, pigment casts, some inflammatory aggregates in the kidney with some blood cells in the kidney, and then they give the amount of mercury in all these various samples that they assayed, which was very, very, very high.

Q So there was no doubt that the death was related to mercury, was there?

A No. This was due to the incorrect constitution of the medication with too much thimerosal.

Q Right. And the second case also given by injection also had black necrotic areas where the injection was given. Isn't that true? That would be the next page, Doctor, page report 2.

A Right. I'm just looking at it.

Q Yes. It's on page 418 at the very top.

A Had an induration and the next day these areas became black and necrotic at the injection sites. Yes.

Q Okay. It says extended over an area of approximately 12 x 6 centimeters on each thigh.

A Right.
Q How big is 12 x 6 centimeters?
A 6 x 3 inches.
Q Three inches on each thigh.
A At the injection sites, yes.
Q Okay. Doctor, this child died, didn't he?
A Yes.
Q And the concentration that he received was quite high?
A Huge.
Q Then the case report of the child who survived. She was a six week old child, correct?
A Wait a second. Let me see. The survivor, yes. She was Case No. 3, and that was six weeks old.
Q Yes. And she had the same problem, didn't she, with the injection site becoming necrotic?
A Yes.
Q But she got sent home, didn't she?
A Initially, yes.
Q And they eventually brought her back in when they discovered the extraordinary dose of thimerosal in the chloramphenicol, correct?
A They found out that she had received this very high dose, yes, and that's right, they brought her back and readmitted her.

Q Now, she was the only one out of these six patients to survive, correct?

A That's correct.

Q They indicate a reason for why they believe she survived, didn't they? If you look on the next column, page 419, the next to the last paragraph.

A Right, right. I'm looking at it, I'm just reading it. It's a classical dose issue. They think that although she received a number of injections of chloramphenicol for the treatment of her pneumonia they think they weren't all contaminated with the very high doses of thimerosal, some of them had the appropriate doses of thimerosal.

Q So she was the lucky one. She got the lower doses.

A That's correct.

Q The others all got the higher doses?

A That's correct.

Q And they all died?

A That's just what I was saying this morning, the dose makes the poison.

Q Yes. Now, Doctor, you also talked about Fagan. Do you recall that?

A Yeah.

Q Now, Fagan is contained at Respondent's

Exhibit L, Tab 17.

A Just seeing if I might have my own copy here.

Q Doctor, before you go to that can I just ask you one last question on that child who survived?

A Yeah.

Q Any long-term follow-ups?

A Hang on. I'll take a look. As I recall it was ambiguous about to what degree that she was followed-up. They say that the cavity that had resulted from the necrosis in the area of injection healed up in two months, and at that point her physical signs were normal on examination and she showed no signs of mercury toxicity.

Q That was at what? The end of two months?

A Two months.

Q Two months?

A Yes.

Q So if we could move on to Exhibit 17, which is the Fagan article?

A Sure.

Q Okay. Now, Doctor, in Fagan there are 13 cases of, they call it omphaloceles.

A Omphaloceles.

Q Omphaloceles. And could you tell the Court

what omphaloceles are?

A Sure. You know, normally at postpartum there is an umbilical stump and when the umbilical cord is cut that stump becomes naturally necrotic. Now, sometimes instead of that happening and it involuting and go away it becomes large and potentially problematic.

At the time what they were doing is they were treating these omphaloceles by putting large amounts of thimerosal tincture on the omphaloceles to get them to see if they would necrose and go away.

Q In many instances it was put on until the children were old enough so that a primary closure could take place. Wasn't that true?

A It's possible. I don't recall. I could look that up in the paper if you'd like.

Q Okay. If you'd like.

A I'll take your word for it.

Q Okay. Doctor, out of these 13 cases 10 of them died, didn't they?

A Right.

Q They did an autopsy on these patients and they had very high mercury levels, didn't they?

A Huge. They got highly overexposed to mercury.

Q But there was one child that they were able to find who survived, correct? Out of the three survivors they found one.

A Okay.

Q If you go to page 963 on the bottom it talks about that one survivor, doesn't it? Last paragraph.

A Under discussions?

Q Yes. Last paragraph on the right-hand side.

A On the right-hand side. We traced one of the survivors. They did a neurological exam 10 years of age, and they looked for evidence of mercury toxicity looking for visual field narrowing, which is what you'd expect to see, or paresthesia, which you would expect to see. They didn't assess intellectual development, but they said the school reports that she was reckless, easily distracted and not interested in schoolwork.

Q So the one survivor, Doctor, they couldn't comment on his intellectual development, and his school says he's reckless, easily distracted and not interested in schoolwork, correct?

A Right. Not very unusual for a 10 year old. No objective signs of mercury toxicity, though.

Q And, Doctor, you mentioned one other case where there was a poisoning and that was the Zhang

case.

A Uh-huh.

MS. CHIN-CAPLAN: The Zhang case is contained at Exhibit 60.

SPECIAL MASTER HASTINGS: Tab 60?

MS. CHIN-CAPLAN: Tab 60.

SPECIAL MASTER HASTINGS: Okay.

BY MS. CHIN-CAPLAN:

Q This was a brain contamination case in China, wasn't it?

A Yeah. Let me just bring up my copy here.

Q With ethyl mercury? Yes?

A I think I have my own copy. Yes, that's right. This was a paper from 1984 from the Peoples Republic in China in Zhang of brain contamination with ethyl mercury.

Q Yes. Doctor, you stated in your opinion on page 17 that 40 of the 41 patients who were exposed, they improved or completely recovered despite the fact that they received estimated doses between 35,000 and 280,000 micrograms of ethyl mercury.

A Uh-huh.

Q Now, Doctor, 40 out of 41 did not recover, did they?

A I believe -- they went through the math --

that was the case. If I could take a look at my report there about this? What page are you on?

Q It's on page 256.

A Okay. What page of my report?

SPECIAL MASTER HASTINGS: Page 18 of your report.

THE WITNESS: Okay. Yes. Thank you. Let's see.

SPECIAL MASTER HASTINGS: Well, it's from 17 to 18.

THE WITNESS: Yes. I see. Thank you very much, Special Master. They improved or recovered.

BY MS. CHIN-CAPLAN:

Q If you look on page 256, the first full paragraph, it says in addition to the 27 cases treated with chelation there were 13 cases that were not treated. Two months later the untreated patients showed little improvement in symptoms and signs. One case deteriorated with the appearance of pathological reflexes. These results indicate that chelation therapy was valuable, albeit with a prolonged clinical course.

So long as mercury persists in tissues continued chelation therapy is recommended. So, Doctor, when you said 40 out of 41 improved that's not

true, is it?

A Let me take a look here. I have to go through the paper and see exactly what I was referring to here. It said one patient died, the other 40 patients still showed a variety of clinical manifestations after five months.

SPECIAL MASTER HASTINGS: Where are you reading from that?

THE WITNESS: That is on the bottom of page 253.

SPECIAL MASTER HASTINGS: All right.

THE WITNESS: So they had clinical manifestations at five months, but I think if you go through the paper that you will find that they were sicker when they came in.

BY MS. CHIN-CAPLAN:

Q Doctor, on page 256, didn't I just read to you that there were 13 cases that were not treated with chelation, two months later the untreated patients showed little improvement in symptoms and signs?

SPECIAL MASTER HASTINGS: That's at the top of page 256?

MS. CHIN-CAPLAN: That's correct.

THE WITNESS: In addition to the 27 cases --

there were 13 cases that were not treated. Two months later one case deteriorated. Right. That's at two months. Let me just take a look here. But then if you go to page 253 they talk about five months out, and they say the other 40 patients still showed a variety of clinical manifestations.

You look at these clinical manifestations, and so, yes, they still have some clinical manifestations. Some of them recovered, some of them still have clinical manifestations. They clearly did not appear to be as sick as when they came in.

MS. CHIN-CAPLAN: Okay. Special Master, I think this is a good time to break. I'm going to start another line of questioning.

SPECIAL MASTER HASTINGS: How long do you anticipate being? I didn't know if we should go through and finish with Dr. Brent.

MS. CHIN-CAPLAN: I may still have quite a bit.

SPECIAL MASTER HASTINGS: All right. Let's take our luncheon break at this point.

(Whereupon, at 1:10 p.m., the hearing in the above-entitled matter was recessed, to reconvene this same day, Friday, June 22, 2007, at 2:10 p.m.)

//

A F T E R N O O N S E S S I O N

(2:12 p.m.)

SPECIAL MASTER HASTINGS: All right. We're back from our luncheon break, and we're going to proceed with the testimony of Dr. Brent. Cross-examination by Ms. Chin-Caplan will proceed at this point.

Please proceed, Ms. Chin-Caplan.

MS. CHIN-CAPLAN: Thank you, Special Master.

Whereupon,

JEFFREY BRENT

having been previously duly sworn, was recalled as a witness herein and was examined and testified further as follows:

CROSS-EXAMINATION (RESUMED)

BY MS. CHIN-CAPLAN:

Q Doctor, in your opinion does mercury have an effect on the immune system at all?

A That's a very good question. The issue there is exactly the same as the other issues that we've discussed about this morning. It depends totally on the dose, and the circumstance of the exposure and the form of mercury. So, yes, at high doses mercury can effect the immune system in many different ways.

In contrast, there's no suggestion whatsoever that the doses of thimerosal that one receives through a vaccination would have an adverse effect on the immune system.

Q So you would admit that mercury does have an effect on the immune system?

A Under the appropriate circumstances of dose, yeah.

Q You mean there has to be a high dose to effect the immune system?

A It has to be a high enough dose to effect the immune system.

Q And do we know what that high enough dose is?

A Well, I think there's no question that it is considerably in excess of that which we get from vaccines because there's no evidence whatsoever of any protivation of the immune system associated with vaccines.

Q Okay. Have you read this article, which is Petitioners' Exhibit 81, *Effects of Mercury on the Immune System*?

A If I could take a look at the article I'll tell you. Thank you very much. The Powell article?

Q The sections on up until I would say

Section 3?

A Yes, I've seen this article.

Q Have you read it, Doctor?

A From page to page?

Q No, no.

A I've read it in the past, yes.

Q Okay. So, Doctor, this article, which is entitled *Effects of Mercury on the Immune System* by Michael Powell and Claire Holzman, does it indicate that low concentrations of mercuric mercury reduces cell viability as a function of glutathione content?

A Can you show me where you're reading from, please?

Q Sure. It's under two, Toxic Effects on Lymphoid Components and Immune Responses.

A Uh-huh.

SPECIAL MASTER HASTINGS: What page?

MS. CHIN-CAPLAN: On page 422.

SPECIAL MASTER HASTINGS: Thank you.

MS. CHIN-CAPLAN: You're welcome.

BY MS. CHIN-CAPLAN:

Q It says that, correct?

A I was trying to find the section that you just read.

Q Okay. Second sentence.

A Shenker and colleagues?

Q Yes.

A Used peripheral blood, mononucleo cells to argue that low concentrations of mercuric, that was mercuric chloride, reduce cell viability as a function of glutathione content with cells having low intracellular glutathiones, which is monocytes, being the most sensitive. You read that correctly.

Q Thank you. Doctor, in the next sentence doesn't it indicate that different members of the lymphoid cell population have different sensitivities to mercury?

A Sure.

Q So the monocytes are apparently the most sensitive, aren't they?

A Let's see. Well, once again, you're talking about micromolar concentrations here, so you have to bear in mind the concentrations that you're using. I can't imagine that following a vaccination how any of these cells could ever achieve an exposure to micromolar concentrations. Also, bear in mind that this is mercuric chloride. It's a totally unrelated form of mercury.

Q The reason we use these doses is so we can see a response. Isn't that correct?

A That's right. You have to get to a high enough dose so you can see a response because if you go down to a low dose there is no effect.

Q Now, this is from Dr. Aposhian's slide, page 6, and it talks about the sources and forms and mercury. We have mercury vapor, methyl mercury and thimerosal, correct?

A Well, he has methyl mercury, mercury vapor and thimerosal, right. Three of them. Right.

Q And thimerosal turns into ethyl mercury, which turns into mercuric mercury, which is what we're dealing with, correct?

A Well, yes and no. It's a small amount of the thimerosal will turn into mercuric mercury, yes.

Q Right. But as it becomes inorganic it's mercuric mercury?

A That small proportion that becomes inorganic is mercuric mercury, yes.

Q Right. And mercury vapor becomes mercuric mercury, correct?

A Some proportion of mercury vapor becomes mercuric mercury.

Q Yes. And methyl mercury becomes mercuric mercury?

A Much less so.

Q Yes. These are the organic forms. Ethyl mercury and methyl mercury are organic, and when they become inorganic they become mercuric mercury.

A They become mercuric mercury, right.

Q So we're looking at mercuric mercury, the inorganic form, correct, in this article?

A Right.

Q Right. Doesn't it indicate that the monocytes are the most sensitive to mercuric mercury?

A Sure, but at concentrations way, way in excess of anything that you'd ever get from a vaccine.

Q Okay. Then it indicates that the *B* cells are next most sensitive, correct?

A Yes.

Q Yes. And the least sensitive are the *T* cells?

A That's right.

Q So there's some hierarchy of sensitivity to exposure to mercuric mercury?

A To mercuric mercury, yeah. Relatively high concentrations of mercuric mercury.

Q Right. Doctor, if you'll go on to the next page. Actually, let's continue on in that sentence. It says electron microscopic examination of mercury killed cells reveals condensation and fragmentation of

nuclei and finally, loss of membrane integrity, features that are consistent with an apoptotic-like cell death. What does apoptotic life cell death mean?

A Well, cells can die in one out of two ways. There is a necrotic cell death and there is an apoptotic cell death. Necrosis is generally when something goes wrong that caused a cell to die. Apoptosis on the other hand is a natural process. It's one that we need to live.

It is also sometimes referred to as programmed cell death. All our cells are programmed to die so that they make room for new, healthy cells. A classical example is our skin cells. We're replacing our skin all the time. Because the top layers die by apoptosis we get nice, new fresh skin cells. We don't have the same skin cells we were born with.

It's why leaves fall off trees in winter. It's apoptosis. You know, our liver cells. You're constantly regenerating new, healthy cells from cells that have been around for a while, and get abused, and starting to function abnormally and then they undergo apoptosis. So apoptosis is a natural response, it's part of normal physiology, we'd be in big trouble without it and it is a preprogrammed cell death.

Q Okay. Does mercury lead to a cell death that resembles a natural cell death? Is that it?

A No. It depends on the concentration, it depends on the dose. If, for example, mercury is given in low doses you don't see an effect. If you get up to these kinds of doses on the other hand, these kinds of exposures, then what they're talking about here is that it induces apoptosis in these cells.

Q Okay. If you go to the very next paragraph it says that the lack of a toxic effect may not preclude significant functional impairment of a cell population. So even though it doesn't kill it it could effect the way it functions, correct?

A Well, they may, and I think this is indicating that it may or may not depending upon what the evidence is. It doesn't say it does. Once again, you know, it's all a question of dose because what they are talking about here, and once again, remember we're talking about mercuric chloride not thimerosal or ethyl mercury, and they're talking about doses that these cells would never be exposed to in the body.

Q Doctor, if you move on to page 425 of this article, the very first sentence, it says reductions in both humoral and cell-mediated immune responses.

That's both arms of the immune system, correct?

A That's correct.

Q In a number of species were reported following exposure to organic and inorganic mercurials. So whether it's organic or inorganic doesn't seem to matter, it affects both arms of the immune system?

A Well, that's true. You can get effects. They won't necessarily be the same, but you can definitely get effects with the various organic mercurials or the inorganic mercurials at the appropriate dose.

Q Okay. The mechanism by which mercury elicits immunosuppression, particularly its responses toward infectious agents, remains unclear and warrants further study. More recent studies, particularly in rodents, have suggested that the genetic background may be a key player in understanding how mercury can tilt immunoregulation towards immunosuppression or immunostimulation. I've read that correctly?

A Yes. You did it very well.

Q Thank you. You wouldn't disagree with that, would you?

A No. There's a lot of data on genetically altered rodent models that show unusual responses to

mercury, so no.

Q So your genetics can determine whether you're going to be resistent to mercury, or whether you're going to be immunosuppressed, or perhaps even whether you're going to tilt toward autoimmunity, correct?

A If you're a rodent.

Q Right. If you're a rodent.

A Yeah.

Q Okay. Now, there have been other articles written on mercury and its effect on the immune system, haven't there?

A There's a huge literature on mercury in the immune system.

Q Yes, there is, and you attached a few to your opinion letter, didn't you?

A I think so.

Q Yes, you did. On Attachment 51 there's an article by B.J. Shenker entitled *Immunotoxic Effects of Mercuric Compounds on Human Lymphocytes and Monocytes. I. Suppression of T-Cell Activation*.

SPECIAL MASTER HASTINGS: Which tab was that?

MS. CHIN-CAPLAN: Fifty-one.

SPECIAL MASTER HASTINGS: Thank you.

MS. CHIN-CAPLAN: You're welcome.

Are you there, Doctor?

THE WITNESS: Yes. I'm just looking to see if I have it on my -- yes.

BY MS. CHIN-CAPLAN:

Q Now, this article looked at methyl mercury and mercuric mercury, correct?

A Right.

Q And what it says in the middle of that paragraph is that both forms of mercury caused a dose dependent reduction in T-cell proliferation, however, the effect was dependent upon the presence of monocytes. In the absence of monocytes mercuric mercury enhances PMA induced T-cell proliferation.

So it sounds like here, Doctor, and please correct me if I'm wrong, if you don't have any monocytes your immune system is in more trouble than if it did have monocytes?

A Are you reading from the first page in the abstract?

Q Yes.

A Both forms of mercury? Hang on. Let me take a look. Here it is. Once again, remember this doesn't deal with ethyl mercury or thimerosal, and of course there's no dose discussion here, but, yeah, you

can get a diversity of effects. Certainly.

Q Okay. In this article it also indicates that methyl mercury is five to 10 times more potent than mercuric mercury, correct?

A You're still on the first page?

Q Still first page.

A In this particular scenario that they've described in the prior sentence, yes.

Q Right. Five to 10 times more potent.

A Right.

Q So the organic methyl is five to 10 times more potent than the inorganic mercuric mercury?

A Right.

Q Okay. Doctor, if you go on to the next page it says at the very top there the results of this investigation clearly show that mercury-containing compounds are immunomodulatory; moreover, the decrease in T-cell function following exposure to mercury indicates that this metal is immunotoxic at very low exposure levels. I read that correctly?

A You've read that correctly.

Q Do you agree with that?

A Well, once again, they didn't define what they mean by very low exposure levels. I point out again this has never been shown, that the exposure

levels you get from ethyl mercury in the vaccine, but it depends on how they're defining low exposure levels. I don't think they had the vaccines in mind when they wrote this.

Q I agree with you. All right. So let us continue, and actually, it's an article that dates back to 1992, correct?

A It is.

Q At that time it was unknown that vaccines contained mercury. Isn't that true?

A It was unknown that the vaccines contained mercury?

Q Right.

A No.

Q In 1992?

A In 1992, of course it was known.

Q It was known?

A Yes.

Q Okay. So, Doctor, if you continue on in the introduction, the third sentence. Epidemiological surveys and laboratory studies have shown that when individuals are exposed to low concentrations of heavy metals the clinical symptoms appear to be "silent" or asymptomatic. However, when the health status of asymptomatic subjects is followed for long time

periods, there is clear evidence of tissue or organ dysfunction.

A Well, I have no idea what heavy metal they're talking about here. I can't think of a single paper with mercury that would suggest this, and certainly there's no reference here for what they're talking about.

Q Well, Doctor, this article is on mercuric compounds, isn't it?

A Yeah, and they talk about heavy metals. They don't talk about mercury here.

Q Isn't mercury a heavy metal?

A Yes, but not all heavy metals are mercury.

Q True, but don't most heavy metals have an effect on the immune system?

A At appropriate doses most heavy metals have effects on the immune system, yes.

Q Okay. Then, Doctor, further down in the third paragraph there's a very long list of what studies of mercury immunotoxicity have indicated could occur, right?

A Right.

Q It says Nakatsuru demonstrated that murine lymphocytes when cultured with mercurials mitogen induced DNA synthesis was inhibited, correct?

A Right.

Q And methyl mercury was 10 times more potent than mercuric mercury?

A Uh-huh.

Q So the organic was 10 times more potent than the inorganic, but the inorganic still had an effect?

A The methyl.

Q Yes. Then Nordlind demonstrated that both murine thymocyte and splenocyte DNA synthesis were inhibited by mercuric mercury. When they say thymocyte and splenocyte are they referring to the organs the thymus and the spleen?

A They are referring to the cells of the thymus and the cells of the spleen.

Q And those are immune forming cells, aren't they?

A More the spleen cells than the thymus cells.

Q They are? They're part of the immune system?

A Yeah.

Q So the cells producing are effected according to this individual?

A Well, you know, once again, I think we can go through many, many, many papers on mercuric chloride, and methyl mercury and the effects on the

immune system. There's a huge literature out there. That literature all says yeah, there's a lot of effects of methyl mercury, there's a lot of effects of mercuric chloride on the immune system.

But that is not ethyl mercury, it's not even thimerosal, and none of this really indicates doses of exposure that you'd expect to see with a vaccine. So we could spend a lot of time going through all these articles, and I will endorse all these statements, but they're completely irrelevant to what we're discussing today.

Q Okay. So your opinion is that all the past literature that's been done on organic mercury and inorganic mercury have no relevance to the ethyl mercury that is contained within the vaccines that eventually turn into inorganic mercury? Is that what you're saying?

A I'm saying that if you want to enlighten this discussion in the true scientific fashion about what happened with ethyl mercury at doses associated with vaccines then we should discuss literature on ethyl mercury at exposures we see with the vaccine. Now, I don't think we're going to have that discussion and the reason being there are no papers that show any adverse effects.

So we can go through the exercise of talking about mercuric chloride, talking about ethyl mercury and talking about high doses if you'd like, and I will agree with all these statements to make it easier for you.

Q Okay. Good. Then we can agree, also, that *T* lymphocyte functions are effected in their responses to mitogens and that mixed leucocyte responses were depressed in mice and rats given mercuric chloride in their drinking water or by subcu injection, correct? We can agree on that then?

A That's probably true.

Q Yes. And we can also agree then that when they state all our results indicate that low doses of mercury have a profound inhibitory effect on human *T* lymphocyte activation. We can agree on that?

A Where are you reading from?

Q That's on page 541.

A You jumped ahead of me there. Right. So the mercuric chloride and methyl mercury under circumstances and doses not associated with vaccines, but yeah, so I think that's probably true what they say.

Q Okay. So loses doses of any other mercury can effect the immune system?

A No. We're talking micromolar doses here. I don't think these are exposures that you're going to get even if this was ethyl mercury.

Q Okay. But it says low doses, correct?

A Yes.

Q Of mercury?

A Correct, but not as low as vaccines.

Q So any other mercury other than ethyl mercury can have a profound inhibitory effect on human *T* lymphocyte activation?

A You can see effects with ethyl mercury, too, but also at doses far in excess of what you get from a vaccine.

Q Okay. Doctor, if we go on to the next article, which is again an article by Shenker, and we'll just do this very briefly.

A That's okay.

SPECIAL MASTER HASTINGS: When you say the next article?

MS. CHIN-CAPLAN: Attachment 52.

SPECIAL MASTER HASTINGS: All right. Thank you.

THE WITNESS: That's okay. Take your time.

BY MS. CHIN-CAPLAN:

Q Now, this study is a little bit of an

expansion from the last one, isn't it?

A I'll tell you in a second. They're both the 1992 Shenker article. Okay.

Q Okay. It's a little bit of an expansion?

A Well, it looks like the same experiment. They're talking about two different aspects of the same experiment, the first dealing with immunosuppression and the second dealing with alterations in cell viability.

Q Right. The last one didn't indicate how long it took for these cells to be effected, did it?

A As I recall in the last one if you took the methyl mercury and you applied it to mitogen, because remember this is mitogen stimulated cells, so you put the mitogen on, stimulate the cells. Put the mitogen on and methyl mercury on at high doses, then you get suppression of cell stimulation.

However, once you go out a couple of hours that suppression is lost. In fact, if you look at this first Shenker article once you go out about 24 hours that suppression is totally 100 percent gone. So this is a very, very trenchant effect that has no persistence in terms of time.

Q Well, this Shenker article doesn't say that, though, does it?

A I think it does. In one of the Shenker articles it does, and I believe it was this one. Yeah.

Q This is the *Immunotoxic Effects of Mercuric Compounds on Human Lymphocytes and Monocytes. Alterations in Cell Variety*.

A No, and I said if you look at the first article, the one on suppression, you can see that. That's in Figure 3 of the article.

Q Okay. But in this article, Doctor, in the abstract it says following treatment with mercuric mercury or methyl mercury there was minimal reduction in lymphocyte viability at one to four hours. However, after exposure to mercury for 24 hours cell death was apparent. In comparison, monocytes exhibited significant loss of viability during the early exposure period.

Again, it says methyl mercury is five to 10 times more potent than inorganic mercury, correct?

A I think at these concentrations it's probably true.

Q So, Doctor, you would agree then that mercury does have an effect on the immune system?

A I think I've been saying that all along, at the appropriate dose, conditions --

Q Now, your contention is that this does not involve ethyl mercury?

A Well, I have two concerns about a dialogue about this data as it applies to the questions that are relevant to these proceedings. One is that we're not talking about ethyl mercury, and the second is that we're not talking about exposures that are related to exposures that you get from the vaccine in terms of dose and concentration.

Q So, Doctor, if you had designed the experiment what would you design it as?

A Well, I would do a number of things. The first thing I would do is I would begin the way you begin in science with cheap and dirty to see if there's anything there, and so I would do an in vitro experiment just to see if there's anything there to test in the animal like the Agrawal study.

Now, in doing that the Agrawal study clearly demonstrated -- except I would have done it with ethyl mercury, but they used thimerosal -- that at exposures you get from thimerosal the doses don't have an immune effect, so at that point I would stop. I would say we don't even see it in this in vitro study, we're certainly not going to see it in the animal.

Although, the one thing I would have done

different is I wouldn't use ethyl mercury, I would have used a more relevant exposure. So I think the best data we've had is that it doesn't happen, but if you want to do the perfect experiment that's the way I would do it.

It's also perfectly possible to assess immune parameters in thimerosal exposed people. That can be done. It's very easy to do. We're still exposing people to thimerosal. I had a patient about two weeks ago who had a rattlesnake bite, and the rattlesnake antivenom that we use has thimerosal in it, and we gave it to the patient.

There's patients out there. A lot of people all over the world are being vaccinated with thimerosal containing vaccines. So it's very easy even in humans to study various parameters of the immune system and to assess whether you see an adverse effect associated with thimerosal administration, but there's not one documentation that there is.

Q Now, Doctor, you indicated that the Agrawal study involved thimerosal?

A Thimerosal.

Q Yes. Were you present when Dr. Aposhian indicated that thimerosal turns almost instantly into ethyl mercury and these other components?

A Well, we know that happens in the body. In fact, some of it happens in the bile as I testified to before. Whether that happens under the conditions of the Agrawal experiment is not clear, and they did not assay that.

Q Okay. When you talk about doing a study of thimerosal ethyl mercury in the individual how would you account for the fact that some people might be more susceptible than other people?

A Well, I think if you're saying if we wanted to determine if there's a susceptible population, I mean, nobody's ever suggested or given data that there was a susceptible population, but if we wanted to go and investigate this further we'd just take a bunch of people being immunized maybe in parts of the world where they're still using thimerosal and assess their immunological parameters.

Q Now didn't the earlier Shenker article indicate that people who are affected by mercury might be more susceptible than others or cells rather?

A Different types of cell types have different susceptibilities.

Q Uh-huh. But didn't it also indicate that individuals might also be more susceptible as in hypersusceptibility?

A As far as we know, there is no hypersusceptible individual population. That is strictly speculation.

Q So you wouldn't say that there's a genetic makeup that might make people more susceptible than others to the effects of mercury?

A I know of no genetic finding that supports that with the single exception of some very preliminary findings on the CPOX 4 gene which really have to do with porphyrin synthesis, and it's still a gene that's present in a very large proportion of the population compared to a typical hypersusceptibility seen that's present in 12 to 15 percent of the population.

Q So roughly 15 percent of the population might be more susceptible to the effects of mercury? Is that what you just said?

A No. Roughly 12 to 15 percent of the population will have a pattern of porphyrin synthesis when exposed to mercury different from the other 85 percent.

Q What does that mean?

A As far as we know, nothing.

Q As far as we know, nothing?

A (Nonverbal response.)

SPECIAL MASTER HASTINGS: I'm sorry. You need to say yes.

THE WITNESS: Yes, that's correct. As far as we know, nothing.

BY MS. CHIN-CAPLAN:

Q Now, Doctor, you had talked about the Holmes study in your presentation today.

SPECIAL MASTER HASTINGS: The which study?

MS. CHIN-CAPLAN: Holmes study.

SPECIAL MASTER HASTINGS: Holmes.

MS. CHIN-CAPLAN: Holmes, yes. I'll find the citation for you. It would be Tab 27.

SPECIAL MASTER HASTINGS: Of his?

MS. CHIN-CAPLAN: Of his.

SPECIAL MASTER HASTINGS: Thank you.

MS. CHIN-CAPLAN: You're welcome.

BY MS. CHIN-CAPLAN:

Q Now, Doctor, we've already talked about this or you've talked about it already in your presentation today, correct?

A That is correct.

Q You indicated they hadn't been reproduced at all. Is that true?

A That's right. That there was no public study that supports it. Dr. Aposhian mentioned the Hu

study, but we had talked about the Hu study and it clearly does not support the Holmes study.

Q Okay. Nobody's reproduced the study is what you said, right?

A Well, people have tried. They haven't gotten the same results.

Q You're probably referring to Ip, correct?

A And Kerns.

Q And Kerns. Okay. Now, in the Holmes study she looked at first baby haircuts. Isn't that true?

A That's correct.

Q Before she looked at first baby haircuts didn't she just look at the haircuts of the children at the time that she saw them?

A I don't recall. Is that in the paper?

Q Yes, it is.

A Where is that?

Q On page 278. If you go down to the first column, the next to the last paragraph, it begins with in a clinical practice one of the study authors submitted hair samples from autistic patients for commercial laboratory testing for toxic metal exposure. Most of these mercury hair levels were found to be low contrary to a first order hypothesis of heavy metal toxicity in autism.

She then asked patients to submit first baby haircut samples for analysis thereby testing a sample that would more accurately reflect early exposure, correct?

A Uh-huh.

Q Now, hair grows at approximately, what is it, half inch a month?

A A centimeter a month, yeah.

Q So if you had a seven year old child the hair that you need to be testing would be how long?

A No. Are you talking about the fact that it would be to get the baby hair?

Q Yes.

A It's clearly not baby hair.

Q Yes. It's clearly not baby hair?

A Right.

Q So when she tested hair that was not baby hair she got virtually nothing?

A Well, no. She says right here that when she tested hair samples in general the results were very low, and then she reports in which on her first baby hair test the results are very low. So she's saying here that general hair does the same thing as the baby hair tested.

Q Okay. When you look at Ip, does Ip look at

first baby hair?

A No.

Q Ip looks at hair that's of seven year old children, don't they?

A I can take a look at the paper. Let's see if I have a copy on my computer.

Q It's the next one. It would be Tab 32.

A Okay. 7.2 years for the autistic spectrum disorder group and 7.8 years for the control group.

Q Were they, what, seven years old?

A Approximately.

Q So at seven years old the hair that they would need would have to be very long, wouldn't it?

A It's not baby hair.

Q Right. It's not baby hair.

Q So it would be hard to say that this really contradicts the Holmes study, wouldn't it?

A I think it definitely contradicts the Holmes study because even Holmes as you have pointed out showed that when you don't look at baby hair she thinks that the results are very low, and here we see, no, you just track these cases seven years and the results aren't very low.

Q Now, would you go to Kerns? I'm sorry. Kerns is 34. Is Kerns a hair test? It's a hair

study?

A Yes.

Q It is a hair study?

A Yes.

Q Yes. But it looked at heavy metals in general, didn't it?

A Heavy metals including mercury.

Q Right. If you look at the abstract doesn't it indicate that the evidence from our study supports the notion that children with autism may have trouble excreting these metals resulting in a higher body burden that might contribute to symptoms of autism?

A Hang on a second.

Q It does say that in the abstract, right?

A Hang on a second. I'm just bringing up my copy of the paper here. Okay. I'm sorry. You were looking at the abstract?

Q Yes.

A Right, but not mercury. He was talking about arsenic, cadmium and lead were significantly lower in the hair of children with autism than in matched controls. With mercury there was no difference.

Q So everything other than mercury?

A In this particular study. Now, another

study has contradicted even I believe the arsenic, cadmium and lead data.

Q Okay. So, Doctor, there's one study that you didn't mention that Dr. Aposhian did mention, and that was the Adams tooth study.

A Yes. Okay.

Q In the Adams tooth study wasn't there the indication that the teeth of autistic children had two times more mercury than controls?

A Well, that's what they reported. Let me pull out the study because I'd like to make a couple of observations about that study. I'm very familiar with that study, and there's a couple of things about it I want to point out.

SPECIAL MASTER HASTINGS: Does anyone have the citation from our record? Thank you. Petitioners' Exhibit 82 I believe.

(Pause.)

BY MS. CHIN-CAPLAN:

Q Doctor, my question to you was wasn't it shown in this article that autistic children had two times the amount of mercury in their teeth as opposed to normal children?

A Well, that's what they reported.

Q Okay. And would that be an indication that

autistic children have difficulty excreting mercury?

A No, for a number of reasons. Number one, teeth, like hair, are not a normal excretory organ for mercury. We don't lose a lot of mercury through our hair. Teeth specifically, you know, a tooth is basically bone. It's basically bone. We don't incorporate mercury very much into bone, so I'm not exactly sure what they're even looking at, but it's just the opposite of what they see in hair.

I mean, the Holmes people have reported, although it couldn't be replicated, that there's low release of mercury through the hair. Even if that were true how do you reconcile it with this study which shows there's an increased release of mercury through the teeth? It doesn't make any sense. Now, the truth is with this study I'm not sure their results are statistically significantly different based on the statistical tests they did because they do have an error in their statistical methodology.

I don't know if you want me to go into it. I'll be glad to if you'd like.

Q Doctor, you're saying that teeth are an excretory organ?

A No.

Q It's tissue, isn't it?

A Teeth, like hair, are not excretory organs for mercury. It is known that some organic mercury gets incorporated in hair. Teeth is more analogous to bone, and you don't usually get mercury in bone.

Q It's tissue, correct?

A Well, it's a tooth.

Q Yes. It's tissue, and it's tissue that contains two times more mercury in autistic children than in that of normal children?

A Well, I'm not sure it's even a statistically significant difference. The group size is small. I can go into that if you'd like, and it doesn't have any meaning. If anybody wanted to know do autistic children have more mercury than nonautistic children all they have to do is get blood levels or get urine levels on the autistic children.

I mean, I know so many autistic children have had this done. Nevertheless, there's not one single study in the peer-reviewed English language literature that reports a difference in blood mercury level in autistic children or in urine levels in autistic children compared to controls, and so I don't know what to make of it. Teeth. It doesn't make any sense. I'm not even sure it's a statistically significant difference.

Q Now, Doctor, you're familiar with the Burbacher study, aren't you?

A Burbacher study? Yes.

Q Burbacher study. Yes. That was a study done on primate monkeys?

A Yes.

Q That was a situation where they tried to recreate the vaccine schedule. Was that it?

A Yes.

MS. CHIN-CAPLAN: Let me find it for you. Twelve.

SPECIAL MASTER HASTINGS: I'm sorry?

MS. CHIN-CAPLAN: Twelve.

SPECIAL MASTER HASTINGS: Tab 12.

MS. CHIN-CAPLAN: Yes.

SPECIAL MASTER HASTINGS: Of Dr. Brent?

MS. CHIN-CAPLAN: Dr. Brent.

SPECIAL MASTER HASTINGS: All right. Thank you.

BY MS. CHIN-CAPLAN:

Q So, Doctor, tell the Court what this study consists of.

A Sure. I would be glad to. Thank you. This was a comparison of mercury levels in infant monkeys who were given either dietary methyl mercury or

intramuscular thimerosal as in a vaccine. They did the intramuscular injections once a week and gave over a period of about three weeks roughly the amount of thimerosal that an infant would receive in about six months of vaccinations on a per kilogram basis.

Then they assessed the kinetics of what happened following the exposure. In other words, where the mercury went, what the rate of excretion was, what was left behind, half-life, that kind of thing.

Q They found out what the half-life was in the primates at least for ethyl mercury, didn't they?

A Right.

Q And it was comparable to what has been noted in humans, correct?

A Very, very close. It was about eight days.

Q Yes. Did they measure the amount of mercury that was in the brain?

A Yes, they did.

Q When they measured the amount of mercury that was in the brain what was the comparison between the inorganic mercury from methyl mercury exposure and that of ethyl mercury exposure?

A Well, it depends on the timeframe. Ethyl mercury entered the brain and then effluxed from the

brain.

Q It what?

A Effluxed. Left the brain. The other process that goes on for both methyl mercury and ethyl mercury is that there is some deorganification of the mercury. In other words, it becomes inorganic mercury. It happens a little bit more with ethyl mercury than with methyl mercury. So as time goes on there is faster loss in the brain with ethyl mercury than with methyl mercury, but there's also faster conversion of ethyl mercury to inorganic mercury in the brain.

Q And the conversion of organic to inorganic in the brain occurred with roughly three times the amount for ethyl as opposed to methyl, wasn't it?

A I can give you the exact amount. Let me just take a look here. It was more like twice the amount, but you might be right. I'm just trying to see where I can find it here in the paper. Well, I can't find it right now. Instead of taking time looking for it I thought it was twice as much, three times as much, that ballpark.

Q Around three times more?

A Two or three times. Yes.

Q Right. So, Doctor, once it turns into

mercuric mercury or inorganic mercury in the brain can it leave?

A There is an efflux. It's very, very, very slow.

Q Dr. Aposhian had given this example about a family who ate a pig that drank mercury, and when the woman died 29 years later the mercury was still 100 times the normal amount that was seen.

A Yeah. This is a very highly exposed population. They had a huge exposure to mercury, and a number of the family members died and there's one survivor who when she ultimately died still had a significant amount of mercury in her brain. That's correct.

Q So inorganic mercury can be pretty toxic to the brain, correct?

A Well, not necessarily. You wouldn't necessarily expect that because the bad news, Ms. Chin-Caplan, is that you, and I and everybody else in this courtroom have nontoxicologically consequential but significant amounts of inorganic mercury in our brain. As a matter of fact, every time we eat a seafood meal we're getting a bolus, some of which becomes inorganic mercury in the brain.

We know that if people ate through both

their diet, maybe to some degree from their dental amalgams if they have it and from just the air around us, which has mercury in it, we naturally accumulate mercury in the brain, which becomes inorganic mercury and stays there for a very long time, and that has no pathological significance at all.

It doesn't cause an adverse effect unless you get to very high levels, and there have been multiple studies demonstrating that. So, yes, you get inorganic mercury in your brain. You get inorganic mercury in the brain from many, many, many different sources. Not only people, every animal on the Earth has a significant amount of inorganic mercury in the brain because mercury is a naturally occurring substance. It's in the air.

We've all developed very sophisticated mechanisms to inactivate the mercury in the brain, and you only actually can get an adverse effect from the inorganic mercury in the brain if you have so much in your brain that you overwhelm the very well-developed defense mechanisms that we have.

Q Now, Doctor, you're a pediatrician, correct?

A I'm a toxicologist.

Q Did I also hear you say that you were a pediatrician?

A I'm a professor of pediatrics, but I'm a medical toxicologist.

Q Okay. You do know that the nervous system and the immune system of infants are continuing to develop for the first two years of their lives, correct?

A To some degree.

Q Yes. And during those first two years is the same time that the thimerosal containing vaccines are being administered, correct?

A They were.

Q Yes. So these vaccines are being administered at one of the most vulnerable periods in their lives?

A Yes, that's right, but very unlikely with any ill effect.

Q How do you know that?

A Well, number one, there has never been, other than the very, very rare allergy -- we're not talking about allergy, you can get allergy with any medication, I assume you don't want to talk about that -- a demonstration that thimerosal in doses in vaccines given to infants causes an adverse effect.

As you know this has been extremely well-studied, this has been extremely well-scrutinized and

as a matter of fact it wouldn't even be plausible, and I'll tell you why. It's a very interesting analysis that was just published from Brazil where their immunization schedule using thimerosal was pretty much similar to the United States.

Q Did you say McGill?

A Brazil.

Q Brazil?

A Yes. The country Brazil. They looked at the mercury exposure from breast feeding, and they breast feed about the same amount in Brazil as they do here, and from the thimerosal in the vaccines. It turns out there's twice as much mercury exposure from breast feeding as there is from ethyl mercury in the vaccines.

So it's hard to imagine how the amount of mercury that we get from breast feeding is going to have an adverse effect or that the amount of mercury that we get from vaccines is going to have an adverse effect.

Q Well, Doctor, you are aware that there's at least one breast feeding study that was done from the Iraqi grain contamination cases, aren't you?

A Well, yeah, but those were very, very highly exposed individuals.

Q You must know that those babies did not demonstrate ill effects for quite some time after they were exposed?

A That's true, but this was following a very large exposure. We've had a number of epidemiological studies now, which I think will be discussed on Monday, where children have been followed for long periods of time following their thimerosal containing vaccines and at least with regard to the question of autism or ASD there's clearly no relationship based on --

Q Well, when you say there's no relationship you're relying solely on the epidemiological studies? Is that it?

A I'm relying on the epidemiological studies and the fact that there's nothing to the contrary that suggests there is a relationship.

Q However, the molecular study seems to indicate that there is an effect, doesn't it?

A What molecular study?

Q Well, the studies that we looked at on the immune system.

A At high doses of mercury chloride or methyl mercury?

Q Yes, those studies.

A Well, no. You can't translate that to say that low doses of ethyl mercury are going to have an effect.

Q So you disagree with the statement earlier that people could be asymptomatic from low doses, but that further on in their lives that it would result in symptomatic disease?

A Which statement was that? Was that the reference statement about heavy metals? Is that what you're referring to?

(Pause.)

Q Maybe it's Shenker. Yes, it's in Shenker.

A Was that the reference statement about heavy metals?

Q Yes. It was on Tab 51 on page 540, and you've already indicated with me that you agree with these statements.

A Let me just take a look here.

Q It says epidemiological surveys and laboratory studies have shown that when individuals are exposed to low concentrations of heavy metals the clinical symptoms appear to be silent or asymptomatic. However, when the health status of asymptomatic subjects is followed for long time periods there is clear evidence of tissue or organ dysfunction.

A That's a heavy metals statement, it's not a mercury statement and it's completely unreferenced. I have no idea what they're talking about.

Q Of course, the title of this article is *Immunotoxic Effects of Mercuric Compounds*, correct?

A That's true. If they were talking about mercury here in a specific study they would have said mercury, and they would have cited the study.

Q So the fact that the title was on mercuric compounds and they mentioned heavy metals makes you think it's not mercuric compounds that they're talking about?

A I think what they were trying to do is try to generalize some other heavy metal and relate it to mercuric compound.

Q Is there any reason to believe that mercury does not act in the same manner as these other heavy metals?

A Absolutely there are. There are no two heavy metals that I can think of that have a similar effect on the immune system. All of them at appropriate doses will potentially have adverse effects on the immune system, but they're different, just like even different forms of mercury have different effects on the immune system.

MS. CHIN-CAPLAN: Okay. Thank you, Doctor.

THE WITNESS: Thank you.

SPECIAL MASTER VOWELL: Dr. Brent, I have a number of questions for you. This is Special Master Vowell speaking.

THE WITNESS: Please.

SPECIAL MASTER VOWELL: You've used two terms, as did I believe Dr. Aposhian, efflux and hypersusceptibility. Would you define those terms for me, and are you both using them in the same way?

THE WITNESS: Thank you very much for asking that question. That's a great question. Efflux. I'm not sure how Dr. Aposhian viewed efflux, but from the context in which he was talking it was clear by the fact that he was stating that he was discussing the hair studies of Amy Holmes and the chelation study of Bradstreet, and in fact he pretty much came out and said this, and it's certainly what he said before the IOM, that autistic children do not excrete mercury well.

When we talk about in biological processes molecules moving from one place to another they either move in or they move out between compartments, and efflux is basically moving out meaning out of the body in this case. So his efflux disorder hypothesis is

that the hair studies of Holmes and the chelation study of Bradstreet are pointing to the fact that these kids don't excrete mercury, don't efflux it out of their bodies.

SPECIAL MASTER VOWELL: So they retain it, and therefore more would be available to work its ill effects on whatever system we're talking about?

THE WITNESS: That's exactly the hypothesis. Precisely. Now, hypersusceptible, Dr. Aposhian did not really define what he meant by hypersusceptible other than, and this is what I infer from his testimony, some hypothesized group of children that react to mercury to get toxic at doses that nobody else in the world would ever get toxic to, so they're hypersusceptible.

Because of that ambiguity in that testimony is one of the reasons I drew up that bell-shaped curve with the second curve showing the hypersusceptible population.

SPECIAL MASTER VOWELL: Yes.

THE WITNESS: There is a formal toxicological concept of hypersusceptibility, and that's what I tried to illustrate by those curves and to say that when there is a hypersusceptible population we have a way of looking for it, we know

exactly what it is, although they've never been found in the autistic group with regard to mercury.

SPECIAL MASTER VOWELL: That was the example I think you used of Wilson?

THE WITNESS: Yes. That's exactly right. That where there is hypersusceptibility to toxins very often with not too much research we've actually identified the hypersusceptibility. Wilson's disease, hypersusceptibility to copper. We know the gene. It's very clear. You can do a genetic test. They either have it or they don't.

SPECIAL MASTER VOWELL: Bear with me for a minute here.

THE WITNESS: Take your time.

SPECIAL MASTER VOWELL: In Dr. Aposhian's testimony he talked about one in 500 children exposed to the teething powder that caused acrodynia or Pink disease developing the disease. Do you know how that figure was derived, the one in 500?

THE WITNESS: Yes. Yes, I do. That I believe derives back from one of the Dr. Warkany articles.

SPECIAL MASTER VOWELL: Doctor? I'm sorry?

THE WITNESS: Warkany, W-A-R-K-A-N-Y.

SPECIAL MASTER VOWELL: Okay. The third

exhibit?

THE WITNESS: Yes. Well, he wrote a couple of articles. I'm not sure if it's that exact one, but it's from that body of research. That number has been carried forward and requoted in the literature. Basically, what that number is is that if you look at kids who were exposed to mercurous chloride from the teething powder not all of them get mercury toxic in the form of acrodynia, only some of them do.

There are two potential explanations for that. One is that it's a hypersusceptible population that does, and the other, which would be the more common reason in toxicology, is it's simply a matter of dose. Some got more, some got less, and it's only the ones that got quite a lot that came down with the disease, so they got the high dose.

In fact, looking at that Warkany study that the Court now has come up with that clearly demonstrates that the children who get acrodynia have very, very high mercury levels, so it appears to be just simply a dose-related phenomenon. The reason that not everybody got it is you had to get a significant dose.

SPECIAL MASTER VOWELL: So you're not aware of any study that looks at a dose response level to

teething powders?

THE WITNESS: No. There's never been a dose response level. We only have the study that shows that children that have it have a very high fiber in terms of urine mercury, but it's never actually been looked at in terms of a formal dose response analogy.

SPECIAL MASTER VOWELL: Right. And this was not a study then that said of 2,000 children in this town, assuming all of them were teething and got teething powders, one in 500 developed this disease?

THE WITNESS: No.

SPECIAL MASTER VOWELL: Okay. All right. Let me move on to a couple of other questions then. One is the term used in much of the medical literature you and Dr. Aposhian cited to refer to toxic I guess levels of mercury is mercury intoxication. Does that term have -- at some point you can say someone is mercury intoxicated? Can you explain that term for me?

THE WITNESS: Absolutely. Intoxication simply means having enough of the substance on board that it is causing some kind of an adverse of a toxic effect. Classic example is alcohol. We use the word intoxication all the time. You just have enough on board, you get alcohol intoxicated, then you start to

stagger and so on.

So toxicologically when you use the word intoxication it simply means you've had a sufficient exposure, you've had a sufficient dose, such that you are now getting adverse effects from that substance.

SPECIAL MASTER VOWELL: Well, let me follow-up on that compared to my previous question then.

THE WITNESS: Sure.

SPECIAL MASTER VOWELL: One of us could have four drinks and the other have two drinks, each drink containing the same amount of alcohol, and we would have different reactions. One of us with four drinks might be able to walk a straight line. If I had two I'm sure I couldn't. Can you analogize the effects of alcohol intoxication to mercury intoxication?

That if someone who is, for example, more used to drinking, can walk that straight line at a higher level of alcohol?

THE WITNESS: Yes. This is the bell-shaped curve that we were talking about that if you look at the dose of a substance, in this case alcohol, necessary to cause a specific response, say walk a straight line, that it's not going to be exactly the same for everybody in the population, and that if you look at enough people in the population it forms sort

of this bell-shaped curve where most people are going to sort of be in the middle, two to three drinks probably do it for most people, but for some people it could be seven and for some people it could be one. So that's how this curve --

SPECIAL MASTER VOWELL: Okay. I'm not articulating this well because I understand that. What I'm getting at is if I'm used to drinking a great deal and then I have two drinks the alcohol might have a less apparent effect on me.

THE WITNESS: That's true.

SPECIAL MASTER VOWELL: So if someone is exposed to low levels of mercury over a period of time would they show intoxication, that is ataxia at the same blood or urine mercury levels as someone else who is getting a bolus dose?

THE WITNESS: I'm sorry. I misunderstood your question. With alcohol there is a very well-known phenomena, which I think everybody has had a chance to see in people who drink a lot, it's known as tolerance, where some people one or two drinks and as we were saying you have an excess, but if people drink quite a bit that curve shifts for them and they develop a tolerance.

They could have six or seven drinks and, you

know, we'd never know they were drinking. That's tolerance. It happens with alcohol, well, for several reasons, metabolic adaptations and so on. There is no similar tolerance with mercury. There are some minor adaptations, but for the most part there is no similar tolerance for mercury.

We already have our body's protection in place and they can up regulate and down regulate a little bit, but they don't change in a marked fashion.

SPECIAL MASTER HASTINGS: So while people might fall at a different place in the bell curve the fact that you were working at a thermometer manufacturing plant would not have any effect on where you would fall on that bell curve?

THE WITNESS: That's exactly right.

SPECIAL MASTER VOWELL: Okay. You've indicated the different species of mercury have different effects. At the level of intoxication how are the effects of methyl mercury distinguished from ethyl mercury in terms of clinical signs and symptoms?

THE WITNESS: Yeah. That's a very good question. This might be in the record. There was a major review on this subject by Tom Clarkson where he had listed all the different kinds of mercury and the clinical effects of the different kinds of mercury to

show how different they are. My reading of that review is that it is a very good reflection of what I believe to be in the literature.

So, for example, with methyl mercury almost all of the effects are in the central nervous system, in the brain, as with methyl mercury. With ethyl mercury because of the rapid separation of the mercury off the ethyl group then it generates this inorganic mercury as we were talking about before. Inorganic mercury tends to effect primarily the kidney.

That doesn't happen much with methyl mercury. So with methyl mercury we would see at high doses effecting the brain, low doses don't worry about having your seafood dinner tonight, it's good for you. Ethyl mercury on the other hand, similarly at high doses you could see the effects in the brain if you have a sufficient dose, but you will also see effects of the kidney.

SPECIAL MASTER VOWELL: All right. Let's leave aside the things that we're not going to observe with our eyes. Let's just talk about the clinical picture of the Iraqi farmer who ate the methyl mercury contaminated wheat walks into a medical clinic along with the Chinese farmer who ate the ethyl mercury contaminated rice. How are their symptoms going to

differ at the level of intoxication?

THE WITNESS: Their central nervous system symptoms would probably be the same, the tunnel vision would probably be the same, the tremor would probably be the same, the paresthesias would probably be the same, but you would also see some renal effects, abnormal renal function, in the ethyl mercury exposed version.

SPECIAL MASTER VOWELL: Okay. Are the amounts of ethyl mercury that would produce those physically apparent toxic effects the same amounts as ethyl mercury?

THE WITNESS: As methyl mercury?

SPECIAL MASTER VOWELL: Yes, as methyl mercury.

THE WITNESS: Right.

SPECIAL MASTER VOWELL: I mean, if we're comparing grain, rice, wheat, whichever we're eating, does the amount of the ethyl mercury in the rice differ from the amount of methyl mercury in the wheat --

THE WITNESS: Yeah. That was well-covered in the Burbacher paper that we were just discussing because one of the things that they considered was this whole business about the difference between the

reference dose for methyl mercury in application to ethyl mercury, and he pointed out that if you use the reference dose for methyl mercury and apply it to ethyl mercury you will over estimate its toxicity compared to what it really is because you would expect the ethyl mercury to be less toxic.

SPECIAL MASTER VOWELL: Okay. So if I understand what you're saying it would take more ethyl mercury to produce the same effect that you would see with a smaller amount of methyl mercury?

THE WITNESS: Right. And in fact, that's only experimentally shown. Laslo Magos published a paper in 1985 where he gave animals equivalent doses of methyl mercury and ethyl mercury and then higher doses, and he showed that you need more ethyl mercury to get a degree of damage to the brain than you need methyl mercury.

SPECIAL MASTER VOWELL: If I ingest a certain amount of ethyl mercury versus having it injected, how does that impact the toxicity of the substance?

THE WITNESS: Well, the toxicity will depend on the blood level, and so you would probably get a little higher blood level from an ingestion than you would from an injection.

SPECIAL MASTER VOWELL: I'm talking about intramuscular injection.

THE WITNESS: That's exactly right. The reason is because it's an intramuscular injection and it's slowly absorbed you don't get very high blood levels.

SPECIAL MASTER VOWELL: So intravenous injection versus ingestion you would get a higher level depending on how you were administering it?

THE WITNESS: Absolutely.

SPECIAL MASTER VOWELL: All right. I think those are all my questions. Thank you very much, Dr. Brent.

THE WITNESS: Thank you.

SPECIAL MASTER HASTINGS: Any redirect for this witness?

MS. RENZI: I just have one question.

SPECIAL MASTER HASTINGS: Please go ahead.

REDIRECT EXAMINATION

BY MS. RENZI:

Q Dr. Brent, Ms. Chin-Caplan spent a great deal of time this afternoon going through the literature on mercury and its effect on the immune system. At one point you said that you would agree with any of the statements that she read from that

literature to the effect of mercury on the immune system. I know you've said this, but I want to make it abundantly clear.

What significant caveats do you place on the statement with respect to the form of mercury, and also, the dose?

A Well, those are the two most important considerations. I hope I haven't been redundant today, but I really wanted to make these points. They're fundamental points.

When we're talking about mercuric chloride, when we're talking about methyl mercury, we're not talking about ethyl mercury, we're not talking about the exposures in vaccines, so you cannot assume that all the statements, which I agreed with -- yeah, methyl mercury at this concentration will cause that, and mercuric chloride at that concentration will cause something else -- have anything do with the exposures to ethyl mercury.

The other issue of course is that ethyl mercury we can make to have adverse effects on the immune system. They won't be exactly the same as methyl mercury or mercuric chloride, but it can be shown to have some adverse effects on the immune system, but you have to go once again to very, very

high doses compared to anything that anybody could possibly expect to experience from a vaccine.

So both of those concepts have to be taken into consideration. You want to know about ethyl mercury you have to ask what the data is on ethyl mercury. If you want to know what happens in a vaccine you have to ask what happens if the dose is associated with a vaccine?

MS. RENZI: Thank you. I have no further questions.

THE WITNESS: Thank you.

SPECIAL MASTER HASTINGS: Anything further for this witness?

MS. CHIN-CAPLAN: No, Special Master.

SPECIAL MASTER HASTINGS: All right. Dr. Brent, we kept you up there all day. We thank you very much. You're excused at this point.

THE WITNESS: Well, thank you, Special Master.

(Witness excused.)

SPECIAL MASTER HASTINGS: Before we break for the day I understand that's all the testimony we have for today.

Mr. Matanoski?

MR. MATANOSKI: That's correct, sir.

SPECIAL MASTER HASTINGS: The schedule for Monday is Dr. Griffin and Dr. Fombonne?

MR. MATANOSKI: That's correct.

SPECIAL MASTER HASTINGS: In what order?

MR. MATANOSKI: I believe it will be Dr. Fombonne first, sir.

SPECIAL MASTER HASTINGS: Okay. All right. So that's the witnesses we have for Monday, and that will conclude the government's case I assume?

MR. MATANOSKI: That's the government's case in chief, yes, sir.

SPECIAL MASTER HASTINGS: Case in chief. Correct. Then we'll be adjourned for today. We'll see you folks Monday morning at 9:00 a.m. Thank you, all.

(Whereupon, at 3:32 p.m., the hearing in the above-entitled matter was adjourned, to reconvene on Monday, June 25, 2007, at 9:00 a.m.)

//

//

//

//

//

//

//

REPORTER'S CERTIFICATE

DOCKET NO.: 98-916V

CASE TITLE: Theresa Cedillo v. HHS

HEARING DATE: June 22, 2007

LOCATION: Washington, D.C.

I hereby certify that the proceedings and evidence are contained fully and accurately on the tapes and notes reported by me at the hearing in the above case before the Office of Special Masters.

Date: June 22, 2007

Christina Chesley
Official Reporter
Heritage Reporting Corporation
Suite 600
1220 L Street, N.W.
Washington, D.C. 20005-4018