

UNITED STATES  
COURT OF FEDERAL CLAIMS

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IN RE: CLAIMS FOR VACCINE )  
INJURIES RESULTING IN )  
AUTISM SPECTRUM DISORDER, )  
OR A SIMILAR )  
NEURODEVELOPMENTAL )  
DISORDER )  
----- )  
FRED AND MYLINDA KING, )  
PARENTS OF JORDAN KING, )  
A MINOR, )  
 )  
Petitioners, )  
 )  
v. ) Docket No.: 03-584V  
 )  
SECRETARY OF HEALTH AND )  
HUMAN SERVICES, )  
 )  
Respondent. )  
----- )  
GEORGE AND VICTORIA MEAD, )  
PARENTS OF WILLIAM P. MEAD, )  
A MINOR, )  
 )  
Petitioners, )  
 )  
v. ) Docket No. 03-215V  
 )  
SECRETARY OF HEALTH AND )  
HUMAN SERVICES, )  
 )  
Respondent. )

Pages: 351 through 661/760

Place: Washington, D.C.

Date: May 13, 2008

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IN THE UNITED STATES COURT OF FEDERAL CLAIMS

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Docket No. 03-215V

SECRETARY OF HEALTH AND )  
HUMAN SERVICES, )

Respondent. )

Courtroom 402  
National Courts Building  
717 Madison Place NW  
Washington, D.C.

Tuesday,  
May 13, 2008

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

BEFORE: HONORABLE GEORGE HASTINGS  
HONORABLE PATRICIA CAMPBELL-SMITH  
HONORABLE DENISE VOWELL  
Special Masters

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C O N T E N T S

<u>WITNESSES:</u>	<u>DIRECT</u>	<u>CROSS</u>	<u>REDIRECT</u>	<u>RECROSS</u>
<u>For the Petitioners:</u>				
Vasken Aposhian, MD	---	355	468	486
Richard Deth, MD	493	582	655	659

E X H I B I T S

<u>For the Petitioners:</u>	<u>IDENTIFIED</u>	<u>RECEIVED</u>
3	--	--



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1 A Thank you. Thank you very much.

2 Q Now, Dr. Aposhian, it's unclear from your  
3 report whether it's the ethyl mercury and the  
4 thimerosal-containing vaccines or if it's the  
5 resulting inorganic mercury that causes autism. Which  
6 one are you causally implicating?

7 A Thimerosal is in the vaccine that is  
8 injected into a child. All the scientific literature  
9 indicates the thimerosal is quickly converted to ethyl  
10 mercury. The ethyl mercury is then quickly  
11 distributed to the tissues, crosses the brain barrier,  
12 gets to the brain, and there it is deethylated to  
13 mercuric mercury. That is the metabolism of, the  
14 metabolic root of what happens once you give  
15 thimerosal.

16 Now, whether it's thimerosal per se or ethyl  
17 mercury per se that you're asking a question about,  
18 I'll ask you to be a little more specific in your  
19 question.

20 Q I'm asking you, it's your opinion that  
21 thimerosal-containing vaccines are causally related to  
22 autism. Is that correct?

23 A That is my opinion, yes.

24 Q And I'm asking you whether it is the ethyl  
25 mercury component or the inorganic mercury component

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1 once that ethyl mercury deethylates that is the cause  
2 of autism.

3 A I don't think ethyl mercury per se stays in  
4 the brain long enough to have an effect that we have  
5 yet measured. I think it is the mercuric mercury that  
6 is the culprit. It is the mercuric mercury that  
7 remains in the brain almost forever, and has very  
8 definite toxic effects in the brain.

9 Q And what's the basis for your conclusion  
10 that the mercuric mercury has toxic effects in the  
11 brain?

12 A The scientific literature. If you read the  
13 scientific -- I mean, I quoted a paper in which they  
14 injected mercuric mercury directly into the brain.  
15 Can we go perhaps -- let's go back to that, actually.  
16 If you have copies of those slides. I don't have --  
17 do you have copies of my slides? You were given the  
18 sheet yesterday with the copies of --

19 Q Which slide are you referring to?

20 A Pardon?

21 Q Which slide are you referring to?

22 A Well, I'd like to see the copy so I can give  
23 you a number.

24 Q Oh, you don't have the slides with you.

25 A If you'd give me a minute, I'll bring it up

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1 on my computer. I certainly do have the slides.

2 Sunday. Here they are. Let's see.

3 (Pause.)

4 Q Doctor, do you know --

5 A Slide No. 68. I'm sorry I'm slow, there are  
6 many slides.

7 SPECIAL MASTER VOWELL: I'm sorry, Dr.  
8 Aposhian, which slide number did you say that was?

9 THE WITNESS: Slide No. 68.

10 SPECIAL MASTER VOWELL: Sixty-eight, and  
11 this is on --

12 THE WITNESS: Six-eight.

13 SPECIAL MASTER VOWELL: This is on  
14 Petitioner's Trial Exhibit 2.

15 THE WITNESS: The paper entitled "Gaugher,  
16 et al, Identity of Ultra-Structural Effects of  
17 Mercurio-Chloride and Methyl Mercury After Inter-  
18 Cerebral Injection."

19 So among other things, they injected  
20 directly into the brain methyl-mercury -- I'm sorry,  
21 mercuric chloride. And found, thus, in spite of their  
22 distinctive clinical syndromes, these two classes of  
23 mercury compounds -- namely, mercuric chloride and  
24 methyl mercury -- are capable of inducing neuronal  
25 necrosis.

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1 BY MS. RENZI:

2 Q And that's the basis for your opinion that  
3 inorganic mercury causes autism?

4 A I didn't say -- I don't think that was the  
5 question you originally asked me. You asked me what  
6 was the evidence for, I thought you asked me what is  
7 the evidence that mercuric chloride does damage to the  
8 brain.

9 Q I asked that question. I also asked the  
10 basis for your opinion that the mercuric chloride is  
11 causally related to autism.

12 A In my scientific opinion, it does.

13 Q What is the basis for your opinion?

14 A Based on papers like this, and a vast  
15 variety of evidence that indicates that the mercuric  
16 ion has a high affinity for sulphhydryl groups, and  
17 will tie up the active centers of enzymes, not only in  
18 the tissues, but in the brain as well, and inhibit  
19 those enzymes.

20 The thyrotoxin system, which was maybe Slide  
21 10 or 11 if we want to go back to that --

22 Q No, that's fine.

23 A Is it necessary?

24 Q No, thank you.

25 A Okay. Is a good indication. The latest

APOSHIAN - CROSS

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1 paper of nanomolar amounts of mercury of mercuric  
2 chloride, nanomolar amounts -- those are very small  
3 amounts, those concentrations -- are inhibiting this  
4 purified thyrotoxin system. And so, yes.

5 Q And that's an in vitro study. I mean, an in  
6 vitro study, correct?

7 A That's an in vitro. But it's an in vitro  
8 study in which we don't have to worry about competing  
9 enzyme reactions, we don't have to worry about the  
10 breakdown of substances, or the formation of  
11 inhibitory substances for other reactions. It's a  
12 very purified DNA-recombinant-synthesized enzyme.  
13 It's the purest kind of system that you can find in  
14 biochemistry.

15 Q And from that in vitro study, you conclude  
16 that inorganic mercury from thimerosal --

17 A I'm sorry, I can't hear you.

18 Q And from that in vitro study, you conclude  
19 that thimerosal-containing vaccines, the inorganic  
20 mercury, causes autism?

21 A Well, that's not what you asked me  
22 originally on that. What I'm saying is there is a  
23 body of information, published information, that  
24 indicates that mercuric ion is, has a high  
25 susceptibility, a great affinity for the active

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1 centers of essential enzymes. And if those enzymes  
2 are inhibited, you're going to have problems.

3 Q And how does that cause autism?

4 A Well, since, in the brain, there are the  
5 centers, actually the control of movements, there are  
6 the controls of thought -- the brain controls our body  
7 and everything that we do about it. And once you  
8 begin inhibiting critical enzymes, inhibiting critical  
9 proteins in the brain with an inhibitor such as  
10 mercuric chloride, you are going to have problems.

11 There is no question we all have a certain  
12 amount of mercuric chloride in our brains. But I  
13 think, and I'll have to think one more -- yes. I  
14 think if you look at the autopsy data, you will find  
15 that mercuric chloride remains in the brains of those  
16 autistic children.

17 Q Doctor, is it your opinion that all forms of  
18 mercury exposure, both prenatal and postnatal, lead to  
19 autism? Cause autism?

20 A Perhaps we can go back to -- no, let's go on  
21 to the other slide.

22 Q And Doctor, I am assuming what you have on  
23 your computer is this slide? Is the testimony from --

24 A If you have a copy, it would be much easier  
25 for me to go through them. I put them in my suitcase,

APOSHIAN - CROSS

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1 which --

2 Q I only have my one copy, I'm sorry.

3 A Okay. But anyway, let me -- so you don't  
4 see this, either. Anyway, there is a diagram in the  
5 slides that were handed out to you anyway showing that  
6 ethyl mercury, that thimerosal is converted to ethyl  
7 mercury. And through various kinds of metabolism, it  
8 ends up in the brain, causing encephalopathy. It  
9 causes autism.

10 Yes, I think ethyl mercury will be, is  
11 metabolized, and mercuric mercury -- thank you very  
12 much -- and ethyl mercury and mercuric chloride itself  
13 are very harmful to the brain.

14 Q Oh, so it's both the ethyl mercury and the  
15 mercuric chloride? And the mercuric --

16 A The ethyl mercury is going to be there for a  
17 short period of time. And it's just --

18 Q Does that do any damage?

19 A Pardon?

20 Q Does the ethyl mercury do any damage that  
21 contributes, or causes autism? Just the ethyl  
22 mercury.

23 A The ethyl mercury is the source of the  
24 mercuric ion that resides in the brain after ethyl  
25 mercury has been metabolized in the brain. And it is

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1 the mercuric mercury that remains in the brain, and  
2 probably has the long-term effect.

3 I think the scientific literature, a great  
4 deal of it supports that hypothesis.

5 Q Okay. My next question was, then, do you  
6 think it's both prenatal exposures to mercury and  
7 post-natal exposure to mercury that cause autism?

8 A I think it depends on the individual. It  
9 depends on what the diagnosis is going to be. I  
10 think, as many people, I think one of the best people  
11 that I know of is Professor Ellen Silbergeld at  
12 Hopkins, who got the MacArthur Award, the Genius  
13 Award, the only toxicologist, male or female, who had  
14 ever gotten that award, told me quite some time ago  
15 that in her opinion, the thimerosal and ethyl mercury  
16 will trigger a response.

17 There is already, in a pregnant woman,  
18 mercuric mercury to some extent. And methyl mercury  
19 to some extent. And there is no such thing that we  
20 know of as a mercury-free human being.

21 And so there can be an effect prenatally,  
22 there can be an effect post-natally. It's going to  
23 depend on the concentration and the species of mercury  
24 that you're talking about. Is that an answer to your  
25 question? Is that suitable?

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1 Q What kind of mercury are in-utero infants  
2 normally exposed to? What species?

3 A The in-utero infant, as you call her or him,  
4 is exposed to what the mother has been exposed to.  
5 The mother may have been exposed to methyl mercury  
6 from fish that she ate, and that methyl mercury and  
7 various forms of it can be stored in the woman's body.  
8 The recommendation that many of us have, and the  
9 recommendation I think that many countries now have --  
10 Sweden, Norway, and we're trying to get it through the  
11 FDA in this country at the present time -- is that  
12 women of child-bearing age and pregnant women should  
13 not eat fish that contain a great deal of methyl  
14 mercury.

15 So one source of the mercury in that infant  
16 would be the methyl mercury that comes from the  
17 mother.

18 Another source of mercury in that infant in  
19 utero would be the mercury that comes from any  
20 amalgams that she may have in her mouth. Those are --  
21 the third source, of course, would be if the mother  
22 has had a vaccination of some kind. I don't remember  
23 which vaccine it is, but certainly some women do get a  
24 vaccine sometimes during pregnancy, or if not before.  
25 And this mercury is stored in a woman's body.

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1           And so when the child, when conception  
2           occurs, and during the maturation of the embryo, there  
3           is mercury passing from the mother in the blood to the  
4           infant. Three possibilities of virus sources. One is  
5           fish, the second is amalgam, and third is vaccination.

6           Q     So does the methyl mercury consumed by the  
7           mother and passed on to the infant, does that  
8           contribute to autism?

9           A     You're asking whether methyl mercury  
10          contributes to autism?

11          Q     Prenatal exposure to methyl mercury. Or  
12          prenatal exposure to dental and --

13                 SPECIAL MASTER VOWELL: Could you talk in  
14          the microphone, please?

15                 BY MS. RENZI:

16          Q     I'm asking if the prenatal exposures to  
17          mercury, you said methyl mercury through fish  
18          consumption, through dental amalgams, do those  
19          contribute or cause autism? That prenatal exposure.

20          A     I said that an infant, in utero, would be  
21          exposed to the mercury that's in the mother. The  
22          mercury in the mother could come from fish, amalgams,  
23          or vaccinations.

24          Q     I understand that. But does it cause or  
25          contribute to the autism? If a child develops autism,

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1 can you look back to the methyl mercury exposures and  
2 prenatal exposures?

3 A Okay. It would be very reasonable to  
4 believe, as some of us do, that the methyl mercury in  
5 the mother will eventually be converted in the child's  
6 brain, to eventually, some of that methyl mercury  
7 would get into the child's brain.

8 And through these various sources, when the  
9 child is born and in early childhood, there will be an  
10 accumulation of mercury in that child. And there is a  
11 prevailing thought by many, that many people have,  
12 that the vaccines could be the trigger, what pushes  
13 the toxicity of the mercury over the threshold to  
14 cause autism. That is one of the theories.

15 Q So is it your opinion that the exposure to  
16 methyl mercury can cause autism?

17 A Again, we're getting into terms that you've  
18 got to be more specific about. The child is exposed  
19 to thimerosal. The thimerosal is metabolized to ethyl  
20 mercury. One might say, as far as the true definition  
21 of exposure, the child is not exposed to ethyl  
22 mercury. The child has thimerosal converted to ethyl  
23 mercury in the body, and that ethyl mercury then  
24 travels to the brain and to other tissues and is  
25 deethylated to get mercuric mercury.

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1           So if you ask me is a child exposed to ethyl  
2 mercury, I would say we're dealing with semantics.

3           Q     You know, it might be helpful if we put up  
4 the chart that you had up yesterday about different  
5 roots, different exposures to mercury.

6           A     Is this the one that you want?

7           Q     Yes.

8           SPECIAL MASTER VOWELL:   And we are on, what  
9 page is this?

10          MS. RENZI:   Slide 23.

11          SPECIAL MASTER VOWELL:   Okay, slide 23,  
12 Petitioner's Trial Exhibit 2.

13          THE WITNESS:   It's entitled, "Influence of  
14 the mother and other sources for mercury exposure of  
15 infants." Is that the one you want?

16          MS. RENZI:   Yes.

17          THE WITNESS:   I'm sorry, I don't know your  
18 name.

19          MS. RENZI:   My name is Ms. Renzi, Linda  
20 Renzi.

21          THE WITNESS:   Pardon?

22          MS. RENZI:   Linda Renzi.

23          THE WITNESS:   Thank you, thank you, ma'am.

24          MS. RENZI:   Sure.

25         //

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1 BY MS. RENZI:

2 Q Now, Dr. Aposhian, from your chart and from  
3 your testimony yesterday, we get methyl mercury from  
4 the mother through fish consumption, through chicken  
5 consumption, and we get inorganic mercury from dental  
6 amalgams, and then if the mother has had a thimerosal-  
7 containing vaccine, the child is exposed to ethyl  
8 mercury. The mother. Is that correct?

9 So in utero, the child would be exposed to  
10 methyl mercury from fish, chicken, inorganic from  
11 amalgams.

12 A Yes.

13 Q And if the mother has a vaccine, ethyl  
14 mercury.

15 A Yes. If the mother has -- yes, yes. Ethyl  
16 mercury, yes.

17 Q And post-natally, the child is exposed to  
18 methyl mercury from breast milk, methyl mercury from  
19 fish consumption, methyl mercury from chicken. Dental  
20 amalgams I guess if the child would be old enough to  
21 have fillings.

22 A Or from the mother.

23 Q Or from the mother.

24 A Via breast milk.

25 Q And then thimerosal-containing vaccines.

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1 Now, what is the basis for your opinion, given all the  
2 methyl mercury exposure, that the child has, both in  
3 utero and post-natally, that it's a vaccine, 12.5  
4 micrograms of ethyl mercury that tipped that child,  
5 triggered that child to have autism?

6 A Well, it also could be 187.5 micrograms of  
7 mercury. That is what a child gets after a set of  
8 vaccinations. So there's a big difference from 187 as  
9 compared to 12.5. However, you could say that 12.5  
10 chronically, over a period of time, might also cause  
11 such effects.

12 What we are pointing out, what we have  
13 proposed as a theory, not only by me, by many other  
14 people, is that one possibility for the cause or the  
15 etiology of autism is that the vaccine is enough to  
16 exceed the threshold of what some children may have,  
17 the amount of mercury that some children may have in  
18 their brain.

19 Q So are you saying today you need 187.5  
20 micrograms --

21 A What about that --

22 Q -- of ethyl mercury? Are you saying that  
23 you need the full vaccine?

24 A I'm not saying how much you need. All we're  
25 saying is there's a good possibility that that amount

APOSHIAN - CROSS

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1 of mercury given in vaccines could trigger the cause  
2 of autism.

3 But please remember, there is a tremendous  
4 variation, as I hope we showed you in the data  
5 yesterday, there's a variation, a variability in how  
6 children respond to the same amounts of vaccine. Some  
7 had eight times greater, I think, or five to eight  
8 times greater amount of mercury in the blood; others  
9 had almost no mercury in the blood at a given time.

10 Q If you have so much exposure from methyl  
11 mercury in utero and post-natally --

12 A I'm not certain, you're saying so much  
13 exposure. It depends on the person's diet. It  
14 depends on the woman, whether a pregnant woman is  
15 going to eat tuna steaks, it depends on whether she's  
16 going to eat a tunafish salad sandwich every day for  
17 lunch, as they used to do in the past. Most of the  
18 women at our university -- we're not an Ivy League  
19 school, our tuition is among the lowest, we get young  
20 women who don't have very much money, and they have to  
21 be very careful in what they eat. And when they come  
22 to us to begin with, they're usually eating tunafish  
23 sandwiches, of which we recommend they do not.

24 It depends on who, if the person you're  
25 talking about is, what their diet is, as far as how

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1 much methyl mercury gets into that person.

2 Q Well, that's actually my next question,  
3 then. If there is a high consumption of methyl  
4 mercury by women, pregnant women, such as in the  
5 Seychelles, is there a higher rate of autism in the  
6 Seychelles, where there is a large fish consumption?

7 A That's a very good question. Because again,  
8 as in the Iraqi study, when the Seychelle Island study  
9 began, no one even thought about studying, about  
10 testing the population for autism. It's my  
11 understanding in conversations I've had with Dr.  
12 Clarkson that they are looking into that now.

13 But let us also state that the Seychelle  
14 Islands may not be an example of what happens in the  
15 rest of the world. The Seychelle Islands, their diet,  
16 being a tropical country, is very high in citrus  
17 fruit. And it has been shown by a superb young woman  
18 epidemiologist in Montreal doing a study in Brazil  
19 that the diet is important as far as the toxic effects  
20 of methyl mercury.

21 The women that ate citrus fruit did not have  
22 as many toxic signs of methyl mercury. So it's a very  
23 complex phenomena, and a complex question that you're  
24 asking.

25 Q Now, have you read the report of Dr.

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1 Clarkson?

2 A Of who?

3 Q Have you read the expert report submitted by  
4 Respondent of Dr. Clarkson?

5 A Yes, absolutely, I did.

6 Q And do you know what he said about autism in  
7 the Seychelles? I have a quote for you.

8 A You can quote. I don't have it with me. I  
9 do --

10 Q It's on your screen.

11 A Oh, fine. It's one of the things that I did  
12 underline when I read it about a couple weeks ago.

13 And what does he say?

14 Q He says -- this is at Respondent's Exhibit K  
15 at page 57. He said, "In some 30 years of detailed  
16 pediatrics, in neuron physiological tests on large  
17 cohorts of these infants who have continuously  
18 elevated mercury blood levels, I have found no  
19 evidence of an increased prevalence in autism.

20 "Admittedly, we did not specifically look  
21 for autistic children. But many of the neurocognitive  
22 tests we carried out, none of which uncovered  
23 neurological deficits would surely have detected such  
24 cases."

25 A Is this published? Is that what you just

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1 said?

2 Q Pardon me?

3 A Did you say --

4 Q I said this is his opinion in his report,  
5 about finding, whether they found autistic signs or  
6 symptoms in the Seychelles.

7 A So one could say that the Seychelle Islands  
8 population may not be typical of the way people react  
9 to methyl mercury, because the Faroe Islands say  
10 something entirely different.

11 Not only are they genetically different, the  
12 seafood they eat, I think most people will agree, are  
13 different, and their diet is certainly different.

14 I don't argue with Dr. Clarkson at all. I  
15 have great faith in what he says. If he says that  
16 they don't find it in the Seychelle Islands, I have no  
17 reason to disagree with that.

18 Q Now, I recall from your testimony in  
19 Cedillo, you said there is no citrus in the Faroe  
20 Islands, is that correct? To your recollection.

21 A When I visited the Faroe Islands, we had an  
22 international meeting on methyl mercury there, I think  
23 about the year 2000, I don't remember the exact year.  
24 To try to find, to buy an orange there, it was very  
25 unusual. There are almost no trees left on the Faroe

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1 Islands. Okay? So I doubt that these people have as  
2 much citrus in their diet as they do in the Seychelle  
3 Islands.

4 Q And do you know whether there is a higher  
5 rate of autism in the Faroe Islands?

6 A I have no idea.

7 Q Would you be surprised if there wasn't?

8 A I'd have to stop and think about that. It's  
9 a very important question, and I just would not like  
10 to make a snap judgment like that.

11 Q I want to refer now to page 9 of your  
12 report.

13 (Pause.)

14 A I'm all thumbs, my apologies. I have page 9  
15 now.

16 Q Okay, you have it. You have a comment on  
17 the top of page 9 of your expert report that says,  
18 referring to the articles authored by Dr. Clarkson and  
19 Dr. Magos, that those articles should be viewed, and  
20 I'll quote, "cautiously, as current scientific  
21 investigations may render some of their conclusions  
22 false, inaccurate, and outdated." And you were  
23 referring to the review articles of Dr. Magos and Dr.  
24 Clarkson.

25 A May I make a comment?

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1 Q Yes.

2 A I'd like to apologize to Dr. Magos and Dr.  
3 Clarkson. I don't quite understand how that got in.  
4 I have a great deal of respect for them.

5 However, times do change. I think both  
6 their papers are very deficient in the idea of  
7 hypersusceptibility and polymorphism. This is not  
8 meant with any disrespect, and I hope it does not harm  
9 my friendship with Dr. Clarkson, who I have a great  
10 deal of admiration for. But their papers tend to be  
11 deficient in the genetic aspects of mercury toxicity.

12 Q Were you aware, Dr. Aposhian, that 47 out of  
13 your 54 peer-reviewed articles regarding mercury refer  
14 to or rely on reports or articles by Dr. Clarkson or  
15 Dr. Magos?

16 A Say that again?

17 Q About 84 percent of the articles --

18 A I have a great deal of respect for them. I  
19 don't know what your question is, ma'am.

20 Q My question is, you don't believe now that  
21 their review articles --

22 A I don't say that.

23 Q -- should be viewed cautiously.

24 A I think all review articles should be  
25 reviewed cautiously. My review articles, they are

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1 some of the most quoted ones in the world on arsenic  
2 that were recently published, I tell my students they  
3 should be viewed cautiously.

4 We have an exercise in graduate school where  
5 we give students a paper and say find out what is  
6 wrong with this. We teach our students to be  
7 skeptical. No paper is perfect.

8 However, I do want to apologize to Dr.  
9 Clarkson and Dr. Magos for this statement that is in  
10 here. I meant no offense, and how it got in there is  
11 difficult for me to understand. "They must be viewed  
12 cautiously, as current scientific investigation may  
13 render some of their conclusions false, inaccurate, or  
14 outdated." I absolutely retract that statement, and I  
15 apologize.

16 However, I do think that no review article  
17 is perfect, including my own, as well as Clarkson's  
18 and Magos's. But no disrespect is intended to these  
19 two fine gentlemen and scientists.

20 Q Doctor, before this trial started, did you  
21 discuss any of the mercury parts of this case with any  
22 of the other experts? With any other of Petitioner's  
23 experts? Did you talk to Dr. Kinsbourne?

24 A Did I discuss this report?

25 Q This report or your testimony yesterday.

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1 A Now, can we do it one at a time?

2 Q Yes.

3 A Is the first question, did I discuss this  
4 report with any expert?

5 Q Yes.

6 A Yes, I did.

7 Q Who did you discuss your report with?

8 A I discussed this, I needed some help in  
9 deciding whether we can make certain assumptions, with  
10 Professor Dean Carter of the University of Arizona.

11 Q I'm sorry, I'll clarify this. With any  
12 experts that are participating in the litigation  
13 today?

14 A Absolutely not that I can recall. I'm  
15 trying to think what mercury experts you -- our  
16 attorneys are fine gentlemen. They know mercury. I  
17 wouldn't call them scientific experts. I'm thinking  
18 about Dr. Gerth, who I know is a superb scientist. I  
19 haven't even had a conference with him about this.  
20 Our neurologist I just saw again for the first time  
21 since the Cedillo trial yesterday.

22 So I guess the answer to your question is  
23 no, I have not discussed this with anyone else that's  
24 connected with this trial.

25 Q Your testimony yesterday, did you discuss

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1 that with any of the experts participating in this  
2 trial today?

3 A Absolutely not.

4 Q I'd like to go back to your report now.

5 A Sure.

6 Q On page 14 of your report.

7 A I'm on page 14.

8 Q Okay. You state that there is increasing  
9 evidence for neuroinflammatory events being involved  
10 with the development of autism. Is that correct?

11 A That's what it states here.

12 Q And you cite Pardo, which is Petitioner's  
13 Master List 72.

14 A You're speaking down to the desk. I'm  
15 sorry.

16 Q I'm sorry, Petitioner's Master List 72, just  
17 to clarify where this is in the record, for the  
18 record. You quote the Pardo paper, or you cite to the  
19 Pardo paper, correct?

20 A I didn't hear that, I'm sorry.

21 Q The Pardo paper, P-A-R-D-O. Is that what  
22 you are relying on for your statement?

23 A That's one of them. There are a number of  
24 papers from the Zimmerman group in particular, from  
25 Hopkins, that are superb papers dealing with the

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1 neuroinflammatory events involved in the development  
2 of autism.

3 Q Well, I'd just like to ask you about the  
4 article in your report, the Pardo report. The Pardo  
5 paper.

6 A Can I have that paper, since I haven't seen  
7 it for a while?

8 Q Sure.

9 A Because he has a number of papers, and I  
10 want to be certain we're talking about the right one.  
11 Thank you. "Neuroinflammation in Autism," by Pardo,  
12 Vargas, and Zimmerman.

13 Q Okay. Did that paper implicate ethyl  
14 mercury causing the neuroinflammation they report?

15 A This review paper I haven't read probably  
16 for two or three months. And let's see what their  
17 diagram here is.

18 Certainly, if you look at figure 4, you can  
19 certainly include ethyl mercury and environmental  
20 effects. "We hypothesize that --" in the conclusions  
21 they state, "We hypothesize that environmental  
22 factors, for example neurotoxins, which would be  
23 mercury compounds, infections, maternal infections,  
24 and presence of genetic susceptibility and the  
25 immunogenetic background of the host influences the

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1 development of abnormalities," et cetera, et cetera,  
2 "for the generation of autistic symptoms."

3 Q And are they referring to vaccines,  
4 thimerosal-containing vaccines in that article?

5 A Do they mention vaccine?

6 Q Yes.

7 A I would have to read the paper now very  
8 carefully. Perhaps if someone has a computer, one  
9 might --

10 Q Well, let's assume that they don't.

11 A Pardon me?

12 Q Let's assume that they don't, okay?

13 A That they don't?

14 Q That they do not, yes. How do you tie the  
15 neuroinflammation to your belief that thimerosal-  
16 containing vaccines cause autism?

17 A My first inclination would be to leave that  
18 to our neurologist, who will be testifying later on  
19 today.

20 Q So you have no opinion on that.

21 A I'm not a neuro -- I don't have an opinion  
22 that I can give you just like that, since this is a  
23 court of law. I would have to go over the slides I  
24 presented yesterday, which do offer a great deal about  
25 neuroinflammation, before I could really make a

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1 statement that would be truthful.

2 And so if you want to give me time to go  
3 back over these slides, which we have right here --

4 Q You gave your testimony yesterday, but  
5 without reviewing your slides you have no cogent  
6 opinions to give me at this moment?

7 A I have an opinion, but it's an opinion that  
8 I don't want to share with you, because I'm not  
9 certain that I, I want to tell the truth. And I'm not  
10 positive that if I give you something quickly off my  
11 mind, that it will be based on scientific fact.

12 We, in science, are not known for making  
13 rapid decisions. We have very simple minds that have  
14 to go in a logical way.

15 Q Well, we'll move on. I will not ask you to  
16 review your slide presentation from yesterday.

17 A All right, thank you very much.

18 Q I'd like to discuss Pink's Disease, Pink  
19 Disease.

20 A All right. You must notice, however, that  
21 we took everything out of the slides. There is no,  
22 there is hardly any mention of Pink Disease in the  
23 presentation I made yesterday, number one.

24 Number two, in the Cedillo trial, I  
25 mentioned Pink Disease as an example of how

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1 conservative and reluctant the medical establishment  
2 was to make, to declare that the mercurous mercury or  
3 teething powder was its cause. And that is an example  
4 of a disease that was stopped by government  
5 regulation, not by good scientific cause.

6 Q But in Cedillo we also discussed whether  
7 this was a dose-related phenomenon --

8 A Could you talk in the microphone? I'm  
9 sorry.

10 Q In Cedillo we also discussed, if you recall,  
11 whether this was a dose-related phenomenon or an  
12 example of hypersusceptibility. Do you recall that?

13 A I recall that, and I recall all the  
14 respondents making a big thing of it, and the  
15 respondents in this trial. And I -- I was just told  
16 to speak into the microphone myself.

17 And I certainly did emphasize  
18 hypersusceptibility during the Cedillo trial, and I  
19 probably emphasized it too much.

20 However, I believe scientifically that there  
21 was a large element of hypersusceptibility in those  
22 children with Pink Disease. Unfortunately, I don't  
23 think anyone can prove it one way or another, because  
24 the literature is very deficient about Pink Disease  
25 during the years that it was a disease affecting our

1 children.

2 Q But you would agree that the mercury urine  
3 levels taken from children with Pink Disease was  
4 elevated.

5 A In some of them there was a variation. In  
6 some of them there was an elevation.

7 Q Which could be a dose-response phenomenon.

8 A Which could be a dose response.

9 Q On page 8 of your report, and I believe in  
10 your testimony yesterday, you discussed porphyrins.

11 A Page 8 of the report.

12 Q Page 8 of your report, you discuss  
13 porphyrins.

14 A Yes, I have page 8.

15 Q Do you consider yourself an expert on  
16 urinary porphyrins?

17 A Do I think I'm an expert on --

18 Q Urinary porphyrins.

19 A I'm not an expert on urinary porphyrins.

20 Q Can a urinary porphyrin profile,  
21 specifically the presence of elevated precoporphyrins,  
22 precoporphyrin levels, can that be used to diagnose  
23 mercury toxicity?

24 A Certainly the porphyrin profile changes in  
25 people who have been exposed to mercury. There is a

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1 correlation between the amount of mercury exposure of  
2 an individual, especially dentists, but not only  
3 dentists, and how the porphyrin urinary profile  
4 changes.

5 Q Can it be used to diagnose mercury toxicity?

6 A It's used by some people.

7 Q Who is it used by?

8 A By a large number of people, of physicians  
9 who treat autistic children. It also is in the  
10 scientific literature, Woods especially, and in most  
11 of the new current books it's cited as a way, as one  
12 of the changes that occur when people are exposed to  
13 mercury.

14 Now, whether someone wants to use that as a  
15 diagnostic tool or biomarker is, of course, up to the  
16 individual physician.

17 Q Do you know if it's accepted in the general  
18 medical community as a way to diagnose mercury  
19 toxicity?

20 A I don't think the general medical community,  
21 probably with the exception of one or two medical  
22 toxicologists, know anything about heavy metal  
23 toxicity. I don't think most medical schools teach  
24 anything about mercury or heavy metal toxicity to  
25 medical students. So that when they get out, very few

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1 of them know about metal toxicity. I think that has  
2 been a complaint by many organizations, and many  
3 national meetings have been held to try to remedy this  
4 situation.

5 Q Now, porphyrin profiles can't be found in  
6 medical textbooks?

7 A Oh, yes.

8 Q To diagnose mercury toxicity?

9 A Again, what I've stated is it depends on who  
10 is making, on what the physician making a diagnosis or  
11 treating the patient wants to do. There are certainly  
12 places in the world now that you can send the urine to  
13 have the porphyrin profile done.

14 Q Can you name one or two?

15 A There's one at Paris. I think it's the  
16 Institute of, I want to say the Pasteur Institute. I  
17 don't know what the institute is, but I can, I think  
18 the paper is quoted here.

19 Q That's fine.

20 A You can also send to the University of  
21 Washington in Seattle, and Jim Woods will be very glad  
22 to do it for you. He has done, we have published with  
23 him, in fact, he had done some for us.

24 Q Is it your opinion that the unique porphyrin  
25 profiles can be used as a biomarker to diagnose

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1 mercury, autism due to mercury toxicity?

2 A You're asking me a question that really  
3 belongs, should be asked of a physician. I don't do  
4 diagnosis. I'm not a physician. I'm a research  
5 investigator. I use various tools at my disposal.  
6 But I do not diagnose humans. That is an MD's  
7 responsibility.

8 Q So an elevated precoporphyrin level, you  
9 don't know if that could be used to diagnose autism.

10 A I'm just trying to give you the most  
11 truthful answer that I know. I know of people who use  
12 it, who use urinary porphyrin profiles as a biomarker,  
13 as a potential biomarker, one of many biomarkers, of  
14 questionable use for autism. But that doesn't mean  
15 that I approve or disapprove. I just haven't really,  
16 I haven't written a paper on the use of urinary  
17 porphyrins as a diagnostic tool. I guess that's the  
18 best way of putting it.

19 Q Now, you just referred to James Wood and the  
20 article that looked at the dentists with chronic  
21 exposure to mercury vapor, correct? That's the  
22 article you were referring to?

23 A That's one of the papers. There were papers  
24 from Paris that showed, I think, that some of the  
25 porphyrins were elevated or changed in autistic

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1 children.

2 Q We'll go to that. Let's just, can we just  
3 focus on the Woods article right now?

4 A Sure, okay.

5 Q And that measured, those were dentists  
6 working with mercury vapor, is that correct?

7 A The dentists were exposed to mercury vapor,  
8 among other things, as a normal individual would be  
9 exposed to mercury and methyl mercury in the diet  
10 primarily.

11 Q And did Woods, he didn't look, though, to  
12 exposure to ethyl mercury, did he?

13 A He does not mention, Woods does not mention  
14 ethyl mercury in his paper. However, I think he may  
15 be doing work along those lines at the present time.  
16 But I know of no paper -- and I could be wrong -- I  
17 know of no paper with Jim Woods's name on it that  
18 deals with ethyl mercury.

19 Q And he didn't look at an autistic  
20 population.

21 A I don't know whether he did or not. I know  
22 of no paper that he did.

23 Q Well, I assume that none of the dentists  
24 were autistic.

25 A I'm not sure that's a good assumption.

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1 There are some very highly performing people, as you  
2 well know, that have Asperger's.

3 Q But he didn't identify any of the --

4 A He did not identify any.

5 Q -- dentists as having autism. Did Dr.  
6 Woods, and you said he -- extrapolate then -- you said  
7 he didn't use or talk about ethyl mercury in any of  
8 his papers. So we can conclude that he didn't  
9 extrapolate that his study can be used to demonstrate  
10 that thimerosal-containing vaccines can cause mercury  
11 toxicity.

12 A I don't think he's been interested at all in  
13 the vaccine. I don't know of any paper by Jim Woods  
14 that deals with vaccines. Again, I could be wrong. I  
15 don't know of any.

16 Q Okay. The second study you refer to is then  
17 the Nataf study? Dr. Nataf in Paris?

18 A Yes, yes.

19 Q Is Nataf important to your opinion about  
20 porphyrin profiles?

21 A Again, it would help me if you talked in the  
22 microphone. Could you move the microphone over  
23 towards you? I'm sorry.

24 Q How important to you is the Nataf study, in  
25 your opinion?

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1           A     It shows that autistic children, I think,  
2     I've forgotten what the number is. I don't have the  
3     paper in front of me.

4                     As I remember it, I want to say probably 120  
5     children, they studied 120 autistic children, I think,  
6     and gave them I think DMSA, also. And if I remember  
7     correctly, I haven't read that paper for at least six  
8     months, but if I remember correctly, the porphyrin  
9     profile in the urine went back to normal after they  
10    gave the chelating agent to bring the mercury up.

11           Q     Did that study measure levels of mercury in  
12    either urine or blood of the subjects?

13           A     I haven't read that paper in six months, so  
14    I'd have to see a copy of it to know what they did.

15           Q     Would you like to see a copy of that paper?

16           A     Thank you.

17                     (Pause.)

18           A     They do porphyrin levels, porphyrin levels.  
19    They did chelation studies. I see nothing in any  
20    figures, I don't know about the text, but I see  
21    nothing in any of the figures that they followed  
22    mercury levels in the urine. But again, I think the  
23    implication is that DMSA would bring out lead and/or  
24    mercury in the urine.

25                     I don't know, I don't see in the abstract

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1 either that urine mercuries were studied, but let's  
2 see in the methods. The impression I have is that  
3 they probably did not do urinary mercury levels, but I  
4 have not studied the paper closely. That's the  
5 impression I have.

6 Q Well, without knowing these levels, the  
7 mercury blood and urine levels, how does the Nataf  
8 study demonstrate an association between mercury  
9 toxicity and porphyrin profiles in autistic children?

10 A They studied autistic children. They gave  
11 DMSA, all right? DMSA we know mobilizes and increases  
12 the excretions of mercury. And so it's a supposition  
13 on their part that these children, when they were  
14 given DMSA, not only had a change in the coporphyrin  
15 excretions, but also had a change in mercury. That is  
16 an assumption on their part.

17 Q The porphyrin studies by Woods and Nataf  
18 were renal porphyrins, correct?

19 A Were?

20 Q Renal. It's kidney, urine porphyrins,  
21 correct?

22 A Again, I --

23 Q The profiles studied in the Nataf and the  
24 Woods papers are renal porphyrins, correct?

25 A Are urinary. You said renal.

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1 Q Urinary porphyrins, correct?

2 A Urinary. That's the problem, I couldn't  
3 connect that word with --

4 Q Now, Doctor, yesterday during your direct  
5 testimony Mr. Williams asked you if the urinary  
6 profiles was one, a semi-quote, I'm not sure since I  
7 don't have the transcript.

8 Mr. Williams asked you if this was one  
9 genetic marker to this efflux problem. And you  
10 responded yes. And can you explain how a pattern of  
11 kidney porphyrins has any relation to a biomarker for  
12 mercury efflux?

13 A I would like to know what my direct quote  
14 was. I wish you --

15 Q Your direct quote was "yes."

16 A -- would give me the direct quotation, in  
17 the context that I made it.

18 Q I believe you said yes to the question if  
19 this was one genetic marker, referring to porphyrins,  
20 one genetic marker to an efflux problem.

21 A To an efflux problem.

22 Q Yes.

23 A Yes. One would expect that if mercury were  
24 accumulating in the tissues, that the porphyrin  
25 profile would change. Does that answer your question?

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1 Q Is it a genetic biomarker for mercury  
2 efflux?

3 A It probably would be, because of the  
4 dentists. It was clearly shown that 15 percent of the  
5 dentists had a different urinary porphyrin profile  
6 because of the difference in the way they metabolized  
7 porphyrins.

8 Q Do urinary porphyrin profiles tell you  
9 anything about the presence of levels of mercury in  
10 the brain?

11 A In the brain?

12 Q Yes.

13 A I don't, I don't know.

14 Q And on page 8 of your report you also  
15 describe a polymorphism that causes elevated --

16 A Can I get to page 8 first, please?

17 Q Sure.

18 A Thank you. What part of page 8 are we  
19 dealing with?

20 Q Pardon me?

21 A What part of page 8?

22 Q The CPOX-4 polymorphism.

23 A Are we talking about the first major  
24 paragraph? The urinary porphyrin profile was found in  
25 85 percent of the dentists, with 15 had an atypical

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1 porphyragenic response? Is that what we're talking  
2 about?

3 Q Yes. Yes.

4 A And what about that, please?

5 Q Are you referring to the CPOX-4  
6 polymorphism?

7 A We are referring to what Jim Woods I guess  
8 would call the changes in the metabolism of  
9 coporphyrins.

10 Q Do you know whether that's a CPOX-4  
11 polymorphism?

12 A I don't have the metabolic shot in front of  
13 me. And with the long names of porphyrins,  
14 coporphyrins and all, I really would rather have a  
15 metabolic chart in front of me so I can trace the  
16 metabolic pathways before I come up with a word  
17 that --

18 Q It's your opinion that there is a  
19 genetically susceptible population who, in response to  
20 ethyl mercury exposure, develop autism, correct?

21 A It's my thinking that there is a population  
22 that, when exposed to the thimerosal vaccines, will  
23 develop, some of them will develop autism.

24 Q In the genetically susceptible population  
25 that you believe exists, those are the children that

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1 cannot excrete mercury? Is that correct?

2 A I would not say they cannot excrete mercury.  
3 I would say they cannot excrete mercury, as much  
4 mercury as is normal, and as much mercury as they  
5 should excrete if they did not, if they were normal.

6 Q And you call this a mercury efflux disorder?

7 A We call it a mercury efflux disorder,  
8 similar to the copper efflux disorder known as  
9 Wilson's Disease.

10 Q And this genetically susceptible population,  
11 we don't know the rate, whether its efflux is reduced  
12 by 50 percent, 25 percent, the excretion of mercury.  
13 We don't know.

14 A We don't know that, because there has not  
15 been enough research yet. The idea of a mercury  
16 efflux disorder was first presented at the IOM  
17 Symposium, which I think was in the year 2004. It  
18 takes time to do such experiments.

19 Q And does the inability to excrete mercury  
20 cause a form of mercury toxicity that results in  
21 autism?

22 A Let's go over that sentence very slowly now.  
23 Would you please repeat it slowly, section by section?

24 Q Does the buildup of mercury, because a child  
25 cannot excrete the mercury, does that result in a

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1 mercury toxicity that leads to autism?

2 A In my opinion, yes.

3 Q And what is the basis for your opinion?

4 A We would have to go back and look at the,  
5 all right, the basis, number one, the experiments by  
6 Holmes and Haley, Haley being at Chemistry at  
7 Kentucky. The experiments by Bradstreet that show  
8 that if you give the DMSA or mercury-mobilizing agent,  
9 more mercury comes out of these kids, as compared to  
10 controls.

11 You must mention the Adams study, in which  
12 baby teeth were used as an indication of the mercury  
13 content of the tissues.

14 Q And Doctor, I don't mean to interrupt, we'll  
15 go over the studies later. I'm not asking the basis  
16 for your belief that there is a mercury efflux; we'll  
17 get into that later.

18 But does that result in the toxicity that  
19 causes autism? Is there a toxic --

20 A I think we're talking about the same thing.  
21 Or if we're not, I don't understand why we're not.

22 We believe, I believe that mercury builds up  
23 in the tissues, and that mercury level in the brain,  
24 because of the metabolism of ethyl mercury to mercuric  
25 mercury, causes, is one of the causes, one of the

1 causes of autism.

2 Again, you must realize the autism spectrum  
3 of disorders are a broad band of diseases. They are  
4 all different diseases. Different kids with so-called  
5 autism react differently to given therapies.

6 Now, if you're asking me whether I think  
7 mercury toxicity in the cells is one of the causes of  
8 autism, there is no question in my mind that it is one  
9 of the causes of autism. And the addition, the  
10 injection of a thimerosal-containing vaccine can be  
11 the trigger, making that child go over the threshold  
12 of a disease process. Does that answer your question?

13 Q I'm not sure. Do you agree with Dr. Deth  
14 and Dr. Mumper that most children with autism suffer  
15 from mercury toxicity?

16 A Yes. Well, let's say, see, science is  
17 quantitative. Science is numbers. I would hate in  
18 this sense to use an adjective, "most." I would say a  
19 great many. Even that's bad. A certain percentage of  
20 children with autism in my opinion clearly suffer from  
21 mercury toxicity. What that percentage is, I don't  
22 know.

23 Q Is your genetically, the genetically  
24 susceptible population that you believe exists, are  
25 they unable to excrete all forms of mercury? Or is it

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1 just ethyl mercury?

2 A I really don't know, because that study  
3 hasn't been done.

4 Q But it's your belief that there is a mercury  
5 efflux disorder. Is it a mercury efflux disorder or  
6 an ethyl mercury efflux disorder?

7 A There's a mercury efflux disorder that they  
8 cannot get mercury out of their cells to any great  
9 extent.

10 Q So you think it's all mercury; methyl,  
11 ethyl.

12 A It can be anything. But the ethyl mercury,  
13 we must understand, when it gets into the brain is  
14 deethylated. Because it's very, very toxic mercuric  
15 mercury, which, when injected directly into the brain,  
16 as you pointed out earlier in the slide that you  
17 brought up, has very toxic, causes neuronal necrosis.

18 Q Methyl mercury demethylates into mercuric  
19 mercury in the brain as well, correct?

20 A Pardon?

21 Q Methyl mercury demethylates --

22 A Yes.

23 Q -- into mercuric mercury in the brain, as  
24 well.

25 A Yes.

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1 Q Thank you.

2 A But it's not the methyl -- more of it is  
3 excreted. It's the excreted part, it's removed more  
4 rapidly from the brain, so that the amount of mercuric  
5 mercury formed from a given dose of methyl mercury is  
6 less than, the percentage is less than the conversion  
7 of ethyl mercury to mercuric.

8 Q Excuse me, did you say methyl mercury is  
9 excreted faster than ethyl mercury?

10 A No, I thought I said -- let me reword it to  
11 be certain -- that methyl mercury is removed from the  
12 brain faster than ethyl mercury is removed from the  
13 brain. This is based on the infant monkey studies of  
14 Burbacher, where speciation was done, and it was  
15 clearly shown that of the two, of the total mercury  
16 remaining in the brain, the animals getting ethyl  
17 mercury had a higher percentage of inorganic or  
18 mercuric mercury.

19 Q Is mercury efflux a lifelong condition?

20 A We don't know that much about it. I would  
21 expect so. We don't know.

22 Q You don't know.

23 A I guess that's the best way of putting it;  
24 we don't know.

25 Q And is the only outcome of mercury efflux

1 disorder autism?

2 A Again, as it took them 100 years to show  
3 that Pink Disease was due to mercurous mercury in the  
4 teething powder, it's probably going to take the  
5 medical community another 50 or 100 years to come to  
6 any conclusion about the mercury efflux disorder.

7 And no disrespect is meant to the medical  
8 establishment. I think it's clearly accepted that the  
9 American medical establishment, one of its strengths  
10 actually is its conservatism.

11 Q So in the mercury efflux disorder, you're  
12 not removing mercury from the tissues as well as the  
13 brain, is that correct?

14 A Yes. It's probably a matter of degree.  
15 There's more mercury accumulation in the brain because  
16 the mercuric mercury cannot get out of the brain.  
17 What mercuric mercury is bound to also cannot get out  
18 of the brain as easily as mercuric mercury gets out of  
19 tissues.

20 The greatest concentration of mercuric  
21 mercury in the body usually is in the kidney.

22 Q Assuming that mercury efflux disorder is all  
23 mercury, and assuming it's a lifelong condition, what  
24 mechanism do you know of that would just cause autism  
25 without resulting in clinical signs of mercury

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1 toxicity?

2 A Well, I think if you talk -- I'm not a  
3 clinician, as you well know, I'm not an MD, as you  
4 asked me many times. I'm not a neurologist, as you  
5 well know.

6 But if you talk to many of the physicians  
7 who treat and diagnose autistic children, they will  
8 say that they see very similar signs of, they see very  
9 similar -- they have similar diagnostic evidence for  
10 mercury toxicity in some of their autistic children.

11 I'm not a clinician. I don't want to make  
12 that statement. I'm telling you what I am told.

13 Q Can you reconcile this position with the one  
14 you took in -- do you remember you spoke at the 2004  
15 Institute of Medicine? Where you said that the signs  
16 and symptoms of mercury poisoning are so indefinite  
17 and non-specific that you can come to any conclusions  
18 that you want.

19 So is that different than your opinion  
20 today, that --

21 A Can I read this?

22 Q Sure.

23 A It's four years ago, you know.

24 (Pause.)

25 A There is a term that we've used, that I

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1 thought we used here, called micromercurialism, all  
2 right? And it's usually meant to be a, people that  
3 have been exposed to what is normally considered  
4 below-toxic amounts of mercury, but will have signs,  
5 some signs, some non-specific signs if you will, of  
6 mercury toxicity. And the term micromercurialism I  
7 think is certainly in the literature.

8 And so what should have been said here, and  
9 what I'm saying is the signs and symptoms of  
10 micromercurialism or micromercury poisoning are so  
11 indefinite and so non-specific that you can come to  
12 any conclusion you want.

13 And to some extent, that's also true with  
14 anything but extremely severe mercury toxicity. Many  
15 of the signs of mercury toxicity are signs and  
16 symptoms seen in other diseases. Many people --  
17 that's one reason why a good clinician, I'm sure  
18 you'll agree, will want a mercury determination done  
19 on the blood, and/or on the urine, before the term  
20 "mercury intoxication" is made. Most of the board-  
21 certified clinical toxicologists that I know of would  
22 make that statement.

23 Q If a person had efflux disorder, the  
24 genetically susceptible population has an efflux  
25 disorder, can they experience mercury toxicity from

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1 eating fish? Too much fish?

2 A Probably. Yes, I would say they could.

3 Again, depending on how much fish they eat, and how  
4 old they are, and what their genetic predisposition  
5 is.

6 Q Is there any evidence that such a thing is  
7 occurring? Mercury toxicity from fish consumption, or  
8 children nursing? Breastmilk with methyl mercury in  
9 it?

10 A The first question is, is there any evidence  
11 of mercury toxicity from fish eating?

12 Q Yes. In this country.

13 A Absolutely. In the Philippines, in Brazil,  
14 many of these people, there are huge amounts of  
15 scientific literature that show that people who eat  
16 fish, especially near gold-mining, where mercury is  
17 used to amalgamate mercury, the mercury gets into the  
18 water. The fish consume that water. There is a  
19 tremendous amount of literature.

20 In fact, that's the Minamata story, also,  
21 where, in Minamata, these people had, the factory  
22 dumped mercury into the river; the river empties into  
23 Minimata Bay. The fishermen, the cats, the birds ate  
24 this, ate these fish, and they got sick. There's no  
25 question about that.

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1 Q There is no question about that, but those  
2 were huge doses of methyl mercury.

3 A Of course. But you didn't mention huge  
4 doses.

5 Q I'm saying we have a genetically susceptible  
6 population who cannot efflux mercury. They eat  
7 tunafish, cans of tunafish. Can they suffer mercury  
8 toxicity?

9 A Yes, they could. If they are  
10 hypersusceptible, or if they have a genetic  
11 predisposition, they certainly could.

12 Q And is there any evidence of mercury  
13 toxicity due to a lack of excretion of mercury that  
14 results in mercury toxicity from tunafish consumption?

15 A There certainly is a paper that one of the  
16 respondents has criticized from, I think it's the  
17 University of California. A physician that's a woman  
18 who showed that many of her patients who were eating  
19 high levels of tuna steaks and other things, and other  
20 high-priced fish, had health complaints. And when she  
21 recommended that they stop eating fish for six months,  
22 the complaints disappeared.

23 The criticism of these papers is that she  
24 did not determine mercury.

25 Q And that's the Hightower study, correct?

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1 A Thank you very much, the Hightower study.

2 Q So we don't know if these people were  
3 genetically susceptible because of efflux.

4 A That's correct.

5 Q So that paper doesn't demonstrate an efflux  
6 disorder.

7 A But you asked me whether I knew of any, I  
8 thought you asked me did I know of any case where  
9 eating tunafish or fish could cause mercury toxicity.

10 Q Due to an efflux disorder. So you would  
11 expect --

12 A Due to an efflux disorder, we have no  
13 evidence in those cases that they had efflux disorder.

14 Q Now, in your testimony yesterday and in your  
15 report, you talk about a spectrum, a band, of autism.  
16 And I think we can pull it up. It's certainly not as  
17 colorful as the one you had yesterday, but we have it  
18 on the screen here.

19 Can you identify where, on this band,  
20 children who develop autism from thimerosal-containing  
21 vaccines would fall?

22 A We don't know the various, the various kinds  
23 of autisms. The various severities of autism have not  
24 been quantifiably presented by the medical community.  
25 So there is no way that I could fill in the bands

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1 between Asperger's, which is high-functioning ASD, or  
2 autism, which is the most critical cases where they  
3 are severely affected.

4 My point is there is nothing that I know of  
5 that we can put in the middle. That I know of. There  
6 are probably physicians that could put some things in  
7 there, but they would not give us very many bands.  
8 That's why it's called the autism spectrum disorder.

9 Q Is there any evidence that there is more  
10 mercury in the brains of autistic children, compared  
11 to non-autistic children?

12 A I thought there was a paper that I quoted in  
13 my presentation yesterday that showed that autistic  
14 children had a high amount of mercury in their brains.  
15 I'd have to go through my -- will you give me a minute  
16 to go --

17 Q You don't know if off the top of your head?

18 A Pardon?

19 Q I mean, you gave this, you gave your  
20 testimony yesterday; you don't recall what article  
21 you're referring to?

22 A I think there are 135 or something slides.  
23 I certainly could not quote every one of those slides  
24 to you.

25 Q Would this finding be critical to your

1 opinion?

2 A I don't understand your question.

3 Q Is this article critical to your opinion?

4 A Is one of a series of articles that I think  
5 is very important -- but again, I would like to look  
6 at it on my slide set before I made a statement about  
7 it, because it has been a very traumatic couple of  
8 days, as I'm sure you realize.

9 Q I won't have you do that. We'll just move  
10 on.

11 A All right.

12 Q Is mercury efflux disorder recognized in the  
13 general medical community?

14 A I would say I don't know. I do know it's  
15 recognized in a large number of physicians who treat  
16 autism.

17 Q Does Dr. Mumper recognize it?

18 A Pardon?

19 Q Does Dr. Mumper recognize mercury efflux  
20 disorder?

21 A You'd have to ask her.

22 Q Okay.

23 A I know that I've been invited to various  
24 think tanks that deal with autism, that are by  
25 invitation only, that have anywhere from 20 to 100

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1 people. And during those talks, people refer to  
2 mercury efflux disorder. Based on the evidence that I  
3 have pointed out, as far as the Adams paper, the  
4 Bradstreet paper, and the Holmes paper. And their  
5 confirmation by the MIT Group.

6 Q What think tanks were you invited to? Do  
7 you have --

8 A There was one think tank, a very, very  
9 interesting one. There is a small reservation owned  
10 by, formerly owned by the RCA Company that was used  
11 for worldwide transmission, north of San Francisco  
12 about 45 miles. It's owned by a foundation whose name  
13 begins with C, and I just don't remember which one.

14 At that time they brought about 20 people  
15 together. They brought two couples with autistic  
16 children; they brought four scientists together, of  
17 which I was one; they brought some MDs. So it was a  
18 small group of people, and mercury efflux, that's one  
19 of the meetings that you're asking, a think tank.

20 The other think tank is by the Autism  
21 Research Institute. That's held about twice a year.

22 Q Is that a part of, DAN is part --

23 A DAN is, excuse me, DAN is part of that  
24 group. And it's a very large group. At meetings  
25 there are probably 6,000 people, not at the think

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1 tank, that show up at a DAN meeting. It has been a  
2 tremendous help to the autism community, the community  
3 with autistic children, because established medicine  
4 for many years would not do anything about treating  
5 autism.

6 Autism is now considered by many people to  
7 be a recoverable disease, by many physicians.  
8 Certainly not by many establishment physicians. But  
9 there are certified cases of recoverable disease.

10 What is sad is that everyone agrees that the  
11 more money the parents have, or had, the more likely  
12 their child was to recover. And that's because the  
13 family could spend all sorts of money in trying every  
14 single kind of treatment. It's almost un-democratic.

15 Q Your hypothesis that thimerosal-containing  
16 vaccines, your hypothesis that thimerosal-containing  
17 vaccines cause autism. Is that limited to just  
18 clearly regressive autism?

19 A I have not talked about that at all, and I  
20 would not want to venture such an important opinion  
21 without thinking about it more carefully.

22 Q You've never thought about this before?

23 A Your question?

24 Q Yes.

25 A No, I have not.

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1 Q Could you think of a mechanism by which  
2 mercury efflux disorder could cause only clearly  
3 regressive autism?

4 A Again, I would want to sit and think about  
5 it before I made such a statement. I think it still  
6 could be an accumulation of mercury at a given time,  
7 plus a genetic hypersusceptibility to the mercury.  
8 That's about all I feel safe saying at the present  
9 time, because this is a court of law and I must tell  
10 the truth.

11 Q You testified at the DO and in your report,  
12 you have it in your report, that there are hypotheses  
13 that there is a specific window of development; that  
14 the reason -- and your second hypothesis is the reason  
15 not all children who receive vaccinations develop  
16 autism is because not every child gets vaccinated at  
17 exactly the same point in time. Is that your  
18 hypothesis?

19 A It is part of my hypothesis to explain why  
20 more children don't get -- if you look at the story of  
21 thalidomide, which is a known, which most -- do you  
22 know the thalidomide story?

23 Q Yes, I do.

24 A Okay. It is probably one of the worst  
25 teratogenic episodes that the human population has

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1 been exposed to. But not every child whose mother  
2 took thalidomide during her pregnancy got, got the  
3 problem, got the thalidomide, the monster formation,  
4 born without arms, born without wrists, et cetera.

5 There is a window for all teratogenic  
6 agents. And there is a tremendous amount of  
7 literature about this. And that window is usually  
8 very narrow, relatively narrow.

9 And so it is very reasonable to me that one  
10 of the reasons, not the only reason, that children,  
11 that all the children getting thimerosal did not  
12 develop autism.

13 Q Now, thalidomide was a prenatal exposure,  
14 correct?

15 A Thalidomide was a prenatal exposure.

16 Q So the window was prenatally.

17 A Yes. But there are other teratogenic agents  
18 known that have an effect on the window post-natally.

19 Q And what are those?

20 A I think, I'm not positive, valproic acid may  
21 be one. But the literature, if you pick up any book,  
22 and I'm not even sure about valproic acid being post-  
23 natally. But if you pick up any toxicology textbook,  
24 there's usually a chapter on teratology, and lists  
25 agents that are affected prenatally and post-natally.

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1 Q And you just listed prenatal ones in your  
2 report, for example.

3 A Pardon?

4 Q You just listed prenatal exposures in your  
5 report, for example.

6 A That's right.

7 Q Is the window, does it apply only to a  
8 genetically susceptible population? Or is it just a  
9 timing issue?

10 A I think it's both. But there is no question  
11 that in teratology, there has to be a predisposition  
12 to that effect of the metal. There has to be a  
13 predisposition.

14 And so time, and since that predisposition  
15 to an agent also has a window, there has to be a time  
16 element there, also.

17 Q And is that predisposition mercury efflux,  
18 and then the window?

19 A That predisposition would be that one, that  
20 the child would be deficient in the mechanism for  
21 bringing mercury out of the cells; just as the  
22 Wilson's Disease patients don't have the gene for the  
23 copper transport protein that brings copper out of the  
24 cells.

25 We use Wilson's Disease, or hepatolenticular

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1 degeneration as it's called, as an example of an  
2 efflux disorder, which is accepted by the medical  
3 community. The conservative ones, also.

4 Q But if there's a very narrow window, how is  
5 there an accumulation? So you're accumulating  
6 mercury, and then there's --

7 A Oh, be careful.

8 Q -- a very narrow window?

9 A Be careful. We're not talking about  
10 accumulation in that window. We're talking about an  
11 effect in that window.

12 In other words, when my arm -- and think of  
13 me as an embryo, if you will.

14 Q I'll try.

15 A When the DNA tells my arm to begin  
16 developing, well, the arm just doesn't shoot out. The  
17 first thing that happens is something, a bud is going  
18 to occur here, and there's going to be some kind of a  
19 formal, or something that will come in and say hey,  
20 make that arm a little longer. And ah, then all of a  
21 sudden we have an elbow. And then again another.

22 So this process can take maybe a week or a  
23 month. But each part of it, each part of it is a  
24 window. Are you with me? So that that window can be  
25 very narrow.

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1           Maybe thalidomide had no effect way out here  
2           when my fingernail was formed, but thalidomide may  
3           have an effect up here when my shoulder is being  
4           formed.

5           So the window, the window is when some  
6           particular morphological event is occurring, so that  
7           the arm will continue to develop. And that  
8           development, if you have a teratogen around, is based  
9           on a number of things. It's based on the width of the  
10          window, the time element, the concentration of the  
11          teratogen, and the predisposition of the mother and  
12          the predisposition of the embryo, through the toxic  
13          effects of that teratogen.

14          Q     So dose is important. Because I thought  
15          from your report --

16          A     Dose is one of the important factors.

17          Q     Okay. With autism, are you talking about a  
18          neurodevelopmental window?

19          A     I'm trying to look at the whole picture.  
20          There certainly is part of the development of autism,  
21          as far as a neurodevelopmental window. Which  
22          neurodevelopmental window that is, we don't know. If  
23          we knew, we would know the cause of autism.

24          Q     So if I put up William Mead's vaccination  
25          schedule, for instance, one of the Petitioners in this

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1 case, can you tell me where the neurodevelopmental  
2 window would be?

3 A You must remember that a child's brain does  
4 not stop maturing, does not stop being formed until at  
5 least puberty. So to ask anyone what window is going  
6 on at this time is almost an impossible question.

7 At each of these times, that child is  
8 maturing, that child is developing. His brain is  
9 developing. Now, what brain function is developing at  
10 2.5 months of age, or how many brain functions are  
11 developing at 2.5 months of age, I would leave that to  
12 a neurologist, or a developmental neurologist, say.

13 Q So you can't tell me what's going on in the  
14 brain when that window is open.

15 A I can't tell you because I don't know which  
16 window you're talking about. We have many windows.

17 Q The window, the window that when they  
18 receive the thimerosal-containing vaccine, it leads to  
19 autism. That window.

20 A If we knew that, we could cure autism. We  
21 don't know it. No one knows it.

22 Q And we don't know what part of the brain the  
23 window, we don't know whether it's during the  
24 development or what part of the brain --

25 A Well, we probably will know it soon because

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1 of a paper that Burbacher may have impressed, or at  
2 least he's about to submit, whereby he has used a  
3 technique to not only determine the concentration of  
4 mercury in the brain of injured monkeys who got  
5 thimerosal, but also is able to localize, visually  
6 localize where the mercury is in various parts of the  
7 brain, in certain sections of the brain. That may be  
8 a very valuable tool to tell us what's going on.

9 But at the present, we don't know.

10 Q Now, you said these windows are very narrow,  
11 correct?

12 A It depends on which window you're talking  
13 about, and it depends on the definition of "narrow."  
14 Some are narrow, some are narrower. They're not  
15 large.

16 Q Well, it's your hypothesis, so why don't you  
17 tell me? I mean, tell me when the window is, how long  
18 it lasts, and how it leads to autism.

19 A It took the thalidomide people almost four  
20 years to come up with the window for thalidomide. We  
21 have not, I don't know of anyone that is looking for  
22 that window at the present time, because the federal  
23 government, the NIH in particular, has been very  
24 reluctant to support research on autism.

25 When you stop and think that more money is

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1 spent trying to keep a man like me alive, an old man,  
2 with research on cancer and high blood pressure,  
3 millions are spent by the National Institutes of  
4 Health. Whereas when I die, it's not going to cost  
5 very many people anything.

6 But when a child gets autism, it's going to  
7 cost society at least, what was the figure, \$3 million  
8 or \$300 million. And very little money in comparison  
9 in this country is spent on research to help the  
10 children, in particular to find out the cause of  
11 autism. And this is where my faith in democracy was  
12 restored, because we would not have autism research  
13 going on in the National Institutes of Health today if  
14 the parents of autistic children did not go to  
15 Congressman Burton, and a whole series of  
16 congressional hearings were set up, and pressure was  
17 put on the National Institutes of Health to do autism  
18 research.

19 It's very difficult for me to say that. I'm  
20 a child of the NIH. My complete education and  
21 research have been supported by the National  
22 Institutes of Health. But it's the one time that I've  
23 been ashamed of the National Institutes of Health,  
24 that they did not support decent research on autism.

25 Q I'm going to go back to your windows.

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1 A All right.

2 Q During this window of vulnerability, does  
3 any, is it just mercury that can have an effect on the  
4 development of this child? Or is it any --

5 A Again, we don't know, because we don't know  
6 what mercury -- I'm sorry, we don't know what window  
7 we're really talking about. But usually, usually  
8 windows are susceptible to many agents.

9 Like the thalidomide window has been  
10 proposed by some people as being the autism window.  
11 But I don't think the medical community accepts that  
12 as a whole.

13 Q Now, in Cedillo you said your narrow window  
14 was a hypothesis. Has anything come out, any peer-  
15 reviewed articles, that is this anything more today  
16 than a hypothesis than it was in Cedillo?

17 A A hypothesis as to the mercury efflux? Or  
18 the hypothesis --

19 Q The window of susceptibility.

20 A Window of susceptibility.

21 Q The timing issue.

22 A I think I would guess that most clinicians  
23 would agree that any kind of a toxin given during the  
24 child's development pre- or post-natally would have a  
25 potential window of effects. I don't think, well, I

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1 don't think any embryologist would disagree with that,  
2 and I don't think any pathologist would disagree about  
3 that. And as far as medical toxicologists, I was  
4 certainly not one to put words in their mouth.

5 Q But your window is not for, your window is  
6 for 12.5 micrograms, or 25.5 micrograms. We're not  
7 talking toxic doses if they're in a particular window;  
8 we're talking about micrograms, is that correct?

9 A We're talking about micrograms that are  
10 being given to a child who may have large  
11 accumulations of mercury in his or her tissues  
12 already.

13 Q Because of mercury efflux disorder.

14 A Pardon?

15 Q Because of mercury efflux.

16 A Because of exposure via the mother, transfer  
17 of mercury through the placenta, and because he or she  
18 has an efflux disorder.

19 Q On page 24 and 25 of your report --

20 A I have so much paper here.

21 Q I'm just going to get a sip of water.

22 A Are you going to show it on here, or no?

23 Q No.

24 A Okay, I have page 24 now. I have page 24.

25 Q Okay.

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1 MS. RENZI: Special Master, I have maybe 35  
2 more minutes of questions. Do you want me to carry on  
3 and finish it up?

4 SPECIAL MASTER VOWELL: I'd say go ahead.

5 MS. RENZI: Okay.

6 SPECIAL MASTER VOWELL: Does anyone need a  
7 break at this point? Dr. Aposhian, could you use a  
8 break?

9 THE WITNESS: I'd love to have five minutes  
10 just to collect my thoughts, but I don't need anything  
11 more than that. But it's not necessary, Special  
12 Master.

13 SPECIAL MASTER VOWELL: Let's go ahead and  
14 take our mid-morning break, then. We'll resume then  
15 at about 10 minutes to 11:00.

16 (Whereupon, a short recess was taken.)

17 SPECIAL MASTER VOWELL: Please be seated.  
18 All right, we're back on the record in the Theory II  
19 and the King and Mead proceedings.

20 Ms. Renzi, you may proceed. Dr. Aposhian is  
21 back on the witness stand. And once again, I remind  
22 you, sir, that you're still under oath. I remind you  
23 that you are still under oath.

24 THE WITNESS: Thank you, ma'am.

25 //

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1 BY MS. RENZI:

2 Q Dr. Aposhian, on pages 24 and 25 of your  
3 report.

4 A Yes, ma'am.

5 Q You list six pieces of evidence that you say  
6 if taken alone leave some doubt, but if taken together  
7 implicate thimerosal as the etiology of some autism  
8 spectrum disorders. Do you agree with that?

9 A Yes, ma'am.

10 Q I'd like to go through those six pillars.  
11 And I know you've discussed this yesterday, and we'll  
12 discuss it today.

13 The first one is the Adams study, the tooth  
14 study. And I believe you wrote and testified that  
15 this study found that teeth from autistic children  
16 contained more mercury than those of non-autistic  
17 children, correct?

18 A Yes.

19 Q And that demonstrated that autistic children  
20 have a higher body burden of mercury than non-autistic  
21 children. Is that an accurate description?

22 A I have the statement here, just that Adams  
23 demonstrated that teeth from autistic children  
24 contained more mercury than those of non-autistic  
25 children.

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1 Q Is it your opinion that that demonstrates a  
2 higher body burden of mercury in autistic children,  
3 compared to non-autistic children?

4 A Do I say here that it does?

5 Q I'm asking if that's your opinion, can you  
6 conclude that.

7 A Oh. The teeth have been used as -- the  
8 answer is yes.

9 Q Can you cite to any peer-reviewed articles  
10 that demonstrate that tooth mercury concentrations  
11 reflect mercury body burden?

12 A Would you repeat the question, please? Talk  
13 into the microphone, please.

14 Q Can you cite to any peer-reviewed articles  
15 that demonstrate that tooth mercury concentrations  
16 reflect mercury body burden?

17 A I can just state that there is evidence that  
18 lead, zinc, and other metals, including mercury, which  
19 are increased in teeth, are a reflection of the amount  
20 of mercury in the body and the other tissues. This  
21 has been clearly shown for lead by Needleman in his  
22 very classic studies on lead, and it's been shown by  
23 other people, too. The teeth have been used as a  
24 marker.

25 Q For mercury body burden?

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1 A For mercury in this case Adams has done.

2 Q You testified in Cedillo that teeth are not  
3 excretory organs, correct? Are teeth excretory  
4 organs?

5 A Did I say it was an excretory organ?

6 Q You said it was not.

7 A Yeah, I haven't thought about it. It's  
8 considered to be a tissue, an organ, that is, that  
9 takes up phosphate, it takes up calcium and many other  
10 things.

11 Q Now, you stated in your testimony today, and  
12 I believe yesterday, that all papers are subject to  
13 review and criticism. You said all papers, any peer-  
14 reviewed article, you show them to your students and  
15 you get criticisms of all papers that are peer  
16 reviewed. Is that correct?

17 A Yes.

18 Q What are your criticisms of the Adams study?

19 A Of the --

20 Q Adams study.

21 A I think most people -- well, probably the, I  
22 don't have the paper in front of me, probably the  
23 number of controls that he got could have been  
24 increased. That's probably true with many studies,  
25 that the number of autistic, the number of teeth, the

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1 number of autistic children that contributed teeth and  
2 the number of control children that contributed teeth  
3 is probably small.

4 Q Do you recall how many controls or --

5 A I don't have the paper in front of me. I  
6 read over 100, I read many papers. And there's  
7 certain things that I know I can just go back and look  
8 at.

9 Q Would you like us to hand you the Adams  
10 study?

11 A Pardon? Okay, thank you.

12 (Pause.)

13 A M was 15 with autism spectrum disorder, and  
14 N was 11 typically developing children.

15 Q Were the levels of mercury found in the  
16 autistic, in the teeth of the autistic children, were  
17 they indicative of mercury toxicity?

18 A I don't think there have been enough studies  
19 performed to have used teeth as an indication of  
20 mercury toxicity, or teeth as a biomarker. I don't  
21 know of any studies that have taken teeth from  
22 severely mercury-toxic people, and examined for  
23 mercury.

24 Q Well, what was the average mercury level of  
25 the teeth in the autistic children, reported by Adams?

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1 And you can see table 2 on page 4, if that's helpful.

2 A For autistic children it was 0.15.

3 Q Is that indicative of mercury toxicity?

4 A I don't know. But it is more than what's in  
5 the controls.

6 Q Do you know whether mercury levels vary  
7 depending upon the tooth? Whether it's an incisor, a  
8 canine, a molar?

9 A I don't know that.

10 Q Would you expect mercury concentrations to  
11 vary depending upon the sex of a child?

12 A Yes.

13 Q Do you know whether the Adams study  
14 controlled for gender?

15 A I don't know where -- usually there are more  
16 autistic boys than there are autistic girls. And I  
17 would just have to see where, number of male and  
18 female, there were 81 percent males in the autistics,  
19 and 45 percent in the control.

20 Q So he didn't control for gender.

21 A No, he doesn't control for gender.

22 Q Does lead concentration affect mercury tooth  
23 concentration?

24 A What?

25 Q Does lead concentration in the tooth affect

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1 its mercury concentration?

2 A Does blood --

3 Q Lead. Does lead.

4 A Does lead.

5 Q Yes. Does lead tooth concentration affect  
6 mercury tooth concentration?

7 A You're asking me whether lead concentration  
8 affects mercury concentration in the teeth?

9 Q In a tooth, yes.

10 A I don't know.

11 Q Do you know what type of mercury was  
12 measured in the teeth? Was it ethyl mercury or  
13 inorganic mercury?

14 A I don't know whether he did speciation or  
15 not. Let's see.

16 (Pause.)

17 A I don't think they did speciation. I think  
18 he's doing total mercury.

19 Q Do levels of mercury in baby teeth reflect  
20 anything, tell you anything about the levels of  
21 mercury in the blood?

22 A In the blood?

23 Q In the circulating blood.

24 A I don't know. I think it would depend on  
25 the particular genetic composition of the child, but I

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1 don't know the answer to your question.

2 Q Do mercury levels in the teeth tell you  
3 anything about the amounts of inorganic mercury in the  
4 brain?

5 A I don't know whether there has been a  
6 correlated study along those lines. I don't think  
7 anyone has done the study.

8 Q The second piece of your pillar is the  
9 Holmes study.

10 A Yes.

11 Q And that's on page 24 and 25 of your report,  
12 if that's helpful, in the Holmes study's Petitioner's  
13 Master List 237. And the Holmes study found that hair  
14 from autistic children contained less mercury than the  
15 controls, is that correct?

16 A That's correct, as I said in the report.

17 Q And then from that, do you conclude from  
18 this study that autistic children cannot excrete  
19 mercury?

20 A That autistic children, I'm not sure what  
21 sentence you're talking about now.

22 Q I'm asking if it's your opinion, based on  
23 that study.

24 A Yeah. I think this is one of the examples  
25 of there's less mercury being excreted into the hair

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1 in autistic children, which is an indication of more  
2 of it being, more of it staying in the tissues of  
3 autistic children, as compared to controls.

4 Q What percentage of mercury gets excreted  
5 through the hair? What percentage of mercury --

6 A A very small percent.

7 Q What percentage gets excreted through feces?  
8 Through the feces or through urine. Can you break  
9 that down?

10 A The feces is a major source of, is a major  
11 out of the excretion of mercury.

12 Q How about urine?

13 A Urine is a route, if you use -- well, first  
14 of all, you can use urine as a measure of mercury  
15 exposure, of how much mercury is in the body. You can  
16 increase the mercury excretion in the urine by giving  
17 a chelating agent, like DMSA.

18 Q Were measurements of either feces or urine,  
19 mercury measurements taken in either feces or urine in  
20 the Holmes study?

21 A No.

22 Q Did the Holmes study attempt to determine or  
23 control for mercury exposure in their test subjects  
24 before they took hair samples?

25 A I'm sorry.

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1 Q Did they control for --

2 A Excuse me, ma'am. But if you would talk  
3 directly into the microphone, it would be a big help  
4 to me.

5 Q Did the Holmes study attempt to determine or  
6 control for mercury exposure in their test subjects,  
7 before taking hair samples?

8 A They just took hair samples, as far as I  
9 know. Again, I read that paper a number of times  
10 after it was published. I don't remember whether they  
11 did any interviews or anything else about mercury.

12 Q What studies have confirmed the Holmes  
13 study?

14 A A study from the MIT Group, which had a  
15 small number of children, but used an entirely  
16 different technique, is an example of a confirmation  
17 of the Holmes study.

18 Q And is that also known as the Hughes study  
19 HU? Is that the Hughes study, HU 2003?

20 A Yes. Yes, it is.

21 Q How many autistic children were included in  
22 that study?

23 A It was either two or three. It was a small  
24 number. I don't -- it's a small number.

25 Q And did the author of that paper control for

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1 dietary intake of mercury?

2 A They state quite clearly that they did not.

3 Q And isn't it true that two of the three  
4 autistic subjects had undergone heavy metal  
5 detoxification prior to being tested?

6 A If the paper says so, that's true.

7 Q And wouldn't dietary intake and mercury  
8 detoxification, wouldn't they be factors that would  
9 affect levels of mercury found in the hair?

10 A It would cause more mercury to be found in  
11 the hair if the intoxication was for a lengthy period  
12 of time. But the hair, it depends on how the hair  
13 analysis was done; whether it was done in segments to  
14 correlate with time, or it was a complete hair sample.

15 Q Are you aware of any papers that dispute the  
16 findings of Holmes?

17 A We have quoted the Ip paper as being  
18 incorrect. And we have quoted other papers. We have,  
19 there are indications that people believe the Holmes  
20 paper makes sense now, especially after the reanalysis  
21 by, I want to say DeSoto is her name, I think it's  
22 DeSoto. It's from yesterday's, it's in the record.

23 Q Now, the Ip study did not find a significant  
24 difference in mercury hair levels between autistics  
25 and non-autistics, is that correct?

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1           A     The Ip study, I want to be certain we are  
2     quoting it correctly. But essentially, that's correct  
3     as I recall it.

4                     But the point is that the DeSoto people  
5     pointed out they reanalyzed the data originally  
6     reported by Ip, et al, in 2004, and found the original  
7     p values were in error, and that a significant  
8     relation does exist between, they did blood levels,  
9     and the diagnosis in autism spectrum disorder.

10                    Moreover, the hair sample analysis results  
11     offer some support for the idea that persons with  
12     autism may be less efficient and more variable in  
13     eliminating mercury from the blood.

14           Q     Did the DeSoto article criticize the  
15     findings of the Ip hair study, or just the blood  
16     findings? Did they find the hair measures to be  
17     incorrect?

18           A     They criticized the blood levels.

19           Q     I've put up on the screen what DeSoto said  
20     about the hair levels.

21           A     You're not talking into the microphone, I'm  
22     sorry. Forgive me.

23           Q     I've put up on the screen what DeSoto said  
24     about the hair studies in the Ip. It's on the screen,  
25     sir.

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1 A Oh.

2 Q It says there was no difference in the mean  
3 hair levels. This is essentially the same result as  
4 reported in the initial, the original article.

5 So the DeSoto study doesn't dispute the hair  
6 findings of Ip, is that correct?

7 A I would have to read the paper again very  
8 carefully. This statement implies that. I just don't  
9 remember this statement, per se.

10 However, could you go on to say what the  
11 "however" is? However, given that hair levels would  
12 normally expect to be higher occurring, it might be  
13 surprising that blood levels could predict an autism  
14 spectrum disorder, but that hair and mercury levels  
15 could not. Indeed, hair and mercury levels for the  
16 whole sample were correlated.

17 Q Are you aware of the Fido article of 2005?  
18 F-I-D-O. And that's Respondent's Master List Article  
19 138. Are you familiar with that article?

20 A Can you expand for me? Oh, this is the  
21 article from Quake. And so I don't know how good  
22 these investigators are. There is no American  
23 investigator associated with this study. I don't know  
24 whether they used the proper techniques. I don't  
25 know. I'm not willing to make, to give an opinion on

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1 this paper.

2 Q But did it dispute the findings of the  
3 Holmes study?

4 A Pardon?

5 Q Did it dispute the findings in the Holmes  
6 study?

7 A They dispute the findings in the Holmes  
8 study. Could you give me the general reference,  
9 what -- that's what I thought, okay. I'm ready to go  
10 on.

11 Q How about the Kern study, 2007? And that's  
12 Respondent's Master List No. 274. Did the Kern study  
13 dispute the findings of the Holmes study?

14 A I think it does dispute it.

15 Q And how about Adams 2006, Respondent's  
16 Master List 2?

17 A Well, let's read that abstract.

18 (Pause.)

19 A I don't see in this particular abstract the  
20 word "mercury," though I could miss it very, very  
21 easily. They have done iodine levels, chromium  
22 levels, potassium levels, zinc, lithium. I don't see  
23 in the abstract the word "mercury." Again, I could be  
24 wrong. So what is the point of this article? Why are  
25 you bringing it up now?

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1 Q Does it confirm the Holmes study, then?

2 A It doesn't try to confirm the Holmes study.  
3 As far as I can see, this article does not, as far as  
4 the abstract is concerned, does not mention mercury  
5 analysis of hair.

6 Q Are you familiar with the rest of -- I won't  
7 ask you to read the article, Doctor, so we will move  
8 on.

9 A I'm just reading the abstract.

10 Q Okay. We'll move on. I want to turn to  
11 chelation now, which you use as -- chelation.

12 A Yes, what about it?

13 Q These are the third and fourth pillars of  
14 your six pillars.

15 A This is the Bradstreet report? Is that what  
16 you're referring to?

17 Q We'll start with the Bradstreet report. And  
18 that report stated that autistic children treated with  
19 DSMA excreted more mercury than controls. Is that  
20 correct?

21 A Yes. They were comparing controls with  
22 autistic children.

23 Q What is DSMA? What is DSMA? DMSA, excuse  
24 me.

25 A DMSA is dimercaptosuccinic acid. It is a

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1 water-soluble, relatively non-toxic chelating agent  
2 that mobilizes metals, such as lead, arsenic, and  
3 mercury. It is approved by the Federal Drug  
4 Administration for the treatment of children with  
5 blood levels of 45 micrograms per deciliter of blood  
6 or more.

7 But it also has an off-label use for  
8 treating mercury intoxication and arsenic  
9 intoxication, because its safety has been proven in  
10 children.

11 Q And it's fair to say that you performed a  
12 significant number of chelation studies, is that  
13 correct?

14 A Bradstreet?

15 Q No, you.

16 A Yes, that's correct.

17 Q And you've published several peer-reviewed  
18 articles on chelation, is that correct?

19 A Many.

20 Q Do you know how many articles you published  
21 on DMSA chelation?

22 A I have anywhere from five to 10. I don't --

23 Q That's okay if you don't know, but several.

24 A I just don't judge my productivity by  
25 numbers. I judge my productivity by quality of the

1 papers in first-class peer-reviewed journals.

2 Q Have you ever published a peer-reviewed  
3 experimental study on chelation where you did not get  
4 both pre- and post-chelation measurements?

5 A In most of our papers, I don't remember  
6 exactly how many, I think in most, but I also have  
7 shortcomings, as almost most beginning investigators  
8 do when they enter a new field. We have usually  
9 always insisted on doing pre and post.

10 Now, whether any of our early papers did not  
11 do pre-urinary mercury levels or heavy metal levels, I  
12 just don't remember.

13 Q And you testified in Cedillo that you always  
14 try to get a baseline; it's the proper way of doing a  
15 test. Isn't that correct?

16 A It depends on what the purpose of the  
17 experiment or the study is. It depends on how easy it  
18 is to get patients. It's very difficult to just make  
19 a statement with no reservations. And if I said that  
20 at the time, then you have the quote that I said it.

21 But let me say that we usually insist on  
22 doing pre and post, but we can understand with  
23 autistic children, to those of us who have worked with  
24 autistic children, how difficult it is to get a blood  
25 sample and a urine sample. And to try to get two in

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1 the same day is, makes it very difficult to do the  
2 experiments.

3 Q So the Bradstreet study didn't take pre-  
4 chelation mercury levels, is that correct?

5 A They did chelation. And they compared not  
6 pre and post, but they compared a group of autistic  
7 children with a group of control children.

8 Q Did the Bradstreet study control for dietary  
9 intake of mercury?

10 A I don't think so, but I don't recall. My  
11 impression is they did not. It's very difficult,  
12 especially with autistic children, to have that kind  
13 of control.

14 Q Could dietary intake affect post-chelation  
15 urine mercury levels?

16 A Absolutely. If, if there was a great deal  
17 of mercury-containing foods in the diet.

18 Q Your fourth pillar is -- and it's on page 25  
19 of your report -- you state, "The most beneficial  
20 treatment for autism as reported by parents of  
21 autistic children was chelation therapy." And that's  
22 the fourth pillar of your six pillars. Do you recall  
23 that?

24 A I recall something like that. Where is this  
25 on the --

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1 Q Page 25.

2 A Page 25. Yes, I see it now. Yes.

3 Q And you rely on the 2006 Autism Research  
4 Institute consensus paper addressing chelation, is  
5 that correct?

6 A Yes, yes. What was the question about that?

7 Q You rely on the consensus paper from the  
8 Autism Research Institute.

9 A Essentially, I also rely, to some extent I  
10 also relied a great deal on what parents told me at  
11 these think-tank meetings, or the meetings associated  
12 with a think tank. Although I realize the  
13 shortcomings supposedly of taking parental views.  
14 It's not a controlled clinical trial.

15 Q Is the consensus paper, it's not a peer-  
16 reviewed paper, it's just a consensus paper issued by  
17 the --

18 A It depends on how you define peer review.  
19 That consensus paper was given to 100, at least 100  
20 think tank members, of which maybe, at least, my guess  
21 is at least 20 peer reviewed it. I did not peer-  
22 review it because I thought it would be a conflict of  
23 interest, because of my interest in DMSA.

24 Q But it wasn't peer reviewed by a journal  
25 editor or --

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1 A It was not published in a journal, per se.

2 Q Can you cite to any peer-reviewed journal  
3 articles that demonstrate chelation improves the  
4 neurological manifestations of autism?

5 A Improves --

6 Q The neurological manifestations of autism.

7 A I don't know whether -- no, Bradstreet was  
8 short term. I know of no good paper that proves it.  
9 The NIH started such a study, but has, for a variety  
10 of reasons, abandoned the study.

11 Q Have any of the authors on the consensus  
12 paper done studies upon which to base their opinion?  
13 Or peer-reviewed studies upon which to base their  
14 opinions that chelation is useful for the treatment of  
15 autism?

16 A I honestly don't know. I just don't have  
17 the names of the reviewers before me.

18 Q Do you remember that Dr. Mumper was one of  
19 the authors on that paper?

20 A I just don't remember.

21 Q Do you know whether Dr. Mumper performs  
22 chelation? Do you know whether Dr. Mumper performs  
23 chelation?

24 A Why don't you ask her? Because she would be  
25 a witness. She is a very reliable physician, and I

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1 would hate to put, I would hate to misquote her.

2 Q Okay.

3 A I think I know what she does, but I would  
4 think since she is going to be here, an expert witness  
5 here, I would rather not make that statement.

6 Q Would you agree that by the time most  
7 autistic children are chelated, the chelator is  
8 removing inorganic mercury from the body?

9 A When most autistic children have been  
10 chelated, what was the rest of it?

11 Q Is it removing inorganic mercury from the  
12 body?

13 A Oh. May I rephrase the question? Are you  
14 asking me whether DMSA will stimulate the excretion of  
15 inorganic mercury and/or methyl or ethyl mercury? Is  
16 that what you're asking me?

17 Q I'm asking you that by the time children  
18 undergo chelation therapy, which is after the  
19 vaccination schedule has been administered, is that  
20 usually correct?

21 A I'm sorry, I don't understand your question.

22 Q Okay. I will ask you, what does DMSA remove  
23 from the body? What does it chelate? What kinds of  
24 mercury does it chelate? We'll go with your question.

25 A Oh, fine. You're asking what DMSA chelates.

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1 Q Yes.

2 A All right.

3 Q In mercury.

4 A That's fine. We're just talking about  
5 mercury.

6 Q Yes.

7 A And let's be very specific about this. DMSA  
8 will chelate, by definition chelate means forms a  
9 ring, with mercuric mercury. It will not chelate  
10 methyl mercury. But it will cause the increased  
11 excretion of methyl mercury, because DMSA will tie up  
12 two individual molecules of methyl mercury, and will  
13 not form the chelate. So that's why many of us prefer  
14 to use the term "metal mobilizing agent" rather than  
15 "chelating agent." Is that clear, ma'am?

16 Q Yes.

17 A Thank you.

18 Q When you chelate autistic children, what are  
19 you removing from the body? Is it mostly inorganic  
20 mercury?

21 A I think it's, I don't know whether anyone  
22 has actually done that study. But in animal studies  
23 that we and other people have done, I think we've done  
24 anyway, and certainly Clarkson has done both human and  
25 others, one would expect that both organic mercury and

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1 inorganic mercury would be, the excretion of both of  
2 them would be increased in the urine.

3 Q What did Bradstreet measure in the urine  
4 when he chelated?

5 A I think he did total mercury. I'm not  
6 positive, but my guess is that since the laboratory  
7 did not do speciation, my guess is he did total  
8 mercury. But I don't know.

9 Q And where is most of that mercury coming  
10 from when you chelate?

11 A Where does mercury come from when you give  
12 DMSA?

13 Q Yes.

14 A The majority of the mercury would come from  
15 the kidney. But from animal experiments that we've  
16 done, we also get mercury from other tissues in the  
17 body.

18 Q Now, you testified earlier that once  
19 inorganic mercury is in the brain, it stays there for  
20 a very long time. Is that correct?

21 A That is what Vahter and other people have  
22 published.

23 Q And you have also performed chelation  
24 studies on animals to determine whether chelation  
25 removes mercury from the brain. Is that correct?

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1           A     We have performed chelation studies in  
2           animals that have been exposed to mercury vapor, and  
3           have been able to show that DMSA did not remove  
4           mercury from the brain. That's your question, and  
5           that's the answer.

6           Q     It did not remove inorganic mercury.

7           A     It did not, we did not do speciation, if I  
8           remember. We did total mercury.

9           Q     And the paper, the consensus paper from the  
10          Autism Research Institute also says chelation does not  
11          lower brain mercury levels, is that correct?

12          A     That's not correct if you just say the word  
13          "chelation." In studies that we are now writing up,  
14          we clearly show that a chelating agent called  
15          Depenicillamine, that Clarkson used in Iraq also for  
16          treatment of humans, that Depenicillamine does  
17          decrease brain mercury.

18          Q     What kind of mercury in the brain, inorganic  
19          or organic?

20          A     I'm trying to think. We have done  
21          speciation. And right off -- it will reduce both.  
22          But it reduces one of them much more than the other.  
23          And I think it reduces the organic mercury in the  
24          brain much, brings much more organic mercury out than  
25          it does inorganic. Although it brings some inorganic

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1 mercury out. That's Depenicillamine.

2 Q And what paper is that? What are you  
3 citing? What is the basis for that?

4 A That's studies that we have been doing for  
5 the last two years in my own laboratory, and we are in  
6 the process of writing it for publication now.

7 Q Does DMSA remove inorganic mercury from the  
8 brain?

9 A DMSA will not remove any metal from the  
10 brain. But penicillamine will.

11 Q So if it's your hypothesis that autism is  
12 caused by inorganic mercury building up in the brain,  
13 how is chelation beneficial if it doesn't alter brain  
14 inorganic mercury levels?

15 A Well, if there's mercury in the intestines,  
16 if there's mercury in other tissues in the body, the  
17 mercury levels can interrupt or inhibit the function  
18 of certain enzymes in those tissues. No one claims  
19 that we are only just dealing with the brain when you  
20 do chelation work, because most people know, most  
21 clinicians that use it know that if they give DMSA,  
22 it's not going to affect brain mercury.

23 And also, you must keep in mind that the  
24 damage to the brain probably has been, has been made,  
25 and it may not be reversed by the mercury.

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1 Q So how has it improved neurological  
2 function?

3 A Did I say it improved neurological function?  
4 Did I say DMSA improves neurological function?

5 Q Do you believe it does?

6 A Pardon?

7 Q Do you believe it does? Do you believe  
8 chelation with DMSA can improve neurological function  
9 in autistic children?

10 A Did I say that?

11 Q I'm asking you for your opinion.

12 A Oh. I think you should ask Dr. Mumper that,  
13 because she has much more experience using chelating  
14 agents and dealing with autistic children.

15 Q But it's one of your pillars. I mean, it's  
16 one of the six pillars that you say leads you to  
17 believe that vaccines cause autism.

18 A Do I say that DMSA cured autism? No, I  
19 don't say that in those six pillars.

20 Q You say that chelation was beneficial.

21 A I said that parents believe it's beneficial  
22 to the, when DMSA was given to their children. A long  
23 list, a questionnaire was given to parents by the  
24 Autism Research Institute. And a long list of  
25 possible, vitamin B-6, thyroxin, a whole bunch of

1 things.

2 What was consistent to almost 68 percent or  
3 whatever figure it is that I quote was that parents  
4 came up with DMSA. Now, no question this is not a  
5 controlled epidemiologically suitable clinical trial.  
6 We are just reporting what was said.

7 Q I know you said that chelation isn't FDA  
8 approved; it has a --

9 A I didn't say that. Pardon?

10 Q It has an off label? You said it has an  
11 off-label use for the --

12 A I said not chelation, I said DMSA.

13 Q DSMA. DMSA.

14 A DMSA has an off-label use for treating  
15 mercury intoxication, or to mobilizing mercury, to  
16 mobilizing, immobilizing arsenic. It has been used  
17 and published in peer-reviewed medical journals for  
18 those purposes.

19 And the FDA approves a drug now for efficacy  
20 and safety. So off-label use usually means that the  
21 physician knows it's safe to use; the physician may  
22 not know how effective it will be in off-label use.

23 Q Do you disagree, then, with the Institute of  
24 Medicine's 2004 conclusion -- and we can put that up.

25 (Pause.)

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1 Q That because it is unlikely to remove  
2 mercury from the brain, chelation is useful only for  
3 immediately after exposure, and before damage has  
4 occurred?

5 A I don't see anything about the brain here.  
6 It says because chelation therapy has potential  
7 serious risks, but now you've changed it. We may not  
8 be looking at the same thing, ma'am. Okay, here we  
9 are now.

10 Q "Because it is unlikely to remove mercury  
11 from the brain, chelation is useful only immediately  
12 after exposure, and before damage has occurred.  
13 Moreover, chelation therapy has serious risks. For  
14 example, some chelation therapies might cause the  
15 release of mercury from soft tissues stored, thus  
16 leading to increased exposure of the nervous system to  
17 mercury.

18 "Because chelation therapy has potentially  
19 serious risks, the committee recommends that it be  
20 used only in carefully controlled research settings  
21 with appropriate oversight by the Institutional Review  
22 Boards protecting the interests of children who  
23 participate."

24 Do you agree or disagree with that  
25 statement?

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1           A     I don't completely agree with it. I am  
2     governed by an Institution Review Board in all the  
3     human experiments I do. And I have had a very firm  
4     connection with established medicine.

5                     However, when I see that someone improves,  
6     even though I'm not convinced that the improvement may  
7     be due to the drug that he's getting, or she's  
8     getting, or the placebo effect; if the child gets  
9     better, in the case of someone in my own family that,  
10    when something was given, the person got better; and  
11    so I don't give a darn whether it was recommended or  
12    not recommended by established medicine.

13                    So if we can go through these sentences one  
14    by one, I'll point out to you some of the problems  
15    with the sentences. And there are just three or four  
16    sentences.

17                    "Because it is unlikely to remove mercury  
18    from the brain, chelation is useful only immediately  
19    after exposure, and before damage has occurred."

20                    Now, first of all, there are now chelating  
21    agents, we have known -- we've had chelation,  
22    chelating agents that will remove mercury from the  
23    brain. British antileurocyte, the name for, the  
24    official name for dimercaprol. It will remove mercury  
25    from the brain.

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1           But when it's first given during the first  
2           couple of days, it will cause a redistribution of  
3           mercury. It will take mercury from the tissues, and  
4           that chelate, the true chelate, will be moved up the  
5           brain and across the blood-brain barrier.

6           So British antileurocyte dimercaprol is no  
7           longer recommended for the treatment of heavy metal  
8           poisoning, because for the first couple of days it  
9           will increase the levels. All right? So there is,  
10          but in the long run the brain mercury level does go  
11          down. But you can do some damage. So the first  
12          sentence isn't completely truthful, all right?

13                 "But moreover, chelation therapy has serious  
14          risks." That's absolutely correct.

15                 "For example, some chelation therapies might  
16          cause the release of mercury from soft tissue stores,  
17          thus leading to increased exposure of the nervous  
18          system to mercury." That statement is also correct.

19                 "Because chelation therapy has potential  
20          serious risks, the committee recommends that it be  
21          used in only carefully controlled research settings,  
22          with appropriate oversight by Institution Research  
23          Boards protecting the interests of children who  
24          participate."

25                 I cannot disagree with that as an academic.

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1       However, when I hear and meet parents who say I got my  
2       child back with tremendous improvement if they are  
3       given DMSA, even though there is no controlled study,  
4       I can't ignore that. And I can't ignore the fact that  
5       some people, some children are given DMSA, and it did  
6       not help them.

7                So I don't know what you're asking me now  
8       about this. As a research person, I certainly agree  
9       with the last statement. But as a, but I'm not  
10      treating a human being; I'm doing research. Dr.  
11      Mumper could probably, Dr. Mumper could probably  
12      address that more clearly.

13             Q     The fifth pillar for arguing thimerosal-  
14      containing vaccines cause autism is the Hornig study.  
15      Do you still rely on the Hornig study as one of your  
16      pillars?

17             A     That's a very difficult question now,  
18      because some people have claimed that they can't  
19      repeat it. But according to the grapevine, she is now  
20      coming up with another study that will. So I just, at  
21      the present time I have no firm opinion.

22             Q     And you are referring to the Berman study,  
23      which is Respondent's Master List 42? They tried to  
24      replicate the Hornig study, and could not? Is that  
25      correct?

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1 A Yes, yes.

2 Q Okay.

3 A And I think I have it in the list of slides  
4 that we showed, actually.

5 (Pause.)

6 A What do you want to ask about the Berman  
7 study?

8 Q I have no questions on the Berman study,  
9 other than it tried to replicate the Hornig study and  
10 could not. Is that a fair assessment of that, of the  
11 Berman study?

12 A But there is also criticism of the Berman  
13 study.

14 Q Okay. I'm not going to ask you about the  
15 criticisms, unless --

16 A You're not going to ask?

17 Q No.

18 A All right, thank you.

19 Q Your sixth pillar, you state -- and that's  
20 on page 25 of your report, the sixth pillar.

21 A Page 25.

22 Q That is that there's evidence of post-natal  
23 loss of brain cells in autism, particularly in the  
24 cerebellum. What's the basis for that statement?

25 A I thought it was, that's mentioned here,

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1 proportionates 203 at page 584 and reference cited  
2 there. But that's all I know at this present time.

3 Q Do you know whether that article discusses  
4 the possibility of thimerosal as a cause of autism?

5 A I don't frankly even remember reading the  
6 article. I don't know when I read it, so I just have  
7 to familiarize myself with the title of the article,  
8 and maybe I can answer your question.

9 I don't recall thimerosal as being part of  
10 that article, but I'm not certain.

11 Q If we take out the Hornig study, which  
12 you're not sure about any more, how many of these  
13 pillars do you need? You said taken individually it  
14 doesn't matter, but if you take them altogether it  
15 shows the vaccines, thimerosal-containing vaccines can  
16 cause autism.

17 What if we take away two pillars? What  
18 three studies or two studies -- how many pillars do  
19 you need, I guess?

20 A As many as I can find.

21 Q What if we only had one pillar?

22 A It would depend on the quality of the paper,  
23 and whether I believe what they did, and whether I  
24 have any confidence in what the investigator has done  
25 in the past. And what the peer-reviewed critiques

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1 are.

2 Q Well, you said taken alone, you really  
3 couldn't draw that conclusion. But taken together,  
4 you could.

5 A In these papers. I certainly feel better  
6 after having more than one pillar, as you put it.

7 Q How about two?

8 A I don't understand the purpose of the  
9 question. The more we have, the better off we are.  
10 The more evidence we have, the more convincing it is.  
11 If you have one piece of evidence, it's one piece. If  
12 you have two pieces of evidence, then it should be  
13 twice as good.

14 Q Did you put these pillars in order of what  
15 you think are the most important studies that show  
16 thimerosal-containing vaccines show autism? Is there  
17 a particular order?

18 A I really put them in the order of their  
19 importance as to the connection of mercury with  
20 autism. I did not have in mind in any of these the  
21 use of thimerosal in vaccines at the time, when I put  
22 these in order.

23 Q Dr. Aposhian, yesterday in your testimony,  
24 and I only have a black-and-white copy, but as I  
25 recall you stated that the parts --

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1 A Give me the slide number?

2 Q All of your slides. It's a general  
3 question.

4 A Oh.

5 Q You said some of it was written in blue, and  
6 some of it was written in red.

7 A Yes.

8 Q What did the blue represent, again?

9 A The blue was either a direct quotation or  
10 what, if you read the article, you could understand  
11 the author was saying. It was in some cases my  
12 abstract of that article, but it was what the author  
13 was saying. That was the blue.

14 The red was my expert opinion. And I tried  
15 to keep those separate, as best as I could.

16 Q You wrote your report in August of 2007, is  
17 that correct?

18 A If that's what the date is.

19 Q And I know you testified yesterday that  
20 following the completion of your report, that you had  
21 health problems in your family that sort of distracted  
22 you from focusing on this litigation. Is that  
23 correct?

24 A That's correct.

25 Q When did you start refocusing on this

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1 litigation?

2 A The word "focus" is not a good term.

3 Q Okay. When did you --

4 A I've always thought about it.

5 Q When did you begin working on this case,  
6 towards litigation? Reworking on this case.

7 A I just don't recall. You know, my guess is  
8 it was always in my mind, and I was always thinking  
9 about it. One just doesn't put things out of their  
10 mind. Anyway, it's not possible for me to put  
11 something completely out of my mind.

12 Q But when did you actually, you don't recall  
13 when you actually started working on it again  
14 preparing for your testimony?

15 A I don't recall. We have the figures. If  
16 it's really important, I have an invoice I can check.  
17 Would you like that?

18 Q Well, was it a month ago? Two weeks ago?

19 A I would guess at least probably, my guess is  
20 December, January, something around that time. Since  
21 this is a court of law, I don't want to say something  
22 that's not --

23 Q I'm not asking for an exact date, so we  
24 don't need to look at your invoice. I was just  
25 wondering.

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1 A Okay. All right.

2 Q So you think December, January some time.

3 A That's what my guess is, but I really don't  
4 know.

5 Q Okay. And in your testimony yesterday, you  
6 cited to quite a few articles that weren't in your  
7 initial report, is that correct?

8 A Did I --

9 Q You referred to articles that were not in  
10 your initial report, is that correct?

11 A Yes, that's correct.

12 Q And one of those articles, for example, you  
13 relied on was Dickey-Bloom, et al. It's an article  
14 from 2006. And we'll show you your slide.

15 A Yes, yes.

16 Q What is that article about?

17 A Can you put it back on?

18 Q Well, if you testified to it yesterday,  
19 let's see what you can --

20 A But can you just have the article up for me  
21 to look at? May I ask the courtesy of --

22 Q Well, we'll put it up. But what I'd like to  
23 ask you first, what do you recall about that article  
24 before we put it up?

25 A I recall it being a very good and clear

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1 article that I emailed to a number of people,  
2 recommending that they should read it. Some of my  
3 associates at the University of Arizona and at other  
4 universities.

5 It explained a great deal about autism in  
6 relatively simple language, that I and many people who  
7 are not MDs might understand. That's what I remember  
8 about the article. And that's why I have slides which  
9 quote them directly. And if I can go there, I think  
10 that's, you have -- thank you, sir. I now have it in  
11 front of me.

12 SPECIAL MASTER VOWELL: And we're referring  
13 to slide 77.

14 THE WITNESS: Thank you very much, Special  
15 Master.

16 BY MS. RENZI:

17 Q How did you find this article?

18 A Can I find 77 first?

19 Q Sure, sure. I'm sorry. It's right up on  
20 the screen.

21 A I still would prefer seeing my own slide,  
22 thank you. Yes, okay. What is your question, please?

23 Q How did you find out about this article? I  
24 mean, it obviously was published prior to you writing  
25 your report, but how did you find this article

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1 subsequent to writing your report?

2 A Let me tell you how I usually work, so that  
3 we can be clear, and so I don't have to, you know, say  
4 I don't know or something.

5 One reads an article. And as one reads the  
6 article, one reads a statement with a reference. And  
7 if that statement is important, then one wants to go  
8 back and check that reference to see whether what the  
9 person is quoting in the article is really correct.

10 And so I suspect that in this case, the  
11 Diccico-Bloom article I picked up because I read some  
12 article, and suddenly "The Development of Neurobiology  
13 of Autism Spectrum Disorder" appeared in the reference  
14 list. And therefore I went to my abstracting service,  
15 which is Hightower Press I think, Highwire Press that  
16 Stanford University puts out, and immediately got the  
17 article. Does that answer your question?

18 Q Yes. Now, you didn't think this article was  
19 important when you wrote your initial report, is that  
20 correct?

21 A I'm not even certain I knew it existed. I  
22 don't know whether -- you're implying that it's not in  
23 my initial report, so I would suspect I didn't even  
24 know it existed. I had less than a month to put this  
25 report together, when I usually take much more time to

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1 very thoroughly and carefully do things.

2 Q I understand that, and that's not what I'm  
3 asking. I'm just asking why, subsequent to your  
4 report, you found this article important to rely on.

5 A Because neurobiology is basic to autism  
6 spectrum disorders. Developmental neurobiology is  
7 even more basic. And so the title intrigued me. And  
8 I read it to learn more about developmental and  
9 neurobiology of autism spectrum disorders. I don't  
10 know everything. And the more I can learn by reading  
11 good, peer-reviewed scientific articles, the better  
12 off my knowledge is.

13 Q Did you find this article before or after  
14 you read Dr. Kinsbourne's report?

15 A Before I read --

16 Q Dr. Kinsbourne's report.

17 A I don't remember, to tell you the truth. I  
18 don't know. I was very impressed by Dr. Kinsbourne's  
19 report. Is this in his report?

20 Q Well, we can ask Dr. Kinsbourne about his  
21 report. I don't know. Actually, I just want to know  
22 why you relied on it, if you relied on it post seeing  
23 Dr. Kinsbourne's report.

24 A The answer is, I don't know, but I doubt it.  
25 I try to stay independent of other people's reports in

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1 a given case.

2 Q Did you create all the slides for your  
3 presentation yesterday yourself?

4 A As far as I know, I did. The only time I  
5 used some help from my young students was if I could  
6 not transfer a picture, a photograph from a journal to  
7 PowerPoint, which sometimes is very difficult for me.  
8 And so then I'd call one of my students on the  
9 telephone, and tell her -- her name is Emily  
10 Goldberg -- and she does it, so it's nice.

11 Q So you wrote all of the parts in blue  
12 yourself?

13 A Absolutely. Absolutely. I type with my  
14 fingers; it's not the easiest thing.

15 Q No, the only reason I was asking, and we'll  
16 pull up a slide, which is slide 4.

17 A I'm sorry. I think this slide was put  
18 together from material that I gave the law office.

19 Q Okay. So the fact that you refer to your  
20 laboratory as his laboratory, those were, okay. So  
21 those were preexisting slides that you put in.

22 A I think so.

23 MS. RENZI: Okay. I have no further  
24 questions.

25 THE WITNESS: Thank you, Ms. Renzi.

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1 SPECIAL MASTER VOWELL: Do we have questions  
2 now, or do we want to wait? I have a couple of  
3 questions, Dr. Aposhian.

4 THE WITNESS: Yes, ma'am.

5 SPECIAL MASTER VOWELL: Dr. Aposhian, are  
6 you aware of any estimates of the average daily intake  
7 -- and I hesitate to use that word -- of mercury in  
8 any, of all species in humans?

9 THE WITNESS: Yes, ma'am. I'm sorry I  
10 didn't show that, because I had gathered that I should  
11 not repeat very much from the Cedillo trial.

12 SPECIAL MASTER VOWELL: This is a separate  
13 theory, a separate case, Doctor.

14 THE WITNESS: Pardon?

15 SPECIAL MASTER VOWELL: This is a separate  
16 theory, a separate case. We're not incorporating your  
17 testimony from Cedillo in this case, that I'm aware  
18 of.

19 THE WITNESS: I'm sorry, I did not know  
20 that. In the Cedillo slides -- and if you want, I can  
21 bring it up, because I think I have that talk here --  
22 there is -- and it's published in the, I think it's  
23 called the Toxicology of Methyl Mercury, the National  
24 Research Council Publication 2007, in the year 2000, I  
25 think, and in the World Health Organization.

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1           There is a wonderful table that lists the  
2           species of mercury with the intake of each one for the  
3           general population, and also the retention.

4           The greatest exposure of the general  
5           population to mercury in general, without speciation  
6           now, is the mercury from amalgams. Of course, that  
7           exposure is mercury vapor, okay?

8           And of that, if I remember correctly, it's  
9           in the ballpark of six to 10 micrograms per day. Of  
10          course, depending on how many amalgams you have and  
11          that sort of thing, but that's the average. It's a  
12          wonderful table.

13          And if the, if our lawyers will remind me,  
14          or if you'll give me your email, I will be happy to  
15          email it to you. It's also, it's published in the  
16          article, in the toxicology chapter that I wrote for  
17          the NRC Monograph.

18                 SPECIAL MASTER VOWELL: So it's available,  
19                 and we could obtain it.

20                 THE WITNESS: Pardon?

21                 SPECIAL MASTER VOWELL: So it is available,  
22                 and we could obtain it.

23                 THE WITNESS: Absolutely. And would you  
24                 like more information now?

25                 SPECIAL MASTER VOWELL: Certainly.

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1 THE WITNESS: Okay. Of all the species of  
2 mercury, the organic mercury they're talking now about  
3 is methyl mercury, that's the far right-hand side;  
4 that of all these exposures of mercury, we retain most  
5 of the methyl mercury that we're exposed to, all  
6 right? And the inorganic mercury, the mercuric  
7 mercury if you will, as far as the general population  
8 is concerned, you're exposed to a little bit of it in  
9 food, but it's generally considered to be of very low  
10 value.

11 So to summarize, the greatest exposure of  
12 the general population to mercury is via dental  
13 amalgam mercury; that the methyl mercury, of them all  
14 methyl mercury is retained the most. It's on order of  
15 I think six to 20 micrograms per day that you retain.  
16 And the inorganic mercury is sort of insignificant.

17 SPECIAL MASTER VOWELL: All right. Now, if  
18 we're dealing with children from birth to age three,  
19 understanding that those children receive some  
20 exposure to mercury from the dental amalgams of their  
21 mother, is there a different table or a different  
22 assessment of an average daily exposure?

23 THE WITNESS: No, ma'am, there is not.  
24 There is not one that I know of, because this question  
25 came up in our NRC meetings.

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1           The closest thing you can find is the  
2           Seychelle Islands and the Faroe Islands and the New  
3           Zealand studies, but it's not in table form at all.  
4           It just gives an idea about low exposure of children  
5           to methyl mercury in fish or in whales. But we don't  
6           have a table like we have for the general population.

7           SPECIAL MASTER VOWELL: All right. You also  
8           refer in your testimony to some of the findings in the  
9           brains of primates and the brains of autopsied  
10          autistic subjects. Are there any studies you are  
11          aware of that measure the brain mercury level of, in  
12          autopsy, of autistic subjects?

13          THE WITNESS: Oh, yes. Let me be sure I  
14          have the question right. You're asking me are there  
15          any studies that have measured the mercury levels in  
16          the brains of autistic children.

17          SPECIAL MASTER VOWELL: That is correct.

18          THE WITNESS: Yes, there are.

19          SPECIAL MASTER VOWELL: Or adults. Autistic  
20          children or adults.

21          THE WITNESS: Of autistics, yes. Yes, there  
22          are such studies.

23          SPECIAL MASTER VOWELL: And did you cite any  
24          of them, either in your presentation or your paper?

25          THE WITNESS: I thought I did, but again,

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1 the cross-examination was so good, my thoughts were  
2 not quite concentrated. But let me very quickly, if I  
3 can.

4 (Pause.)

5 THE WITNESS: I think there's one from, I'm  
6 positive there is one from Hopkins, if I can put my  
7 finger on it. Ah.

8 I'm not positive, but I would suggest that  
9 one look at a paper by Vargas, et al. I'm not  
10 positive. That would be, it's slide 79.

11 SPECIAL MASTER VOWELL: Thank you, I will  
12 look at that.

13 THE WITNESS: If it's not that one, and if I  
14 find one, I'll try to tell --

15 SPECIAL MASTER VOWELL: Bring it up to the  
16 attorneys, and they can bring it up to us at a later  
17 time.

18 THE WITNESS: Thank you. My apologies for  
19 not being able to come up with it right away.

20 SPECIAL MASTER VOWELL: That's not a  
21 problem, no one expects that. I'm just trying to get  
22 the questions answered while we have you here.

23 THE WITNESS: All right.

24 SPECIAL MASTER VOWELL: You also mentioned  
25 yesterday, in talking about thimerosal and ethyl

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1 mercury, you seem to equate thimerosal with  
2 merthiolate. Was I misunderstanding what you said, or  
3 is that correct?

4 THE WITNESS: I think that's correct.

5 SPECIAL MASTER VOWELL: And when we're  
6 talking about merthiolate, we're talking about that  
7 topical antiseptic that you and I were probably  
8 painted with as children, but --

9 THE WITNESS: Did you say anesthetic?

10 SPECIAL MASTER VOWELL: Antiseptic.

11 THE WITNESS: Yes, antiseptic. Yes, yes.

12 SPECIAL MASTER VOWELL: Yes. It certainly  
13 wasn't an anesthetic, as I recall it.

14 THE WITNESS: That's correct. And that has  
15 been prohibited now.

16 SPECIAL MASTER VOWELL: Prohibited now. But  
17 at the time you and I were children, and some of the  
18 people over 40 in this room, it was fairly common in  
19 use as an antiseptic.

20 THE WITNESS: Yes, ma'am.

21 SPECIAL MASTER VOWELL: Okay. And that  
22 would also refer to mercurochrome.

23 THE WITNESS: Yes.

24 SPECIAL MASTER VOWELL: I think chrome was  
25 another formulation of that.

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1 THE WITNESS: Yes, ma'am.

2 SPECIAL MASTER VOWELL: And then finally, I  
3 got a bit confused during the cross-examination, so  
4 let me make sure I understand what you're saying.

5 Thimerosal is injected. It is converted by  
6 the body rapidly to ethyl mercury, and then the ethyl  
7 mercury at some point is, and I have forgotten the  
8 term, but it is converted to mercuric mercury.

9 THE WITNESS: It enters the tissues.

10 SPECIAL MASTER VOWELL: It enters tissue.

11 THE WITNESS: And then it's deethylated.

12 SPECIAL MASTER VOWELL: Deethylated.

13 THE WITNESS: Yes, ma'am.

14 SPECIAL MASTER VOWELL: Okay, deethylated as  
15 opposed to demethylated, which is what happens with  
16 methyl mercury.

17 THE WITNESS: Yes, ma'am.

18 SPECIAL MASTER VOWELL: Okay. It is  
19 deethylated to mercuric mercury.

20 THE WITNESS: Mercuric mercury.

21 SPECIAL MASTER VOWELL: And that is the form  
22 of mercury that persists in the brain.

23 THE WITNESS: Yes, ma'am.

24 SPECIAL MASTER VOWELL: Okay. And it  
25 doesn't matter whether it comes from ethyl or methyl

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1 mercury.

2 THE WITNESS: Correct.

3 SPECIAL MASTER VOWELL: Except that more  
4 ethyl mercury is converted to mercuric mercury in the  
5 brain.

6 THE WITNESS: A greater percent.

7 SPECIAL MASTER VOWELL: A greater  
8 percentage, all right.

9 THE WITNESS: I'm sorry, let's be careful.  
10 There is a greater percentage of the total mercury --

11 SPECIAL MASTER VOWELL: Correct.

12 THE WITNESS: -- that becomes mercuric  
13 mercury in the case of ethyl mercury exposure.

14 SPECIAL MASTER VOWELL: All right. Now, my  
15 question is, is it mercuric mercury in the brain that  
16 you are contending is what causes autism? The  
17 mercuric mercury in the brain? Is that correct?

18 THE WITNESS: Yes. Of course, we cannot  
19 rule out that some of the organic mercury is also  
20 doing it, but the mercuric mercury is what stays  
21 there, and stays there for a long time. And the  
22 mercuric mercury has an extremely high affinity for  
23 the enzymes of the brain, the have sulphhydryl group.

24 The methyl mercury is too big to get into  
25 certain enzymes that have an SH.

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1 SPECIAL MASTER VOWELL: But once it's  
2 demethylated, it becomes mercuric mercury, it doesn't  
3 matter how it got there.

4 THE WITNESS: Yeah. Once it becomes  
5 demethylated, then it can go in as a mercuric ion and  
6 inhibit an enzyme.

7 SPECIAL MASTER VOWELL: All right. Those  
8 are my questions. Any redirect, Mr. Williams?

9 MR. WILLIAMS: Yes.

10 REDIRECT EXAMINATION

11 BY MR. WILLIAMS:

12 Q Dr. Aposhian, I want to start by going over  
13 the DeSoto criticism of the Ip study, and the analysis  
14 of the hair data from that study.

15 You were shown on cross the first DeSoto  
16 paper criticizing Ip, but you weren't shown the second  
17 DeSoto paper that responded to Dr. Aschner's letter  
18 about the hair analysis? Do you recall that?

19 Let me put that up. This is Petitioner's  
20 Exhibit 612.

21 THE WITNESS: Can you make it bigger for me,  
22 Scott?

23 MR. WILLIAMS: Show the title first, Scott.

24 BY MR. WILLIAMS:

25 Q Just to remind the Special Masters, Ip did a

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1 study comparing the blood levels and the hair levels  
2 of mercury in autistic children and controls. And the  
3 first paper published by Ip said there was no  
4 difference. And it was interpreted as therefore a  
5 negative study on whether there was this efflux  
6 disorder, correct?

7 A True.

8 Q But then DeSoto and colleague published a  
9 reanalysis of the Ip data that concluded there was a  
10 statistical significant difference between the  
11 autistic children, the blood levels in the autistic  
12 children of mercury, and the blood in the controls.  
13 That was where it was higher in the autistics, right?

14 A Yes, sir.

15 Q And then Dr. Aschner wrote a letter to the  
16 editor, which is what we have up on the screen here  
17 now, and I want to show what his criticism was of the  
18 DeSoto --

19 MR. MATANOSKI: Actually, counsel?

20 MR. WILLIAMS: Yes?

21 MR. MATANOSKI: Are you going to pose a  
22 question? I mean, I understand background, but it's  
23 going on quite -- do you have a question to pose to  
24 the witness?

25 MR. WILLIAMS: Yes. I can ask it.

APOSHIAN - REDIRECT

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1           SPECIAL MASTER VOWELL: Let's direct your  
2 question, queries, up here, okay? Rather than  
3 engaging in colloquy among counsel. Please address  
4 your inquiries to the Bench, or your objections to the  
5 Bench.

6           Mr. Williams, I do think you need to get to  
7 a question, however.

8           MR. WILLIAMS: Okay.

9           BY MR. WILLIAMS:

10          Q     Did Dr. Aschner write a letter to the editor  
11 of the Journal criticizing the DeSoto reanalysis of  
12 the Ip data?

13          A     Yes, sir.

14          Q     And I have highlighted a section that I  
15 believe summarizes -- let me ask you. Does this  
16 highlighted portion here, does that summarize what Dr.  
17 Aschner is criticizing DeSoto's reanalysis for?

18          A     That's not necessarily so.

19          Q     No, I'm just asking you, is this what Dr.  
20 Aschner was arguing?

21          A     Yes.

22          Q     Yes. And then DeSoto and Hitlan, did they  
23 write a response to Aschner's letter, that starts on  
24 the second column of this same paper?

25          A     Yes, they wrote an answer. Sorry.

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1 Q Okay. Now, if we go to the second page of  
2 their reanalysis, I've highlighted some sections that  
3 I want to ask you about. The first one is, it says  
4 here that a case in point of apparent misunderstanding  
5 is this letter by Aschner. And they quote his  
6 criticisms. And then they say, "We believe that it  
7 should be clear that our conclusion was not related to  
8 the hair analysis, and the statement by Aschner  
9 appears to reflect a misunderstanding of our article."

10 Now, toward the bottom of this page they  
11 start reanalyzing the hair analysis data, and that's  
12 what I want to ask you about. It says, there's a  
13 paragraph that says, the hair analysis data, "I'm  
14 going to pull it up here.

15 Do you see where they say, "The hair  
16 analysis data is in fact interesting, but is of  
17 secondary importance. That said, because it was  
18 brought up in Aschner's critique, we address the rest  
19 of his criticism."

20 And it goes on. They reiterate his  
21 criticism, which is, can you explain what his  
22 criticism was again, about the chelation therapy?

23 A Yes. He says the chelation therapy and  
24 changes in the diet in fish consumption, both most  
25 likely to occur in the ASD group supposedly, in the

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1 two months preceding the mercury analysis, are likely  
2 to affect blood, but not hair mercury samples.

3 Q Okay. Then on the start of the next column,  
4 on the second half of this page, would you read what  
5 they say there about whether they agree with Aschner's  
6 critique or not?

7 A "To some, chelation among autistic patients  
8 could, as Aschner suggests, cause a correlation  
9 between blood and hair to be different in the autistic  
10 group, compared in controls. So do we agree with  
11 Aschner's critique? No."

12 Q And then I've highlighted a section just a  
13 little bit lower on that same page, where they start  
14 to explain why they disagree with Aschner. Could you  
15 read that? And then I may have some questions to ask  
16 you about that.

17 A "In other words, the autistic sample has  
18 lower hair levels of mercury than their blood levels  
19 would predict, and not the higher levels, as would be  
20 the case if they had undergone successful chelation  
21 therapy. They are consistent with the idea that the  
22 autistic sample might perhaps be worse at ridding the  
23 body of circulating mercury, and not consistent with  
24 the idea that the autistic group might have recently  
25 experienced a high level of mercury removal from blood

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1 circulation in controls."

2 Q So what are they saying here now, about the  
3 hair levels and the chelation criticism of Dr.  
4 Aschner?

5 A They are not agreeing with Aschner's  
6 criticisms, and they say they are consistent with the  
7 idea that autistics might perhaps be not good as  
8 ridding the body, or may have an efflux, if you will,  
9 disorder.

10 Q So is it fair to say that the current state  
11 of back-and-forth about Ip's data on hair, that DeSoto  
12 and Kaplan interpret the hair analysis to be  
13 consistent with your theory that autistic children  
14 have a mercury efflux disorder, that you can see in  
15 their hair analysis?

16 A It is consistent.

17 Q Now I want to turn to the teeth paper by  
18 Adams.

19 A Uh-huh.

20 Q This is Petitioners' Exhibit 138. You were  
21 asked quite a few questions about this this morning.  
22 What I want to go to, what you were asked is whether  
23 this is indicative of body burden; whether the  
24 additional -- just to summarize, the tooth study found  
25 that in autistic children, there was more mercury in

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1 their teeth than in the controls. Is that right?

2 A Correct.

3 Q Okay. And you were asked whether that was  
4 indicative of a body burden or not, right?

5 A Correct.

6 Q Let's see what the authors say about that.  
7 If you look at the second page, middle of the second,  
8 first column, I have highlighted a sentence about  
9 that. What do the authors of this paper say about  
10 whether this reflects a body burden or not?

11 A "A decreased ability to excrete mercury  
12 should result in a higher body burden."

13 Q And then on the right-hand side of this  
14 paper, this right-hand column, would you read what was  
15 highlighted there about baby teeth studies?

16 A "Baby teeth are formed in utero, and during  
17 the first few years of life, so they provide a measure  
18 of cumulative exposure during that critical period of  
19 development. Previous studies have demonstrated that  
20 mercury can be reliably measured in teeth."

21 Q And do you agree with those statements?

22 A Absolutely. Yes.

23 Q And then finally, over in their discussion  
24 section on page 1049 of the article, the first  
25 sentence of the discussion, I'll ask you to read that,

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1 please, once we blow it up here.

2 A "The two- to threefold-higher level of  
3 mercury in the baby teeth of children with autism is  
4 important, because it strongly suggests that they had  
5 a higher body burden of mercury during several years  
6 of prenatal/infant development."

7 Q And do you agree with that interpretation of  
8 the data?

9 A I do agree.

10 Q Then on the last page of the article, start  
11 with the paragraph on the bottom left. Would you read  
12 that, please? And then I'll ask you some questions  
13 about it.

14 A "It is interesting to note that the median  
15 mercury level in control teeth was 50 parts per  
16 billion, which is similar to the level of mercury, 40  
17 to 50 parts per billion, found by Burbacher, et al,  
18 2005, in the brains of infant monkeys following dosing  
19 of the monkeys with thimerosal in a manner designed to  
20 mimic the U.S. childhood vaccination schedule.

21 "If baby teeth levels correlate with brain  
22 levels, then this suggests children with autism in  
23 this small study had median brain levels of mercury in  
24 the range of 140 parts per billion, which is  
25 approaching the range of what has previously been

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1 calculated as necessary to result in mercury-induced  
2 neurological disorders by Takeuchi and Eto, 1975."

3 Q In fact, I want to show you the very next  
4 sentence of this, too, that I didn't highlight, but  
5 it's the last sentence of that paragraph. If you  
6 could just pull that up, Scott. If you'd just read  
7 one more sentence, please.

8 A "They found that levels of 260 to 630 parts  
9 per billion were able to induce Minimata Disease,  
10 which was a severe form of mercury poisoning."

11 Q All right. And again, do you agree with  
12 this interpretation of their teeth data and  
13 Burbacher's data?

14 A I do, yes.

15 Q And then their conclusion, this two-sentence  
16 conclusion of the paper, I'll have you read that.

17 A "The results of this small study suggest  
18 that children with autism have a higher body burden of  
19 mercury, probably due to a decreased ability to  
20 excrete mercury that is likely in part due to a high  
21 usage of oral antibiotics."

22 Q And do you agree with that statement?

23 A Yes, I do, sir.

24 Q Now, you were also asked some questions  
25 about the 2004 IOM report. And I just want to show

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1 you some, the references to this 2004 IOM report for a  
2 moment.

3 Could you blow the references up, Scott?

4 Thank you.

5 First of all, do you note that the IOM  
6 committee cites you as one of the authorities they  
7 have consulted in writing this report? Is that your  
8 name there?

9 A That is my name, sir.

10 Q Okay. But then let's look to see if this  
11 IOM 2004 report cites any of the adult monkey studies  
12 that were published back in the mid-1990s, that we  
13 spent quite a bit of time with yesterday.

14 A The Charleston --

15 Q The Charleston and Vahter. Let's see if  
16 there's any Charleston papers in the citations to this  
17 2004 IOM report.

18 Would you pull up the Cs, Scott? We lost  
19 the citation page. Will you blow up the difference  
20 between, yes, that part.

21 So there's a Chin and Akomi, but there is no  
22 Charleston paper cited, right?

23 A That's correct.

24 Q Okay. Let's go to the V section of the  
25 citations. Let's see if any of the Vahter papers are

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1 cited. You need to show the one above that, Scott.

2 So we have Verstraeten, Verstraeten,  
3 Verstraeten. We have Vericcio. We have Vulman. But  
4 there are no Vahter papers cited there, are there?

5 A There are none, sir.

6 Q Do you know how the IOM austere committee  
7 could have overlooked those adult monkey studies from  
8 the mid-1990s?

9 A Do you want my opinion, sir?

10 Q Yes.

11 A The problem with that committee was there  
12 was no toxicologist, no biochemist, no physiologist,  
13 no one who deals with toxicity, per se. This  
14 committee was almost completely made up of  
15 epidemiologists who study, or vaccine people. There  
16 is a gross, in all the IOM reports that have been  
17 published about vaccine safety, there have been no  
18 toxicologists, certainly in this one and the one that  
19 I attended that committee. No toxicologists who would  
20 be an expert, or no biochemists who would be an expert  
21 on how methyl mercury and thimerosal and inorganic  
22 mercury would affect a child.

23 Q Now, I'm going to represent to you that  
24 there is no discussion of neuroinflammation in that  
25 2004 IOM report, in relation to autism. Would that

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1 surprise you?

2 A I have not read the complete report, but  
3 that is a shock to me, really. Because, it's just a  
4 shock. The Zimmerman work is going to be classic.  
5 And I would suspect as he continues, he'll probably  
6 have a Nobel Prize.

7 Q Now, I want to show and go to your report  
8 for a moment, the one from last year, and look quickly  
9 just to see some of the topics that you had in your  
10 report, that you have not been cross-examined about.

11 Let's turn to page 13. Do you see the  
12 topic? Just pull up the bottom paragraph there,  
13 Scott, no. 5, the brain and mercury.

14 Now, here you're analyzing the Vehrbacher  
15 and Pichichero numbers. If we go to the top of the  
16 next page of your report, explain what you were doing  
17 there in these calculations.

18 A We were trying to estimate -- and it is an  
19 estimate -- of the amount of mercury in the brains of  
20 these children. And we had to, it was a very tricky  
21 thing, so tricky that I had to go ask another  
22 toxicologist who just got a prize from our society,  
23 whether it made sense to him what I was doing.  
24 Because of the assumptions that were being made.

25 Essentially what we were trying to do was to

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1 find out how much mercury was in the brain after the  
2 thimerosal vaccinations.

3 Q And my recollection is, you weren't cross-  
4 examined about this analysis at all. Is that your  
5 memory, also?

6 A That's correct.

7 Q Now, also on this page, same page 14, do you  
8 have a section of your report entitled,  
9 "Neuroinflammation in Autism?"

10 A Yes, sir.

11 Q And you cite the Pardo paper, the review at  
12 2005, at the bottom of that?

13 A Yes.

14 Q And then on the next page, you talked about  
15 the Connors twin study on terbutaline?

16 A Yes.

17 Q And later I'll show that you went into the  
18 animal model. In fact, we can jump to that right here  
19 in just a second.

20 No one asked you any cross-examination  
21 questions about the Connors paper or terbutaline  
22 model, did they?

23 A That's correct. No one asked me about  
24 terbutaline. Very important paper, very important  
25 concept. These are papers coming from mostly the

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1 Johns Hopkins Group, and they've done very, very good  
2 work.

3 MR. MATANOSKI: Your Honor, at this time I  
4 will properly address my observation to you.

5 Typically, redirect is about the matters  
6 that have been gone over on cross. Just because we  
7 haven't referred to a matter in the report doesn't  
8 mean we don't believe it's important, or that we won't  
9 cover it.

10 I'm not going to object to Mr. Williams  
11 going through parts of the report we didn't cover, but  
12 perhaps Dr. Aposhian didn't cover yesterday, because  
13 it would be enlightening to us about what his report,  
14 what parts of his report are important to his opinion.

15 However, if this is just argument about what  
16 Respondent didn't ask in cross, then this is not the  
17 time to argue one's case.

18 SPECIAL MASTER VOWELL: Mr. Williams?

19 MR. WILLIAMS: I think it's proper in  
20 redirect to point out areas of his testimony in his  
21 report which were ignored by the cross. That's what  
22 I'm trying to do.

23 SPECIAL MASTER VOWELL: Okay. Remember that  
24 you're not pitching this to a jury; you're pitching it  
25 to three people who have read these reports.

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1 MR. WILLIAMS: Okay.

2 SPECIAL MASTER HASTINGS: And you can also  
3 argue this on brief, too.

4 MR. WILLIAMS: Okay. Then I'll turn to one  
5 last topic, and that is the Pardo paper itself that  
6 you cited in your report, and which you were asked  
7 some questions about on cross. It's Petitioner's  
8 Exhibit 72. Let's show the title first, please.  
9 Scott.

10 BY MR. WILLIAMS:

11 Q This is the 2005 Pardo review paper, right?

12 A Yes. A very good paper.

13 Q The first thing I want to ask you about is  
14 on page 4 of this exhibit, where there is a section of  
15 the paper called, "Infections and Autism."

16 Could you read the first sentence of that  
17 section, please?

18 A "Infections have been associated with autism  
19 in small numbers of children, and include prenatal  
20 rubella (Chess, Fernandez, and Corns, 1978), and  
21 cytomegalovirus (Sweetner, et al, 2003, Yamashita, et  
22 al, 2003) and post-natal herpes encephalitis (Long,  
23 Bean, and Brown, 1981).

24 Q Now, but when they cite post-natal herpes  
25 encephalitis as a cause of autism here, is that

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1 consistent with your conception that there are post-  
2 natal insults that can lead to neuroinflammation in  
3 autism?

4 A Yes, sir.

5 Q Then on page 6 of the Pardo review, it's the  
6 very middle of this paragraph, Scott, here, with all  
7 the figures. Pull that up.

8 Let me read this to you, because it's hard.  
9 Does it say in here that neuroglial activation in  
10 autism may be part of responses that result from  
11 disturbances of neuroglial function, or neuronal  
12 neuroglial interactions during brain development, and  
13 secondary extrinsic effects resulting from unknown  
14 factors that disturb post-natal CNS development? Does  
15 the paper say that?

16 A That it does say. Yes, sir.

17 Q And is that consistent with your general  
18 theory that it's the inorganic mercury post-natally  
19 inducing neuroinflammation leading to autism?

20 A Yes, sir.

21 Q And then at the very bottom of this column,  
22 and the very top of the next column, does this paper  
23 also say that a potential explanation of the CNS  
24 dysfunction --

25 A I don't have that yet, sir.

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1 Q -- in neuroinflammation is extrinsic  
2 etiological factors, non-genetic neurotoxic or  
3 environmental, involved in the pathogenesis of autism  
4 that can produce neuronal and cortical abnormalities  
5 to which neuroglial reactions are only secondary  
6 responses? Do you see that?

7 A Yes, I see it now. I'm reading it slowly  
8 because it just didn't come up until just a few  
9 seconds ago. Yes, I see that, sir.

10 Q And is that consistent with your notion that  
11 the extrinsic factor of inorganic mercury in the brain  
12 can lead to these problems?

13 A Yes, sir.

14 Q Then finally, on the last page of the paper,  
15 in their conclusions, if you blow up just the top half  
16 of that conclusions paragraph, Scott -- this is on  
17 page 9 of the exhibit. You have part of it  
18 highlighted. It says -- well, let me ask you to read  
19 what I've highlighted there, Doctor.

20 A And you have to give me more of a view,  
21 Scott, please. I need the complete sentence. Thank  
22 you. Yes, we have just about it, yes.

23 "We hypothesize that environmental  
24 factors -- for example, neurotoxins, infections,  
25 maternal infections, in presence of genetic

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1 susceptibility and immunogenetic background of the  
2 host influences the development of abnormalities in  
3 cortical organization and neuronal circuitry and  
4 neuroinflammatory changes responsible for the  
5 generation of autistic symptoms."

6 Q And when they say that neurotoxins could be  
7 responsible for the generation of autistic symptoms,  
8 is that consistent with your notion that inorganic  
9 mercury is the cause, in some cases?

10 A Yes, sir.

11 Q And then let's look at figure 4 quickly, the  
12 last thing I want to ask you about. Let's blow up  
13 figure 4 that they just referred to.

14 Over on the left, they have a balloon there  
15 for environmental toxins.

16 A Yes, sir, I have it.

17 Q Do you see that?

18 A Yes.

19 Q And what does that, what does the arrow  
20 point to from the environmental toxins that goes  
21 around the top, over to the middle?

22 A To the central nervous system, neuronal  
23 organization synapse in neural transmitters,  
24 neuroglial activation, and you can go on to CNS,  
25 cytokines, et cetera.

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1 Q All right. And then at the very bottom of  
2 this diagram, over in the right-hand corner, do you  
3 see where it says "autistic phenotype?"

4 A Yes.

5 Q What's the first word under "autistic  
6 phenotype?"

7 A "Regression."

8 MR. WILLIAMS: Thank you. That's all I  
9 have.

10 MS. RENZI: Just a couple questions. Could  
11 we pull that slide back up, please?

12 RE-CROSS-EXAMINATION

13 BY MS. RENZI:

14 Q Dr. Aposhian, I just have a couple of  
15 questions.

16 A Yes, ma'am.

17 Q In 2004, you presented to the IOM, is that  
18 correct? They invited you to present? The 2004 IOM.

19 A I think that. I don't keep date straight,  
20 but I think it was 2004.

21 Q And you presented your theory that autism  
22 was caused by a mercury efflux disorder. Is that a  
23 fair summary of your contention?

24 A I think that's quite correct.

25 Q And you stated today you were very surprised

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1 that the Charleston and the Vahter paper were not  
2 presented to that IOM, is that correct?

3 A It was not listed as one of the articles,  
4 one of the papers in the bibliography that was shown.

5 Q So you didn't present the Charleston article  
6 in 2004.

7 A You must realize that I was told I could  
8 speak for a short period of time. And I thought it  
9 was much more important to bring up the Wilson's  
10 Disease model than to do a complete survey of all the  
11 work that many good people had done.

12 Q And you didn't present the Vahter article,  
13 either, did you?

14 A The Vahter article?

15 Q Vahter.

16 A Vahter? No. She's a very good friend of  
17 mine, I know her work. We just didn't have time to go  
18 into all of that.

19 Q You just presented your theory on mercury  
20 efflux, is that correct?

21 A I don't know. I'm sure there was  
22 introductory material and other theories. But the  
23 major point was to present the mercury efflux theory.

24 Q Did you discuss neuroinflammation with the  
25 IOM?

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1           A     I did not, because my knowledge of  
2     neuroinflammation at that time was practically non-  
3     existent.

4           Q     Did the IOM, didn't the IOM reject your  
5     hypothesis, that autism was caused by a mercury efflux  
6     disorder?

7           A     I really don't know. I don't know that.

8           Q     Okay. I just want to return to this chart  
9     for a minute that Mr. Williams asked you to look at.  
10    It's on your screen, that chart.

11          A     Yes.

12          Q     And they call this "Hypothetical  
13    Interactions of Environmental and Genetic Factors."  
14    So how do post-natal insults lead to  
15    neuroinflammation? What's the mechanism? What's the  
16    process?

17          A     How does post-natal --

18          Q     Insult.

19          A     -- insult, an environmental insult --

20          Q     Lead to neuroinflammation.

21          A     I would much rather have our neurologist  
22    answer that later on.

23          Q     So you don't know.

24          A     I think I know, but since it's a cause where  
25    I just don't want to make a mistake in saying what I

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1 think, and so I would rather pass it on to the  
2 neurologist.

3 Q But you offered your opinion today that you  
4 agree with this Pardo hypothesis, that's correct? And  
5 you just accept it because it's --

6 A I agree with the Pardo hypothesis.

7 Q But you don't understand why.

8 A That doesn't mean I have to be an expert in  
9 every single part of the hypothesis.

10 Q But do you have an understanding of the  
11 mechanism of how this occurs that you can accept this  
12 hypothesis?

13 A In my own mind, I have such a mechanism,  
14 which I'm not confident in presenting in public.

15 Q So it's not one you could articulate to the  
16 Court at this moment.

17 A Pardon?

18 Q It's not one you could articulate to the  
19 Court today.

20 A It's not one that I can be absolutely 100-  
21 percent certain that I would be giving the correct  
22 information at this time.

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

25 SPECIAL MASTER VOWELL: All right. It would

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1 appear to be an appropriate time, I understand Dr.  
2 Aposhian needs to leave this afternoon, so we would  
3 excuse him.

4 Mr. Matanoski, does the government wish a  
5 sort of caveat in terms of further cross-examination  
6 of Dr. Aposhian?

7 MR. WILLIAMS: In the future?

8 SPECIAL MASTER VOWELL: In the future.

9 MR. WILLIAMS: Yes, ma'am. With the caveat  
10 that we may not be asking for that.

11 SPECIAL MASTER VOWELL: I understand. And  
12 this had to do with an off-the-record discussion that  
13 we'll put in the record at some point, but a  
14 discussion that we held before we began this morning,  
15 concerning Dr. Aposhian needs to leave today. There  
16 may be more cross-examination of him later based on  
17 the matters in his testimony that were not included in  
18 this report. Have I correctly stated that, Mr.  
19 Matanoski?

20 MR. MATANOSKI: That's correct, ma'am.

21 SPECIAL MASTER VOWELL: And Mr. Powers, you  
22 all did not object to that.

23 MR. POWERS: That's correct, Special Master.

24 SPECIAL MASTER VOWELL: All right. Then Dr.  
25 Aposhian, you are excused at this point, with the

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1 understanding that there may be questions for you at a  
2 future time.

3 THE WITNESS: Thank you.

4 (Witness excused.)

5 SPECIAL MASTER VOWELL: And it would appear  
6 to be a good time to take our lunch break. Do we want  
7 to discuss the plan for proceeding this afternoon  
8 before we all break?

9 MR. WILLIAMS: Yes, ma'am.

10 SPECIAL MASTER VOWELL: Okay. So what's the  
11 plan from Petitioners on what we intend to do this  
12 afternoon?

13 MR. WILLIAMS: This afternoon, just looking  
14 at the expected length of testimony, and without  
15 really knowing the expected length of cross, but  
16 anticipating fairly extensive cross of Dr. Deth, who  
17 is our next witness, my best guess is that Dr. Deth  
18 will take the balance of the afternoon today. And  
19 that we would therefore shift our schedules to have  
20 Dr. Kinsbourne take the witness stand Wednesday  
21 morning.

22 I expect he would be done before the lunch  
23 break on Wednesday, and Mylinda King and George Mead  
24 would be available. We anticipate completing both  
25 direct and cross in that remaining afternoon session.

1 That's what we would propose.

2 And we would still be able to get Dr.  
3 Mumper. That would leave all day Thursday for Dr.  
4 Mumper, and I anticipate we would have no problem  
5 being done with Dr. Mumper in that one day.

6 SPECIAL MASTER VOWELL: And we still then  
7 have Friday available for overflow, should cross or  
8 directs take longer than expected.

9 MR. WILLIAMS: That's correct, Special  
10 Master. So that's what we would propose as a  
11 schedule, actually for today and running through the  
12 rest of the week.

13 SPECIAL MASTER VOWELL: Okay. So we will  
14 plan on taking up Dr. Deth after lunch. So let's  
15 reconvene then at 1:25, 1:30.

16 MR. WILLIAMS: Thank you. It's such an  
17 easier number, what's the difference, Special Master?

18 SPECIAL MASTER VOWELL: Fair enough, 1:30.  
19 Thank you.

20 (Whereupon, at 12:25 p.m., the hearing in  
21 the above-entitled matter was recessed, to reconvene  
22 at 1:35 p.m. this same day, Tuesday, May 13, 2008.)

23 //

24 //

25 //



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1 Massachusetts.

2 Q And how long have you been at Northeastern?

3 A I have been there a long time. I believe  
4 it's been, let's see, it will be 32 years this coming  
5 September.

6 Q And would you just summarize your education  
7 for us, please?

8 A Sure. I have a, my original Bachelor's  
9 Degree is in pharmacy, so I am actually a pharmacist.  
10 I received that pharmacy degree from the University of  
11 Buffalo School of Pharmacy in 1970. And in 1975 I  
12 completed my PhD in pharmacology. I received that  
13 degree from the University of Miami in Florida, and  
14 then went ahead to do a post-doc, a post-doctoral  
15 fellowship in Belgium, in the University of Louvain in  
16 Belgium.

17 I returned briefly to Florida, to Miami, but  
18 then took a faculty position in 1976 at Northeastern,  
19 where I am now.

20 Q And you've been there ever since.

21 A I have.

22 Q Now, do you have a laboratory in which you  
23 do research?

24 A That's right. Throughout this period of 30-  
25 several years, I have maintained a lab. I originally

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1 did cardiovascular research, where I was studying  
2 contractions of blood vessels, things relating to  
3 hypertension. And then that moved to studies of  
4 receptors: the molecules that respond to  
5 neurotransmitters.

6 As we studied the receptors in these blood-  
7 vessel preparation, we ultimately discovered a process  
8 that relates very much to the autism and the issue at  
9 hand today.

10 Q Was your cardiovascular research funded by  
11 NIH?

12 A It was. I had cardiovascular grants from  
13 the National Institute of Heart, Blood, and Lung for  
14 almost 15 years. I had also from the American Heart  
15 Association, grant support.

16 Q Now, do you have students that you both  
17 teach and supervise in research?

18 A Certainly. One of the pleasures of being a  
19 university professor is to be able to participate in  
20 the development of the young scientists. And in fact,  
21 I have two PhD students now in the lab; they'll be the  
22 14th and 15th doctoral students that will have been  
23 trained in my lab. The previous 13 have graduated and  
24 gone on to different careers. And there is also a mix  
25 of undergraduates and other students, as well.

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1 Q And have you published some of your original  
2 research in the peer-reviewed literature?

3 A I have, and I certainly make an effort on a  
4 continual basis to do that. I have I guess just short  
5 of 70 publications at the moment.

6 Q Have you also written some book chapters?

7 A I've written several book chapters; several  
8 more relating to autism are in press at the moment.

9 Q And you also had one book you've written.

10 A An important thing for me was several years  
11 ago now, about five years ago, I wrote a book called  
12 The Molecular Origins of Human Attention, the  
13 Dopamine-Folate Connection. And the work that  
14 prompted me to write that book and the content of that  
15 book are again closely related to the issues at hand  
16 today.

17 Q Then how long have you been doing research  
18 related to autism?

19 A Well, the key event that brought us in this  
20 direction was in about 1998. And this will come out  
21 by a matter of course as I review some of our work,  
22 but it involves discovery about a dopamine receptor in  
23 1998. We discovered a new signaling activity of one  
24 of these receptors. And that signaling activity  
25 prompted us to, it prompted me to make the decision to

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1 pursue that, and to eventually leave behind the  
2 cardiovascular work, and bringing us into the field of  
3 neuroscience and neuropharmacology.

4 And so I guess that wasn't an immediate  
5 decision by any means to pursue autism. It was only  
6 when that line of work became coincident with some of  
7 the theories and concerns about autism that it really  
8 became autism-related research. Now, that, I would  
9 suppose, is about five years now.

10 Q And you've prepared some slides to  
11 illustrate your points today?

12 A I certainly have, that's correct.

13 Q Let's turn to slide 2, please. And would  
14 you explain what this slide depicts?

15 A Yes. Thank you for the opportunity. And  
16 this slide says we're here to discuss thimerosal  
17 actions, especially in the brain, where our work has  
18 greatest reference. I thought it would be a good  
19 introduction to the previous testimony, Dr. Aposhian  
20 in particular.

21 But this slide just serves to outline how  
22 the thimerosal, or in fact the organic mercury gets to  
23 the brain, and some of the critical things that it  
24 does once it gets there.

25 And so I've tried to depict in this slide

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1 here the molecular structure -- and you'll pardon,  
2 this has got a lot of science in it, and I hope you  
3 can gather what you can from it -- but it would be the  
4 actual chemical formula of thimerosal, with the ethyl  
5 mercury being attached to a sulphur on the carrier,  
6 which is thiosalicylate.

7 And in fact, the mercury is released from  
8 that sulphur carrier to release the ethyl mercury that  
9 we talked much about here. And the released ethyl  
10 mercury then has different fates or possibilities, and  
11 excretion from the body, and detoxification directly  
12 is one of those possible fates.

13 But alternatively, because of the ethyl  
14 group's ability to make the mercury atom more easily  
15 penetrant of the blood-brain barrier, the ethyl  
16 mercury can cross this normally sufficient barrier and  
17 bring the mercury into the brain. And once it has  
18 breached that barrier, then, as we again earlier  
19 discussed, you get a process of de-alkylation or  
20 deethylation in this case, in which the inorganic  
21 mercury is released on the other side of the blood-  
22 brain barrier. So it's now behind the barrier, as  
23 inorganic mercury is unable to recross the blood-brain  
24 barrier back out to the rest of the body. And  
25 therefore, is more or less trapped, as inorganic

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1 mercury, in the brain.

2 In addition, the de-alkylation step is very  
3 important in establishing the toxicologic activity of  
4 the mercury, because when the ethyl mercury has, when  
5 the mercury in ethyl mercury has ethyl group bound to  
6 it, that one ethyl group leaves only one remaining  
7 binding opportunity for the mercury. So it can only  
8 bind to one thing more than the ethyl group.

9 Once it becomes inorganic mercury, it has  
10 two binding opportunities. And it can bind  
11 simultaneously to, for example, to thiol or to sulphur  
12 groups as long as they are positioned close enough to  
13 each other. And when the inorganic mercury is  
14 simultaneously bound to two such SH or thiol groups,  
15 and even if one bond breaks, which happens rarely but  
16 does happen, the other bond keeps the mercury in  
17 place. So even if I lose one, I'm still not going  
18 anyplace, I still have a second one.

19 So when an inorganic mercury binds  
20 simultaneously to two thiols, it stays for an  
21 extraordinarily long time, much more longer than even  
22 if it was just one. And as it turns out, the kind of  
23 molecules that have two thiol groups in such a  
24 position to be bridged by a mercury, you know,  
25 inorganic mercury ion here, those molecules tend to be

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1 involved in sulphur metabolism. And they tend to be  
2 the key regulatory proteins that are determining the  
3 amount of the antioxidant glutathione, as we'll  
4 discuss in more detail later on.

5           These properties of inorganic mercury, in  
6 general terms, mean that it's going to target sulphur  
7 metabolism, which is really the focus of my research  
8 now, and the focus of my comments here today. And it  
9 disrupts sulphur metabolism, not only in neurons,  
10 which of course provide the function of the brain that  
11 we're most familiar with, but it will disrupt sulphur  
12 metabolism in the other cell types, not only in the  
13 brain, but the liver and other tissues of the body, as  
14 well.

15           So the inorganic mercury disrupts sulphur  
16 metabolism in all cell types, I could say that  
17 broadly, and in the brain in particular, where it's  
18 trapped behind the blood-brain barrier, this is a  
19 particular problem.

20           Q     Why does mercury and sulphur tend to go  
21 together?

22           A     Well, it turns out the electrons that  
23 populate the mercury atom that are available for  
24 bonding are, I'll say a perfect match with the sulphur  
25 atom, in especially the so-called thiols, where the

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1 sulphur has a hydrogen that can come off. And if the  
2 hydrogen comes off of the sulphur and the mercury  
3 comes on, the strength of that bond, because of the  
4 reciprocal nature of their electrons that they share  
5 in that bond is a strong one. And it's very difficult  
6 to break that bond.

7 And so this gives rise actually to the  
8 naming of these thiols that can start to form such  
9 strong bonds as mercaptans. The name "mercaptans,"  
10 after mercury itself, because of the well-recognized  
11 likelihood that mercury in the body will be found  
12 bound to sulphur, bound to these thiols, otherwise  
13 named as mercaptans.

14 Q Now, when we see -- I know in the United  
15 Kingdom at least they call thimerosal thiomersal, T-H-  
16 I-O. Is the "thi" in thimerosal, is that related to  
17 the fact that it has a sulphur in it?

18 A That's right. The original you could say  
19 construction of this molecule by Lilly as a  
20 preservative recognized the fact that the molecule,  
21 thiol, which otherwise would be an H if the mercury  
22 wasn't there, that this thiol here was a perfect place  
23 to attach a mercury to. But then had the probability  
24 of being released, and releases the active ingredient  
25 here, the ethyl mercury.

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1           And in fact, as we sit here and discuss the  
2 potential of that ethyl mercury as a causative factor  
3 in autism, we can recognize that the preservative  
4 value of thimerosal, as formulated and as included in  
5 the vaccine, that preservative role is fundamentally  
6 identical to the role that I am describing here. That  
7 is, the way that it acts as a preservative by  
8 interfering with sulphur metabolism in organisms such  
9 as bacteria, and as a result of interfering with their  
10 sulphur metabolism at the concentrations present in  
11 vaccine formulations, is liable to preserve or  
12 otherwise decrease the growth of bugs in those  
13 containers.

14           Q     And it also has the same effect on fungus,  
15 doesn't it?

16           A     That's right. It's the non-specific ability  
17 of mercury binding to thiols and sulphur compounds to  
18 disrupt sulphur metabolism that makes it an effective  
19 preservative against many different life forms.  
20 Because it's so critical for life forms to have normal  
21 sulphur metabolism.

22           Q     And by preservative, we're preserving the  
23 integrity of the vaccine itself from the invasion of  
24 these bugs or fungus, is that right?

25           A     That's right. The word "preservative" is a

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1 relatively comforting word. I like my materials  
2 preserved, more or less.

3 But in this case, the preservative in the  
4 mercury has more or less an infinite lifespan. That  
5 is, the inorganic mercury especially can never be  
6 mutated to anything else other than inorganic mercury.  
7 Whereas a different preservative that we might think  
8 of, like sodium benzoate for example, might be able to  
9 be metabolized to other things, and might have a  
10 halflife in the body that's much shorter.

11 But the choice of mercury guarantees that  
12 wherever that mercury goes, it will have a toxic  
13 potential for the rest of its existence.

14 Q Is it fair to say that another word for a  
15 preservative in thimerosal as a preservative would be  
16 as a bactericide, or a fungicide?

17 A In a sense, yes. It has the ability to kill  
18 bacteria, although there are certain bacteria that  
19 apparently are resistant. Because in fact, different,  
20 lots of vaccines, for example, have been found to be  
21 contaminated despite the presence of the thimerosal.

22 So to a significant extent, it is a  
23 bactericide and a fungicide, but it's not infallible,  
24 even in those regards.

25 Q Are we ready to move to the next slide?

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1           A     I'm ready, except I did want to point out  
2     where we're going here. I specified these three cell  
3     types here, which we have heard and will develop  
4     further. But I want to make it clear that we'll next  
5     move on to it in a short time.

6                     So the effects that are distinctive in  
7     neurons or neuronal cells, or microglial and astrocyte  
8     cells, so different cell types respond in their own  
9     way to the presence of the inorganic mercury. And so  
10    if we couldn't move ahead now, the next slide was  
11    really intended by me to be sort of a vocabulary  
12    builder here to make sure that all parties concerned  
13    recognize some of the terminology.

14                    When I talk about thiols or talk about  
15    sulphur metabolism, it's necessary of course to use  
16    the biochemical terms. And here I'll just introduce  
17    three important thiols. And so the three here would  
18    be cysteine, which is the normal sulphur-containing  
19    amino acid that is, in fact, a thiol. It has an SH as  
20    a part of it. And it's also the limiting factor  
21    inside of cells for making glutathione, the anti-  
22    oxidant. So the concentration of cysteine and the  
23    availability of cysteine is critical for making the  
24    anti-oxidant glutathione, and its sort of cousin here  
25    would be homocysteine.

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1           It turns out that it's an unusual amino  
2           acid; it's only formed in the body, typically, and is  
3           a homo part of it here, refers to the fact that it has  
4           an extra carbon, compared to cysteine, and that gives  
5           it the name homocysteine. It's formed during the  
6           process of methylation, a cycle called the methionine  
7           cycle that I'll refer to. And so it's formed from the  
8           amino acid, and it can be a precursor for making  
9           cysteine as needed.

10           Q       Now, I'm sure you call these the three most  
11           important thiols. Why are they the most important?

12           A       Well, they are important especially for the  
13           consideration here, because they are a part of the  
14           core sulphur metabolism that's involved in maintaining  
15           the anti-oxidant, or the reduced state of cells;  
16           maintaining a normal redox status of the cell.

17                   And this is the area which I believe, and  
18           others, is the most critical problem in autism, and  
19           it's an area that mercury is active in. These  
20           compounds, each of them actually can bind to mercury  
21           directly. They are all thiols; they can bind mercury.  
22           Although, in fact, the effects of mercury are more  
23           than simply binding to these three molecules here.

24           Q       Now, you used the word "reduce." Can you  
25           explain, you know, oxidation and reduction?

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1           A     Yes. I'm glad you asked me to do that, and  
2     actually I wish I had a better slide to present it.  
3     But let me try to illustrate here.

4                     Each of these thiols, as a sulphur, let's  
5     say the tip of my finger would be the thiol. And when  
6     it's in its reduced state, the sulphur has a hydrogen  
7     atom attached to it. That's a reduced thiol.

8                     But if we have two such reduced thiols, the  
9     hydrogens can be removed from both of them, and the  
10    two sulphurs join together. In this case you have a  
11    disulfide, which also is referred to as an oxidized  
12    form of the thiol, because the reducing equivalents,  
13    the hydrogens are off, and now they are oxidized as  
14    they are going together here.

15                    So we could have a diathiol of two cysteines  
16    bound to each other, or two homocysteines bound to  
17    each other. Or most importantly, two glutathiones  
18    bound to each other that would be oxidized  
19    glutathione. And this would be reduced glutathiones  
20    with two hydrogens on either one.

21            Q     Okay.

22            A     And the glutathione I'm mentioning here,  
23    which one might consider the star player in this  
24    important drama here that we're a part of, the  
25    glutathione is actually a small peptide made of three

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1 amino acids; and the cysteine is the important  
2 functional part, and it's the middle one. And on one  
3 other side there's a glutamate, and on the other side  
4 of the cysteine is a glycine. So there is three, this  
5 peptide has three amino acids to make it up.

6 And in fact, it is the major anti-oxidant in  
7 all of our cells. And by all, I mean not only neurons  
8 and anthrocytes and microglia, but I mean cardiac  
9 muscle cells, I mean liver, kidney, and whatever. It  
10 has, through evolution, been chosen as the anti-  
11 oxidant that's going to keep us from oxidizing. We  
12 need to have enough glutathione in every cell in order  
13 to be able for that cell not to be damaged by  
14 oxidation. So it's our primary anti-oxidant. And  
15 when we run short of the reduced glutathione, then in  
16 fact that cell is in danger of not only dying, but  
17 certainly losing normal function and things like that.

18 And really, it took me a while to understand  
19 how important the glutathione synthesis is, to  
20 recognize the concentration in cytocells -- I make a  
21 note here that the concentration is 10 millimolar.  
22 Inside a cell, it's a typical value. Now, this is  
23 scientific terminology, and I recognize that. But we  
24 compare that to the sodium ion, salt, which is an  
25 important part of the blood and all of our fluids.

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1 This is actually just about the same amount of the  
2 glutathione as there is of sodium ions floating  
3 around. So it's a really impressive amount of this is  
4 produced and maintained by cells in order to stay  
5 alive in a oxygen environment.

6 Q Anything more about this one?

7 A I think I've covered all those aspects. And  
8 this again was meant as sort of background for the  
9 more detailed considerations of what the thimerosal  
10 does to cells.

11 Q Okay. Then we're ready for the next slide,  
12 please, 4. This is slide 4.

13 A So here I've tried to provide a little more  
14 detail about the brain, and about those three cell  
15 types that I alluded to before. And they are  
16 represented here as in the middle, a neuron, two  
17 astrocytes, and then one microglial cell.

18 And in the brain, these three cells work  
19 together. And they work together to maintain a  
20 satisfactory or a homeostatically normal redox  
21 environment. And the way they work together, I've  
22 tried to illustrate here, and I'll start the  
23 description here with the -- well, let me start with  
24 the astrocytes, if I could, up at the top here.

25 Q Let me ask you this.

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1 A Okay.

2 Q Are astrocytes also called glial cells?

3 A Yes. Excuse me for not specifying, but yes,  
4 it's one kind of glial cells. A microglial would be  
5 another type of glial cell. That means non-neuronal  
6 generally speaking.

7 Q Yes.

8 A So if I start with the astrocytes here, the  
9 astrocytes take up the oxidized form of cysteine that  
10 I mentioned before, which comes from the liver. Just  
11 by way of background, it's cysteine, it's called here,  
12 the name for the oxidized cysteine, is provided by the  
13 liver in the bloodstream, and it crosses the blood-  
14 brain barrier readily. And in the brain it's taken up  
15 by the astrocytes, and converted into glutathione.  
16 And the astrocytes, because of their makeup, have the  
17 ability to make an excess quantity of reduced  
18 glutathione, GSH.

19 And so they have so much extra capacity that  
20 they export some of this reduced glutathione out of  
21 the astrocyte, into the environment around the neuron.  
22 And in that extra-cellular environment, that  
23 glutathione is converted into cysteine first by the  
24 removal of the glutamate, and then by the glycine, and  
25 now the cysteine content of the glutathione is taken

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1 up by the local neuron cells by a particular  
2 transporter. And once inside of the neuron, this  
3 cysteine is now available to the neurons to make their  
4 own glutathione.

5 It's kind of an odd relationship between  
6 these two cells, why don't neurons simply take up the  
7 cysteine and do it themselves? Why do they need the  
8 astrocytes to make it into the glutathione first, and  
9 then break it down? Well, this is how nature  
10 carefully controls the access of cysteine to these  
11 neurons. The amount of cysteine available is dictated  
12 by the astrocytes.

13 And so they have like a working  
14 relationship. But astrocytes are sometimes considered  
15 to be nurse cells, taking care of neurons. And this  
16 is a very important way in which they do that: by  
17 providing a source of cysteine to neurons they  
18 influence the fate and the functionality of neurons  
19 that way.

20 I should mention that these transporters  
21 that take up the cysteine by astrocytes, as well as  
22 the ones that take up the cysteine in neurons, are  
23 transporters that can take cysteine and/or glutamates,  
24 the excitatory neurotransmitter glutamate. And in  
25 fact, this can be either together with the cysteine in

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1 the same direction or in opposite directions; they can  
2 exchange for each other with the cysteine. And so  
3 this alerts us that there is a close relationship  
4 between the oxidative mechanisms of metabolism in the  
5 brain and the excitatory neurotransmitter, glutamate.  
6 We'll hear more about that from Dr. Kinsbourne.

7 But otherwise, this is how neurons get their  
8 glutathione. And this leaves us with the microglial  
9 cells, which serve as really vigilant sentinels for  
10 the redox status of the brain. Actually, they are  
11 positioned almost like in a matrix in the brain. Each  
12 one has their domain, their area around the microglial  
13 cell, and they monitor the redox status in their zone,  
14 in their area.

15 And when they detect something there that's  
16 not supposed to be there, perhaps a bacterial toxin,  
17 perhaps a metal ion, when it is in that area and they  
18 are impacted by that, the microglial response is to  
19 undertake an activation mechanism and to clean up the  
20 area. This is much the same as in the periphery, the  
21 so-called macrophage as part of our white blood cells.  
22 They go out and they scavenge things and they grab  
23 some host bacteria and so forth.

24 In a similar way, the microglial cells  
25 monitor materials, and the redox state in their

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1 environment. And when they come in contact with or  
2 are affected by, in this case let's say inorganic  
3 mercury, they become activated. And the activated  
4 microglial actually change shape. They change  
5 morphology. They become phagocytotic, to take up  
6 materials, and they also put out oxygen species that  
7 are damaging, called reactive oxygen species, or ROS.

8 And I will say here, what those could be,  
9 they can be hydrogen peroxide, that we're sort of  
10 familiar with. They can be another one in the middle  
11 here, super-oxide anion, or hydroxyl radical. And  
12 these oxygen species are meant to kill bacteria. This  
13 is how our innate immune system works, is that certain  
14 cells, by producing these nasty oxygen species, can  
15 damage bacteria that are nearby, and kill them. And  
16 by damaging them and then taking up the bacterial  
17 remnants, they can clean up their areas here.

18 But they are creating an oxidative  
19 environment. And so when the microglia are activated,  
20 it creates near the neurons, or in the neuronal area,  
21 a certain amount of oxidative stress, or an extra sort  
22 of load of oxygen species that the neurons have to  
23 deal with themselves, because they are in that same  
24 environment.

25 Q Now, you said that the microglia not only

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1 detect and take in bacteria, but also metal ion.

2 A Well, I hesitate even again here, because  
3 the microglial interaction with metal ions, it's  
4 really one, I don't know whether they're like designed  
5 to take up the metal ions. But more precisely, they  
6 are actually affected by the metal ions. And they do  
7 respond to the metal ions. They don't have a choice.

8 For example, if the mercury ion is there,  
9 and it binds to sulphur groups and sulphur proteins in  
10 microglia, the microglia are affected by that metal  
11 ion. And they develop oxidative stress as a result of  
12 the interference with their metabolism.

13 So in a sense, they are sensing metal ions,  
14 but it's a slightly different way. They don't have  
15 receptors for mercury, whereas they do have receptors  
16 on the surface to detect bacterial components. So  
17 it's subtly different, but similar.

18 Q Okay. Anything more about the --

19 A Well, I think I've covered this. I just  
20 want to make sure the word neuroinflammation here is  
21 meant to describe the state where, as a result of this  
22 oxidative condition here and the effects of the  
23 mercury on each of these three tissues, cell types  
24 rather, that we can call that oxidative stress as a  
25 chemical term. But as a pathologic term, it's very

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1 closely related, it is a part of inflammation, in this  
2 case neuroinflammation.

3 So the term neuroinflammation as it's used  
4 in different articles and so forth implies the  
5 presence of oxidative stress, and the sulphur  
6 metabolism changes. Please, the next slide.

7 Q The next slide.

8 A This is a simpler one. And the concept here  
9 is to say that sulphur metabolism, as I tried to  
10 allude to here, has an important role in maintaining  
11 cellular oxidative status, because of the glutathione  
12 synthesis. But at the same time, sulphur metabolism  
13 has other roles. And it has to balance these  
14 different roles.

15 One of the other important roles that I'll  
16 develop here is that of methylation, a process that's  
17 dependent on sulphur metabolism. And when thimerosal  
18 or inorganic mercury interferes with sulphur  
19 metabolism, it's going to affect both of these  
20 processes, because it's like having a limited amount  
21 of resources. You're either going to attend to the  
22 oxidative needs of the cell, or the methylation  
23 processes; and you have to make, the cell has to make  
24 decisions about that.

25 And so when thimerosal shifts the needs of

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1 the cell toward oxidative needs, then in fact the  
2 methylation needs may suffer by default. And so to  
3 understand, it's a reciprocal relationship between  
4 these two, in that thimerosal interferes with the  
5 normal regulation.

6 Q And methylation means?

7 A I'm about to specify. I think the next  
8 line, if I have the order correct here.

9 Q Okay, you're right.

10 A I'd better check myself. I think that slide  
11 6 gives us a chance to introduce methylation.

12 So methylation relies on the transfer of a  
13 methyl group, which is the CH<sub>3</sub>, in chemical terms.  
14 It's a carbon atom, one carbon atom; and it can be  
15 transferred from a donor, which is usually the methyl  
16 donor, adenosylmethionine, here SAM. And that  
17 donation's molecule can give up its methyl group and  
18 physically attach it to another molecule.

19 So as the methyl group leaves and it gets  
20 attached to something else, the something else gets  
21 methylated. And that's the process known as  
22 methylation. It's like a methyl transfer reaction.

23 And the molecule that does the methyl  
24 donating, SAM, adenosylmethionine, is itself a sulphur  
25 amino acid. Because as it turns out, the chemistry

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1 again of the sulphur here, when it has a methyl group  
2 attached to it, that bond is weak enough to be broken  
3 so the methyl group can be transferred. So sulphur  
4 atoms are chosen for methylation because of the  
5 ability to transfer a methyl group from this sulphur  
6 atom to something else.

7 And when the sulphur atom, excuse me, the  
8 methyl group is transferred from SAM, the remainder of  
9 the molecule is referred to as adenosylhomocysteine,  
10 or SAH, which is simply SAM without the methyl group.  
11 It's the leftover part.

12 And when we're talking about methylation,  
13 you can say it's just one of those biochemical  
14 reactions, another esoteric, something like that. But  
15 nature has found it useful, again during evolution, to  
16 develop many methylation reactions. And there are  
17 almost 200 different methylation reactions.

18 So when something affects methylation, it's  
19 going to affect 200 different processes, not just one.  
20 And examples are pretty important examples. Because  
21 perhaps the most important example and relevant to  
22 autism is the methylation of DNA, or genes.

23 When genes are methylated at certain  
24 locations where they are methylated, it leads to a  
25 process by which they become hidden, or silent, and

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1 unavailable for expression. So methylation of DNA is  
2 the mechanism by which genes are turned on or allowed  
3 to be on if they're not methylated, or off if they are  
4 methylated. And so it's a pretty important process,  
5 and it's particularly important during development,  
6 because during development is when genes are turned on  
7 or turned off, and so forth.

8 This happens in conjunction with another set  
9 of proteins that are involved with the DNA, and that  
10 is the histone protein. Histones are proteins, I  
11 think of them as like a sphere that the DNA wraps  
12 around. And methylation of the DNA starts that  
13 process going, and methylation of the histones helps  
14 it along, as well.

15 So both DNA methylation and histone  
16 methylation are involved in gene silencing, which is  
17 also referred to as epigenetic regulation of genes.

18 Other things besides those two can be, other  
19 proteins can be methylated. Another important  
20 methylation target, the individual phospholipid  
21 molecules, the fats that make up the membranes of  
22 neurons and other cells. And that's where our work  
23 originated, was from studying phospholipid  
24 methylation. I'll talk more about that.

25 But also neurotransmitters are methylated in

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1 order to terminate their activity. For example,  
2 dopamine, the neurotransmitter involved in attention  
3 awareness. It's a release of neurons, and then the  
4 enzymes that put methyl groups onto the dopamine. And  
5 when the dopamine is methylated, it no longer binds to  
6 its receptors, it terminates its activities. And any  
7 problem with methylation will therefore affect  
8 neurotransmission that way. And I could go on and on,  
9 and I'll try to restrict that. But in fact,  
10 methylation has a lot of different targets.

11 I mentioned methylation here, and the bottom  
12 point on this slide is we emphasize that whenever you  
13 have oxidative stress, you have reduced amount, or  
14 less methylation. It's like a reciprocal  
15 relationship. More oxidative stress, less  
16 methylation. That's the way the cells work.

17 Q Okay.

18 A So next slide?

19 Q Next slide, slide 7.

20 A And again, this takes us a little further,  
21 to our understanding of the relationship with  
22 glutathione here, we, humans, are aerobic organisms.  
23 And we take in oxygen bravely. We use it to make ATP  
24 and energy. But it's a risk. What we're doing is  
25 breathing in a risk of oxidation, and using it, which

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1 works great for us as long as we have enough anti-  
2 oxidants to counter-balance the risks.

3 And I've tried to represent that here by  
4 saying usually there's a certain amount of oxygen  
5 radicals or damaging oxygen forms. And as long as we  
6 have enough glutathione, or buffer capacity to offset  
7 that, we're fine. And this is why we have so much  
8 glutathione in cells, as I mentioned earlier.

9 But under certain circumstances, which can  
10 be partly genetic and partly environmentally induced,  
11 under certain circumstances this balance shifts in  
12 favor of the oxidative conditions. And this would be  
13 the oxidative stress condition that I alluded to  
14 before, which can be -- you can conceptualize this --  
15 as being either because you made too many oxygen  
16 radicals, so you have an over-production of them. For  
17 example, your mitochondria is not efficient in making  
18 ATP from oxygen; they have too many of these oxygen  
19 radicals. Or on the other hand, your defense  
20 mechanism, anti-oxidant glutathione levels might be  
21 too slim, or too limited, in which case the oxygen  
22 state is more on the oxidated side, rather than the  
23 reduced side.

24 So in any case, this balance can be due to  
25 genes that we carry. And if we do carry some genes,

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1 whatever negative potential they have might be  
2 amplified by exposure to things that make the  
3 situation worse, that otherwise damage mitochondria,  
4 or otherwise limit the glutathione antioxidant  
5 synthesis.

6 So we can see the genes and the  
7 environmental factors, generally speaking, can give  
8 rise to oxidative stress, or contribute to  
9 neuroinflammation.

10 Q Let me ask you, you have different arrows on  
11 there. The arrow beside the word "oxygen radicals"  
12 pointing up, does that mean that that's increased?

13 A Yes. This would be under this condition on  
14 the right, compared to this condition. If you have a  
15 higher or increased level of oxygen radicals, or ROS,  
16 then they could be excessive with regard to the  
17 buffering capacity that you have.

18 Q And you have a down arrow beside redox  
19 buffer.

20 A Right. As compared to here, there's less  
21 buffer capacity; compared to here, there's more oxygen  
22 radicals. Either one could create the imbalance. And  
23 I think reasonably, probably they both contributed  
24 commonly to the imbalance.

25 Q And then another question. We've heard the

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1 word occasionally the last two days, mitochondria.

2 What are mitochondria?

3 A Okay. Mitochondria are a so-called sub-  
4 cellular organelle. That is, if the cell is a whole  
5 unit here, within the cell are these little factories,  
6 energy factories called mitochondria, where oxygen,  
7 molecular oxygen, O-2, is taken up by the  
8 mitochondria; converted into water, H2O. And in the  
9 process, the energy in the oxygen is converted into  
10 the energy molecule ATP. And it's a way in which we  
11 can use oxygen metabolically as an energy source, as  
12 long as we convert all of the O-2 into water. If we  
13 did that perfectly, we would have zero risk.

14 But inherently, that process releases some  
15 of the oxygen as hydrogen peroxide or super-oxide  
16 action, the dangerous forms which then can otherwise  
17 attack other molecules, damaging the cells.

18 Q And do neurons and microglia and astrocytes,  
19 do they have mitochondria?

20 A Absolutely every cell in the body, and I  
21 know what I'm thinking of is red blood cell ghosts,  
22 but I think even they have mitochondria in them; they  
23 just don't have a nucleus. But every cell in the body  
24 has a number of mitochondria in them; and they need  
25 that, of course, as a source of energy for those

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1 cells.

2           So just the bottom part of this, what if you  
3 have oxidative stress? If you have that, then in  
4 neurons in particular there are some consequences.  
5 And the most dire consequence would be on the right  
6 side here. That is to say, degeneration, which is  
7 another way of saying the cell could die. And  
8 certainly Alzheimer's Disease, Parkinson's Disease,  
9 other neurodegenerative disorders would be examples of  
10 neurodegeneration.

11           But at a lesser level, you would lose  
12 function. And inhibition of methylation is one way  
13 that function is lost. Because one example that's  
14 pertinent to our work on dopamine receptors is the  
15 fact that methylation activities are important for  
16 those dopamine receptors to provide for a synchronized  
17 firing of neural network areas of the brain together.  
18 And since that activity is dependent on methylation,  
19 then any oxidative stress that lowers methylation will  
20 give a functional consequence here. You'll lose the  
21 ability for this neurosynchronization, as well as  
22 other activities.

23           So the point I am trying to make is that  
24 short of cell death, which can happen from extreme  
25 oxidative stress, there is also a loss of the usual

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1 abilities or the usual function of cells during  
2 oxidative stress.

3 Q Now, you mentioned Alzheimer's Disease and  
4 Parkinson's Disease. Are those associated in any way  
5 with neuroinflammation?

6 A In fact, both of those conditions are well  
7 known in the medical literature to be associated with  
8 oxidative stress, and with neuroinflammation in  
9 microglial activation. I have to be careful; I can't  
10 say as I remember the microglial part, I'll take that  
11 back. But I will say that they're associated with  
12 oxidative stress. And in particular with Parkinson's,  
13 recent evidence associated with pesticide exposure  
14 indicates that environmental exposure to xenotoxins is  
15 part of the pathologic circumstances for that  
16 condition.

17 Q Okay. Are we ready for the next slide?

18 A We could move on to slide 8, if we could.  
19 And we could probably do that a couple of times,  
20 because as we consider the sulphur metabolism, I  
21 mentioned before there's the glutathione, it's a  
22 really important molecule here. It's the main anti-  
23 oxidant.

24 So how do we get this glutathione? We get  
25 it from converting the amino acid cysteine to

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1 glutathione. And again, the cysteine is limiting for  
2 that. And where do we get the cysteine from?

3 Well, one of the places we can get it from  
4 is from the homocysteine, through a pathway that goes  
5 through an intermediate -- again, this is terminology  
6 here -- cystathionine. I believe, I won't go there  
7 now, but later I'll have a slide with some vocabulary  
8 glossary terms, but the idea here is that the cysteine  
9 to make the glutathione can come from the homocysteine  
10 down here. And this pathway is called  
11 transsulphuration, as a homocysteine is converted to  
12 the cysteine. And it's the intracellular way to make  
13 glutathione from homocysteine.

14 Now, if you advance to --

15 Q Wait, hold on, Scott, if you would.

16 A Okay. Well, we can stay there, okay.

17 Q Just first of all, the thio in glutathione  
18 and the thio in cystathionine, are those indicated in  
19 the sulphur groups?

20 A That's right. Really, with all of these  
21 compounds here, and I have to beg beware of those next  
22 ones that I introduce, are all sulphur-containing  
23 compounds. I'm showing you sulphur metabolism. And  
24 each of these, there's a sulphur in homocysteine;  
25 there's a sulphur in the cystathionine; there is

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1 sulphur in cysteine. There is cysteine now attached  
2 to glutamate, so it's still here and still here.

3 And sulphur metabolism, I'm not going to  
4 launch into my evolution story here, but since the  
5 origins of life under the ocean, it's recognized that  
6 sulphur metabolism is critical for life, and for  
7 oxidative control. And so that's why we're looking at  
8 it.

9 Q Okay. Now we're ready.

10 A So where do we get that homocysteine from,  
11 that we can use as needed to make glutathione? We get  
12 that from the methionine methylation cycle is now  
13 added to the diagram here. And this cycle starts with  
14 the lower left, with the amino acid methionine, and  
15 essential amino acid thrusts we can get from the diet.  
16 It's activated by ATP to be the methyl donor that I  
17 referred to, SAM, before, adenosylmethionine, which  
18 gives up the methyl group to things like DNA. And  
19 then the leftover is the adenosylhomocysteine, and the  
20 adenosylhomocysteine is then converted to the  
21 homocysteine.

22 And this reaction, by the way, is reversible  
23 if those who can see it, the arrows go back and forth.  
24 And in fact, this reversibility is a key feature of  
25 this cycle.

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1 Well, once a homocysteine is formed, nature  
2 has a decision to make: whether to send a  
3 homocysteine toward transsulphuration, to make more  
4 glutathione; or to reinvest it back in methylation.  
5 This is like a T junction here. And that decision  
6 that nature makes is guided by the redox state of the  
7 cell.

8 If the cell has the need for more  
9 glutathione, it's going to send more to the  
10 glutathione pathway, to desulphuration. If not, it  
11 sends the homocysteine back to methylation.

12 So we can see from these relationships how  
13 methylation is related to redox status of the cell.

14 The next slide introduces the enzyme, the  
15 key enzyme, the critical enzyme, methionine synthase.  
16 And this enzyme is obviously in a position to control  
17 the fate of the homocysteine. Because if the enzyme  
18 methionine synthase is not working or is turned off,  
19 the homocysteine instead of going down to making the  
20 methionine in methylation, the homocysteine  
21 accumulates and goes north to make the glutathione.

22 So regulating the methionine synthase  
23 activity is how nature controls the fate of the  
24 homocysteine. And this represents a switch mechanism.  
25 You can relate to this in any way you can. You can

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1 give it water flowing, and shifting water from one  
2 direction to the other. In this case you might  
3 consider that oxidation is like a fire that has to be  
4 put out by the glutathione.

5 So as needed, you can divert more water  
6 towards that oxidative need, and less towards your  
7 methylation problem. And the methionine synthase does  
8 that.

9 Now, the last part that has appeared here as  
10 well is the part that has got into this story.  
11 Because through a coincidence, you could say, through  
12 our own molecular studies of receptors when we were  
13 studying cardiovascular systems, we discovered that  
14 there is a receptor for the neurotransmitter dopamine,  
15 specifically the D-4 dopamine receptor, that has its  
16 own methylation cycle.

17 This receptor, and I'll show it in just a  
18 second in the next slide, this receptor has a  
19 methionine sticking out from the receptor that has its  
20 own sulphur with a methyl group at the end of it; and  
21 it's able to activate that methionine to be a methyl  
22 donor methionine, a SAM, and then to give the methyl  
23 group to the membrane-fossil lipids that are right  
24 next to the receptor, causing them to be methylated.  
25 And then to pick up a new methyl group using the

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1 enzyme methionine synthase, and the new methyl group  
2 comes from the folate pathway.

3 And this enzyme, methionine synthase, is,  
4 number one, fully dependent. It's dependent on methyl  
5 folate for those methyl groups to keep the cycle going  
6 here. And number two, it's a B-12, or cobalamin-  
7 dependent enzyme. And vitamin B-12, again essential  
8 for humans, even for vegans to survive, is essential  
9 for methionine synthase.

10 So we discovered this activity again in  
11 1998, which prompted our own interest in what's nature  
12 doing here. Why does it allow this one receptor, and  
13 only this one dopamine receptor, to carry out a  
14 methylation activity like this?

15 The next slide I hope --

16 Q Let me stop you. I want to ask, the picture  
17 that you have here, all of this is inside of a cell,  
18 is that right?

19 A That's correct. This is a segment, and even  
20 only a small segment, of cellular metabolism. Since  
21 this includes now a dopamine D-4 receptor, it's going  
22 to be cells that have that receptor, and not all cells  
23 do. And typically, neuronal cells have this dopamine  
24 receptor; in particular, the kind of intra-neurons  
25 called gabaergic or inhibitory into neurons, are rich

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1 in the D-4 receptor.

2 So it's best to think of this as typically a  
3 neuronal cell, although some non-neuronal cells also  
4 have these D-4 receptors.

5 Q And then the fossil lipid methylation,  
6 that's the cell surface, is that right?

7 A The third possible lipid refers to the  
8 surface membranes, and actually makes the cell. The  
9 sort of bag-like structure is actually made of these  
10 fossil lipids. And they're getting methylated.

11 And as I'll see in a second, I guess, the  
12 methylation of the membrane fossil lipids changes the  
13 membrane.

14 Q And the ATP cycle down there, that's what  
15 the mitochondria produce?

16 A That's right. The, well, it can be produced  
17 in several ways. It can get ATP from glycolysis and  
18 non-mitochondrial sources. But the mitochondria is  
19 the main source of ATP.

20 Q And did the mitochondria also depend on this  
21 kind of regulatory pathway?

22 A Mitochondria depended upon the glutathione  
23 availability to protect them against the very oxygen-  
24 damaging species that they are producing.

25 Mitochondria, however, to my knowledge, don't carry

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1 out methylation directly in the mitochondria. That's  
2 more of an activity within, left to the cytoplasm of  
3 the cell.

4 Q Okay. Now, the next.

5 SPECIAL MASTER VOWELL: Let me interrupt  
6 again, Mr. Williams. I remind you to use the slide  
7 numbers so we'll have an adequate reflection in the  
8 record.

9 MR. WILLIAMS: Okay, thank you.

10 SPECIAL MASTER VOWELL: The last testimony  
11 was on slide 8.

12 MR. WILLIAMS: It was actually the one --

13 SPECIAL MASTER VOWELL: I think we'll be  
14 able to pick it up, given the diagrams, but stay on  
15 the safe side.

16 MR. WILLIAMS: Thank you. So now we are on  
17 slide 8?

18 SPECIAL MASTER VOWELL: Nine.

19 MR. WILLIAMS: Slide 9.

20 BY MS. RENZI:

21 Q Excuse me, slide 9. I want to make the  
22 record clear.

23 Q Slide 9 is meant to provide a pictorial  
24 illustration of what I described in the previous one.  
25 And in the context of the membrane of the cell. So

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1 these ocular-shaped molecules here, this is a slice of  
2 a cell membrane. The outside would be at the top, and  
3 the inside of the membrane at the bottom. So the  
4 cytoplasm would be down below here, and the  
5 neurotransmitter, dopamine, would be released from  
6 other cells, and would come into its receptor, which  
7 is represented here by these blue spirals, and define  
8 the binding site.

9 And when the dopamine finds its binding  
10 site, it causes a rotation of one of these receptor's  
11 helices or spirals, and the helix that moves is the  
12 one that has the methionine that's going to be the  
13 methyl donor. I've shown that in yellow here. So the  
14 dopamine makes that available for donating a methyl  
15 group, and the methyl group is transferred from the  
16 receptor to the fossil lipid, and the new one to  
17 replace it comes from the enzyme, this ion in sensate,  
18 and the methylfolate co-factors that it requires.

19 So this process, when we were able to  
20 estimate how rapid it occurs, occurred in one second's  
21 time, about 20 to 50 times for each receptor molecule.  
22 Twenty to 50 times per second is a very robust  
23 activity. And it startled us to learn that. And when  
24 we did, we realized that the methylation of the  
25 membrane around this receptor, the methylation of it

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1 would change the physical properties in a short period  
2 of time; would make that membrane, now methylated,  
3 makes it more fluid. It makes it biophysically a  
4 little different. And this seems to be the role that  
5 this methylation plays. And when dopamine does that,  
6 it's really changing the membrane of the neuron in  
7 this local area.

8 Moving ahead now to slide 10. What role  
9 does that methylation play in the brain? We don't  
10 know, step by step, exactly that. But we have  
11 proposed, I have proposed that it plays, the fluidity  
12 of the membranes that the dopamine causes plays an  
13 important role in attention. And I proposed that in  
14 the books that I wrote a number of years ago, in part  
15 because this D-4 dopamine receptor is the genetic risk  
16 factor for attention deficit hyperactivity disorder,  
17 or ADHD.

18 That is to say, if you have a particular  
19 form, a genetic form of that receptor, then your risk  
20 of ADHD is three- to five-fold higher than other  
21 people's. And this suggested that this receptor plays  
22 a unique role in attention and awareness. And I have  
23 proposed that this might involve the synchronization  
24 of information during attention.

25 And the study that's shown here, and the

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1 data that's shown on this slide -- again, number 10 --  
2 supports this suggestion or hypothesis. And this data  
3 shows that the synchronization during attention is  
4 stronger if you have the so-called seven repeat form  
5 of this D-4 receptor, and the strength of this  
6 synchronization is indicated by the more brilliant red  
7 color here, compared to other people with a different  
8 form of the receptor, with two or four repeats.

9 And as the title suggests, the D-4 receptor,  
10 polymorphisms or repeats, modulate the human, we call  
11 them gamma band responses. But this is gamma  
12 frequency synchronization between neural networks in  
13 the brain.

14 And if I can try to capture the idea here,  
15 during attention, let's say that I'm attending to, for  
16 example, my pointer here. If I focus my attention on  
17 that, everything else gets kind of blurry, and the  
18 attended information becomes sharp. And it turns out  
19 in your brain the gamma activity is associated in, the  
20 areas that are receiving this information are showing  
21 gamma activity.

22 And so it indicates this kind of information  
23 suggests to me, although it's not proven step by step,  
24 that the special methylation activity of the D-4  
25 dopamine receptor is related to attention and

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1 awareness, and to gamma synchronization of neural  
2 networks.

3 Q Now, do all people that have the seven  
4 repeat gene structure, do they develop ADHD?

5 A No. I indicated that there's a higher risk  
6 if you have this, three- to five-fold. There's more  
7 than 100 peer-reviewed papers now confirming this.

8 But in fact, it's not a guarantee.  
9 Interestingly, it's also associated with a personality  
10 trait of novelty seeking, which is a positive virtue,  
11 compared to a loss of attention, which is a disorder.  
12 And it's been suggested that this seven repeat that's  
13 associated with improved gamma activity is actually,  
14 places some people at risk of ADHD when they're  
15 exposed to environmental pollutants, or even -- the  
16 people who published this didn't specify -- but  
17 environmental factors that took a good gene, a gene  
18 with a positive evolutionary value, and now converted  
19 it into a risk factor.

20 And now it probably means that not everybody  
21 who has it has ADHD. But if you have an environmental  
22 exposure and you have that, chances are your, the  
23 chances of ADHD are greater.

24 Q Are we ready for the next slide?

25 A I am. That would be number 11. Here is the

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1 same pathway that I illustrated before, but now I want  
2 to point out what happens during oxidative stress.  
3 The oxidative stress turns off this enzyme, methionine  
4 synthase. I'll in a second be explicit about how that  
5 happens, but when it does turn it off, we can see that  
6 the beneficial effect, which we are all happy to have  
7 occur, is that the homocysteine is now diverted to  
8 make more anti-oxidants, the perfect solution for the  
9 oxidated stress. You want more anti-oxidants.

10 However, the two methylation processes shown  
11 here, one involving let's say DNA and gene expression  
12 during development, the other that D-4 dopamine  
13 receptor I just talked about, they suffer the  
14 consequences of oxidative stress by having less  
15 methylation, or less methyl groups even available to  
16 support their activities. So the consequence you  
17 might expect to have, impaired attention, impaired  
18 gamma synchronization, as well as problems during  
19 development with inappropriate gene expression.

20 So how is it that the enzyme methionine  
21 synthase responds to this? Actually, the next slide I  
22 meant to expand on it. And if you'll excuse me, the  
23 slide 12 illustrates some additional methylation  
24 reaction, some of which I alluded to before, but I  
25 wanted to reemphasize that many different things

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1 happen during the inhibition of methylation during  
2 oxidative stress. I'll leave that as such, and then  
3 ask that we move ahead to the next slide.

4 Which is a result from a paper published by  
5 a researcher, Dr. Joe James.

6 SPECIAL MASTER VOWELL: And we will be on  
7 slide 13.

8 THE WITNESS: And now we are on slide 13.  
9 Thank you for that.

10 And this slide and this data, gathered from  
11 a study of autistic children and neural typical  
12 control, 80 autistic, 73 neural typical controls. And  
13 Dr. James measured in the plasma of these individuals  
14 the levels of those same materials that I just showed  
15 on the previous slide.

16 In fact, excuse me, the slide before that,  
17 slide number, would that be 9?

18 BY MR. WILLIAMS:

19 Q Yes.

20 A Excuse me. On slide 11, if we go back to  
21 slide 11, if we could just go backwards through this  
22 pattern here of showing impaired methylation and the  
23 diversion of more homocysteine here is expressed in  
24 those data. And when you don't have enough  
25 glutathione, when your glutathione is low, then this

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1 pathway will be emphasized, and these pathways will be  
2 inhibited.

3 And what we should expect to see during  
4 oxidative stress is too little glutathione, associated  
5 with lower activity of the methylation pathways.

6 And now moving ahead two slides, again  
7 returning to slide 13 here with this data, we can see  
8 what she found. And what she found was the levels of  
9 glutathione in its reduced form in the plasma were  
10 reduced by 36 percent. So this means that these  
11 individuals, these autistic subjects had too little of  
12 the reduced glutathione that they needed to combat  
13 oxidative stress; whereas the methylation activity,  
14 reflected as the ratio of the methyl donor SAM to the  
15 SAH without the methyl group, that was reduced by 30  
16 or 28 percent. That reduction means that methylation  
17 is decreased in the presence of oxidative stress, and  
18 suggests that these autistic subjects do suffer from  
19 oxidative stress and impaired methylation.

20 So how is it that the enzyme, methionine  
21 synthase, is regulated? Let me provide that detail in  
22 the next slide, which is no. 14. It illustrates the  
23 molecular structure of the enzyme methionine synthase.

24 And this is a molecular model from an x-ray  
25 crystal structure. And the enzyme has five distinct

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1 parts to it. I'm going to start with the pink part in  
2 the upper right. This is the part, or the domain as  
3 it's called. It's substrate homocysteine. And here  
4 the homocysteine is in yellow. And attached to the  
5 pink is the green domain, and here is the methylfolate  
6 bound onto that domain, so that is the folate domain.  
7 I'll get back to the intervening yellow-cap domain.  
8 But the B-12, the cobalamin, is bound to the red  
9 domain, and the final domain is this blue one, called  
10 the SAM-binding domain, because it binds a molecule of  
11 the methyl donor's SAM.

12 The way the enzyme works, in brief -- and  
13 it's easy to understand, even though this is like a  
14 molecular science -- if you just think of it as  
15 TinkerToys or something like that you can understand  
16 how it works. The B-12, in the middle of it is a  
17 cobalt atom. It's the heart of the B-12. And the  
18 cobalt atom, like the tip of my finger, sits there and  
19 waits for the green methylfolate domain to bring the  
20 methylfolate to it. And now the methyl group is  
21 transferred from the methylfolate to the cobalt.

22 So now I have methylcobalamin, or methyl B-  
23 12, in the red domain. Then this green domain backs  
24 away, rotates in space.

25 Now the pink domain comes in and brings the

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1 homocysteine close enough to pick up that methyl  
2 group, and becomes methionine. So that completes a  
3 reaction cycle. The homocysteine has now been  
4 converted to methionine, and the methylfolate gets  
5 replaced with a fresh one, and that cycle can continue  
6 until interrupted by oxidation.

7 Q Now, a chemical term you're using,  
8 methionine synthase. What does synthase mean?

9 A Well, the word "synthase," I can clarify  
10 that. Synthesis means making something. In this case  
11 it's making methionine. It's methionine synthase.  
12 And it's making the methionine by adding a methyl  
13 group to the homocysteine, which makes it methionine.

14 So methionine synthase, the name of this  
15 enzyme as a whole describes its activity.

16 Now, as I indicated, the reaction continues  
17 of the formation of methionine; but the cobalamin,  
18 when it's waiting for the next methyl group, while  
19 it's bare, it turns out that it's the most easily  
20 oxidized substance in our whole body. It's the most  
21 easily oxidized material that we have.

22 And that means that if there's anything in  
23 its environment that could oxidize it, it will oxidize  
24 it. And so it's a censor of oxygen status. And if  
25 there is something around, it oxidizes the cobalt and

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1 stops the reaction.

2 Well, while the reaction is stopped, the  
3 homocysteine accumulates and goes toward glutathione  
4 synthesis, so that we have more anti-oxidant. And now  
5 when the environment calms down, we can repair the  
6 oxidized cobalamin. And the oxidized cobalamin is  
7 repaired by the blue SAM domain, which comes in,  
8 brings a methyl group from SAM to put on there to make  
9 it into methyl B-12. And there's an auxiliary  
10 protein, methionine synthase reductase, that brings  
11 electrons just to help that reaction.

12 So this is how the enzyme is sent to do the  
13 oxidation. It's because the B-12 gets oxidized.

14 The last component to mention here is the  
15 yellow domain or region, which is called the cap  
16 region. It's called the cap because, in fact, it  
17 floats above the vulnerable cobalt, while it's  
18 exposed. And when you have a cap domain, it limits  
19 the oxidation. And as a result, we fix the stoppage  
20 of the enzyme.

21 And I won't present this data today, but  
22 what we've found in elder humans in their brains is  
23 that that cap domain can be removed with aging, so  
24 that more anti-oxidant can be made by trading greater  
25 vulnerability for the cobalt atom.

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1           So in any case, it's a marvel of engineering  
2           at the molecular level, including an oxidative sensing  
3           ability which helps the cell to make more glutathione  
4           anti-oxidant.

5           So in any case, this is the description of a  
6           standard enzyme. The next slide no. 15 indicates that  
7           in cases of human neuronal cells that we've studied in  
8           the lab, and we've also done related studies on rat  
9           cortex, we find that in those cells, the ability to  
10          reactivate the enzyme using this blue SAM-binding  
11          domain is not working. It doesn't function.

12          In order to reactivate the enzyme in these  
13          human neuronal cells, you need to take out, physically  
14          let the oxidized cobalamin or B-12 float off and be  
15          replaced with a new B-12 that's already methyl B-12.  
16          And this, in net terms, shows us that the neuronal  
17          cells, human neuronal cells, need methyl B-12 to  
18          reactivate the enzyme.

19          And as the next slide no. 16 shows us, the  
20          methyl B-12, or methyl cobalamin as it's otherwise  
21          known, in order to have that methyl cobalamin  
22          available to reactivate the enzyme, you need to have  
23          enough glutathione to synthesize it. Because the  
24          synthesis of methyl B-12 is glutathione-dependent.  
25          This first step requires glutathione.

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1           Now, putting this together, what you can see  
2           is that what nature has in mind in neurons, in human  
3           neuronal cells, is to keep the enzyme off unless there  
4           is enough glutathione to make methyl B-12 available.  
5           And if there's any deficit in glutathione, you won't  
6           have enough methyl B-12, and the enzyme will stay off,  
7           making more glutathione until you do have enough  
8           glutathione.

9           So it's like another solution to the problem  
10          of how to control the flow of homocysteine by keeping  
11          the enzyme in need of methyl B-12.

12          Q       Now, the same need for glutathione that you  
13          say is in neurons, is that also true of microglia in  
14          the astrocytes?

15          A       We don't know that. And I can't really  
16          comment with any authority about that. We've only  
17          been able to confirm this in human neuronal cells, and  
18          in whole brain preparations, which contain a mixture  
19          of neurons and microglia and astrocytes. So at this  
20          time, I can't say whether or not the properties of the  
21          whole brain reflect the neurons, or the microglia, or  
22          some complement.

23          So in any case, having made that point, I  
24          also want to extend the idea that human neuronal cells  
25          don't operate the same as other species. And to

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1 illustrate that, the next slide no. 17 shows the  
2 levels of the SAM sulphuration intermediate  
3 cystathionine in human brain on the left, compared to  
4 the monkey brain, the rat brain, guinea pig, cat, cow,  
5 chicken, and duck.

6 And what we can see in this progression here  
7 is that as evolution or whatever is driving human  
8 development, that we have an extraordinarily higher  
9 amount of this cystathionine, which is the first step  
10 in making the glutathione from homocysteine, which is  
11 the first step in transsulphuration. But because it's  
12 accumulating, we can see that it's not getting any  
13 further than this first step. There appears to be a  
14 block in human brains after the cystathionine that  
15 limits its ability to go all the way to cysteine and  
16 glutathione.

17 And moreover, this is exclusive to the human  
18 brain. Because on the far right of this illustration,  
19 the levels of cystathionine in human liver, human  
20 kidney, and human muscle are 40-fold lower, indicating  
21 this is a brain-specific phenomenon.

22 So the point I wanted to make with this  
23 slide is that human brain -- and again, this includes  
24 a mixture of cells. We're not sure that this is all  
25 neurons. But if it was neurons, there would be an

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1 even higher, if it was restricted to neurons, an even  
2 higher distinction. But otherwise, the human brain is  
3 different than other, I will say lower species here,  
4 even though it's a self-flattery to humans. The  
5 possibility is that our evolution and our abilities  
6 depend somehow on limiting the transsulphuration  
7 mechanism.

8 The next slide no. 18 illustrates that.  
9 Here I've tried to illustrate the human brain  
10 situation by introducing an arrow and a dotted line  
11 here, to indicate the limited transsulphuration  
12 activity, with the blockage here, would cause the  
13 accumulation of the cystathionine, as we just saw in  
14 that previous slide.

15 And if this is the case, if cystathionine is  
16 not fully allowed to go forward to make the anti-  
17 oxidant glutathione or cysteine, the consequence for  
18 the cell is that it needs to find extra amounts of  
19 cysteine from outside the cell. And it makes human  
20 neuronal cells all the more dependent upon the uptake  
21 of cysteine from outside the cell. Now, that's the  
22 cysteine that comes from the astrocytes that I  
23 introduced earlier. Now we can see in more detail,  
24 here is the glial cells or astrocytes releasing that  
25 glutathione that they have an excess amount of. And

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1 the cysteine derived from that is now taken up by  
2 neuronal cells to a very specific transporter. A  
3 transporter labeled here EAAT-3, which stands for  
4 excitatory amino acid transporter 3, which transports  
5 the neurotransmitter glutamate -- that's why it's  
6 named excitatory amino acid transporter -- or  
7 cysteine. It can take glutamate or cysteine across  
8 the cell membrane.

9 Here we're thinking about its capacity for  
10 cysteine transport. And in neurons, when this is  
11 blocked at the level of transsulphuration, the EAAT-3  
12 uptake of cysteine becomes absolutely critical for  
13 survival and normal function of neurons. And that  
14 extra importance is now, is attached to this  
15 transport, is taken advantage of because we have found  
16 that that transporter is regulated by growth factors,  
17 like brain-derived growth factors and signalling  
18 pathways that control that.

19 In any case, the bottom line here I'm trying  
20 to make is that human neuronal cells have extra  
21 vulnerability to oxidative stress because they don't  
22 have a robust transsulphuration pathway. And the  
23 remaining pathways really have to function normally;  
24 otherwise, a deficit of oxidative status will occur  
25 here.

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1           So we can now move ahead. I'm going to do  
2           the next slide, just as in slide 19, has a list of,  
3           again, a sort of glossary of terms for those  
4           abbreviations for reference purposes here.

5           Q     Right. I asked you to prepare this, even  
6           though we don't need to repeat them all here, just for  
7           reference if people are looking at this later.

8           A     I have to apologize, but it's sort of  
9           necessary to use this terminology here.

10           So I'm moving now ahead to slide 20. I'm  
11           now going to review the results that we found for the  
12           effects of thimerosal at different dosage levels in  
13           most cases on the various processes, which I hope this  
14           background has provided identification of.

15           And this work, looking at the effects of  
16           thimerosal, is an offshoot of our earlier publication,  
17           Waly, et al, in molecular psychiatry, where we found  
18           and published there that the activity of the enzyme is  
19           thioneine synthase. And the activity of this dopamine  
20           methylation system that we were investigating was  
21           inhibited by thimerosal, by mercury, and also by lead  
22           and aluminum. And we were curious, having made that  
23           observation of the enzyme, as to what was causing  
24           that.

25           So we undertook a series of studies to probe

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1 deeper into that observation, and find out at what  
2 point was the thimerosal doing what it does.

3 So in any case --

4 Q You've written inorganic mercury underneath  
5 thimerosal there.

6 A That's right. Because while the general  
7 terminology here is thimerosal role, we recognize that  
8 the culprit, if you will, or the active species here  
9 is likely to be inorganic mercury released from  
10 thimerosal.

11 So slide 21 brings us to some result here.  
12 What I'm showing you is that transporter, EAAT-3. We  
13 measured its activity by using radioactive cysteine  
14 and cultured human neuronal cells, and measured the  
15 uptake of cysteine. And even though I have not shown  
16 them here, we have otherwise confirmed through  
17 primatologic inhibitors that this transport is EAAT-3-  
18 mediated.

19 And here we see the inhibitory effects of  
20 thimerosal as a function of its concentration.

21 Q Now, the left-hand column there, with the  
22 numbers from 50 down to zero, what does that  
23 represent?

24 A Okay. On this graph, these are amounts  
25 expressed in chemical terms as nanomolars per

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1 milligram protein of cysteine uptake. So this is the  
2 amount of cysteine being taken up during the three-  
3 minute interval in these cells, and then we've pre-  
4 incubated the cells in various concentrations of  
5 thimerosal for 60 minutes, one hour. And after those  
6 pre-incubations, we then went ahead to measure the  
7 cysteine uptake.

8 And as you can see, exquisitely low  
9 concentrations here caused a substantial two-thirds  
10 reduction in the uptake of cysteine. So this process  
11 of cysteine uptake is exquisitely sensitive to  
12 concentrations of thimerosal at or below the  
13 concentrations which occur in plasma, for example  
14 after vaccination, and concentrations what have been  
15 estimated to occur in human brain.

16 For example, earlier this morning we heard  
17 testimony suggesting that the concentration in the  
18 brain, based on Burbacher's study, might be on the  
19 order of 30 nanomolars. Thirty nanomolars would be  
20 somewhere here between 10 to minus-8 and 10 to minus-  
21 7. And these concentrations have at this point more  
22 or less completed the inhibition, again amounting to  
23 about two thirds of the uptake of cysteine here. So  
24 this is a very substantial, very potent effect.

25 The left side of this figure compares the

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1 effect of 100 nanomolar thimerosal, 10 to minus-7,  
2 which is the far-right mark, with equal concentrations  
3 of inorganic mercury, which is close to, but not  
4 significantly different from, the thimerosal. They're  
5 almost the same, each one slightly less than aluminum  
6 at that concentration, arsenic at that concentration,  
7 and lead at that same 100-nanomolar concentration.  
8 This would be the normal uptake here.

9 So what we can see from this comparison is  
10 that this, while it's not a unique activity of  
11 inorganic mercury or of thimerosal, even though they  
12 are the most effective at this concentration, it's an  
13 effect shared by other heavy metals which also have an  
14 affinity for thiols, and can do the same thing.

15 So if we were concerned about which of these  
16 materials might be important here, we would have to  
17 say that certainly the mercury and the thimerosal  
18 would qualify. But the other materials, should they  
19 be at these levels, would produce at least partially  
20 the same effect.

21 Q Let me ask you about the difference between  
22 the monkey brain and the human brain that we saw at an  
23 earlier slide.

24 If the cysteine uptake is being interfered  
25 with by thimerosal or by inorganic mercury, would you

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1 expect, given that difference between human and monkey  
2 brain, the effect would be greater in humans?

3 A That's exactly correct. When the  
4 transsulphuration pathway is restricted, then this  
5 pathway becomes all the more important. So humans,  
6 based upon that comparison, would be more dependent on  
7 this pathway, and therefore more vulnerable to  
8 inhibition.

9 Q Even than the monkeys.

10 A Than monkeys, for example, or the other  
11 lower species even further down the chain there.

12 Q Okay.

13 A Slide no. 22, the next slide is again  
14 provided for convenience, as a comparison of the  
15 scientific nomenclature of concentrations which I use,  
16 such as molar concentrations, with other more  
17 toxicologic common expression, parts per billion here.  
18 And so we can see the conversion levels that can be  
19 applied here.

20 Again, the concentrations that we're using  
21 in finding effects of thimerosal are very low, either  
22 in the parts per billion or in the molar terminology.

23 Down at the bottom I've also included here  
24 the EPA's referenced dose, which is a dose per day  
25 that is considered by the EPA as safe, or without

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1 effect. This dose of course is being given outside of  
2 the brain, to the body as a whole, and that  
3 corresponds to .1 micrograms per day per kilogram.

4 And the EPA also provides what it considers  
5 to be a safe reference level in the blood. That is,  
6 the blood levels of inorganic mercury that the EPA  
7 considers safe is this 5.8 micrograms per liter. Now,  
8 that's in the blood compartment. What we're talking  
9 about are neurons that are behind the barriers in the  
10 brain. So that concentration in the blood that's  
11 considered safe would be 30 nanomolar, whereas I  
12 suppose a lesser concentration would occur in the  
13 brain because of this restrictive  
14 compartmentalization. But nonetheless, our results  
15 show that concentrations of thimerosal, 30 nanomolar  
16 or less, if they occur in the brain, are going to  
17 inhibit this process.

18 Q And what did you say the level in Burbacher,  
19 in the infant monkeys, what was the level then?

20 A Well, the estimate, depending on the  
21 calculations used, gave I believe around ranges  
22 between approximately 15 to 30. It depends on the  
23 weights, the ages, so two months versus six months and  
24 so forth, of infants. They were estimating -- excuse  
25 me, that was human estimates in human equivalents.

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1 But it was in the range of 15 to 30 nanomolar  
2 concentrations, which would correspond to this, but in  
3 the brain, not in the plasma.

4 Q But we also saw from the Burbacher paper  
5 there is a figure that shows the blood level of  
6 mercury going up, and then clearing fairly rapidly  
7 after each injection. And while the mercury is  
8 clearing out of the blood over a few days, it is still  
9 building up in the form of inorganic mercury in the  
10 brain.

11 A That's correct.

12 Q So is that relevant to the levels we're  
13 talking about here?

14 A Very much. We considered the organelle  
15 mercurials; that is, the ethyl mercury. It's really a  
16 passport to the brain, the ethyl group. That means  
17 that even this level, which is the EPA's inorganic  
18 mercury in the plasma, if we attached an ethyl group  
19 to that and then let it have a passport to the brain,  
20 and equilibrate across the blood-brain barrier, then  
21 this concentration would reach the brain.

22 But in fact, the inorganic doesn't. It's  
23 only the organic form that are able to penetrate  
24 across the blood-brain barrier and achieve those brain  
25 concentrations. And now when they are hydrolyzed to

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1 the inorganic form and are trapped behind the blood-  
2 brain barrier, then they gradually accumulate in  
3 concentration with, for example, every vaccination or  
4 other source of exposure, for years at a time.

5 So moving ahead, if I might, to slide 23.  
6 So having shown the inhibition of the uptake of  
7 cysteine, we would predict, if the cysteine uptake was  
8 blocked by thimerosal, and if cysteine was limiting  
9 for the synthesis of glutathione, then in the same  
10 cultured-cell model, which has limitations -- it's a  
11 cultured-cell system that we can use truthfully for  
12 these studies, but it's not a brain as such -- we  
13 would predict that the blockade here should lead to a  
14 reduction in the glutathione levels. And indeed, the  
15 slide 24, the next slide, shows us the effects of  
16 these doses of thimerosal, again, a one-hour  
17 incubation at these concentrations, and this time the  
18 glutathione levels in the cell.

19 And we can see a graded reduction in the  
20 intracellular concentrations of glutathione, which  
21 reflect the blockage of the cysteine coming in, so you  
22 don't have enough to make glutathione. So naturally  
23 the cell has less of the antioxidant glutathione, and  
24 is therefore at risk intracellularly of the effects of  
25 oxidated stress. So these two things are very much in

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1 correlation with each other.

2 Q And now again, explain the bottom numbers,  
3 those negative numbers along the bottom.

4 A This is the scientific terminology for  
5 concentrations of thimerosal here, in terms of molar  
6 concentration. The one nanomolar, or ten to the minus  
7 ninth, would be right here. I indicated before this  
8 30-nanomolar level, that would be right here. So we  
9 can see that the concentrations that are estimated by  
10 some means to be present in the brain after a regimen  
11 of thimerosal exposure of monkeys, for example, in the  
12 Burbacher study, would produce significant inhibition,  
13 or significant reductions in this case of the  
14 glutathione that are attributable to the blockade of  
15 the transport that we saw in the previous data.

16 Q Now, when you said "right there," we --

17 SPECIAL MASTER VOWELL: You're using your  
18 pointer, and unfortunately we're not going to have  
19 your pointer when we go back and review your testimony  
20 next to your slides.

21 THE WITNESS: I'll try to --

22 SPECIAL MASTER VOWELL: So will you  
23 explicate what you just did, in terms of --

24 THE WITNESS: Excuse me, let me do that.

25 //

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1 BY MR. WILLIAMS:

2 Q I'll ask the same question. You were  
3 pointing up and down between the numbers negative-7  
4 and negative-8 there. And when you said "right here,"  
5 would you explain that again?

6 A Excuse me for not recognizing the problem.  
7 Yes, I was indicating that if the data of Burbacher  
8 suggests that there is approximately a 30-nanomolar  
9 concentration of inorganic mercury in the brains after  
10 a treatment with thimerosal, then that 30 nanomolar  
11 would lie somewhere between 10 to the minus-8 molar,  
12 which is 10 nanomolar, and 10 to the minus-7, which is  
13 100. So the 30 would be approximately halfway between  
14 10 to minus-8 and 10 to minus-7 molar concentration,  
15 which on this figure provides for approximately 75  
16 percent of the full effect of thimerosal, a reduction  
17 amounting to two thirds of the normal level of  
18 glutathione, or reduction by two thirds.

19 Q So let me just try to summarize that. The  
20 level of organic mercury in the brain of those infant  
21 monkeys is equivalent to your 30 nanomolar, is that  
22 right?

23 A That's correct. Somewhere between minus-8  
24 and minus-7 on this graph.

25 Q And on this graph, at that level of

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1 thimerosal, how much of a reduction in glutathione did  
2 you have?

3 A Well, you can see that the Y intercepted at  
4 the left-hand side is about 750. And just looking at  
5 it myself here, I see that the area that would  
6 correspond to 30 nanomolar would be about 300, between  
7 250 and 300. So a reduction approaching two-thirds  
8 reduction in the level of intracellular glutathione  
9 here. Substantial, an obviously significant  
10 reduction.

11 Q Your slide 25.

12 A Going further in the process here, if there  
13 is a reduction in the glutathione levels, as we just  
14 observed, then one might anticipate that thimerosal  
15 would also cause a reduction in the synthesis of the  
16 methyl B-12, or methylcobalamin, because its synthesis  
17 is dependent upon glutathione level. And the next  
18 illustration, slide 26, shows a biograph in which a  
19 single concentration, a 100-nanomolar thimerosal, is  
20 used. And again, after a one-hour pretreatment of  
21 these cells, we see that the level of methyl B-12 is  
22 reduced to almost zero. This is a greater-than-90-  
23 percent reduction in methyl B-12.

24 And if we stop to reflect, we can see how  
25 the strategy of the neuronal cells pays off here.

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1 That is to say, a reduction in glutathiones, such as  
2 we just confirmed on the previous slide, here is  
3 turning off synthesis of the needed co-factor for  
4 methionine synthase. It's turning it off very  
5 efficiently. So that this assures that without methyl  
6 B-12 or methylcobalamin, that methionine synthase will  
7 stay off until the glutathione synthesis returns  
8 toward a normal level.

9 In fact, if this is not resolved, it will  
10 stay off indefinitely. That is to say, one can expect  
11 that methionine synthase and the activities it  
12 supports, including the D-4 dopamine receptor  
13 methylation pathway, will remain in inhibited until  
14 normal oxidative status is regained. And if it's  
15 never regained, it's never allowed to reactivate.

16 So we can expect a persistent loss of  
17 whatever role it is that that D-4 receptor provides.  
18 And evidence is that it's necessary for neural  
19 synchronization during attention and awareness.

20 Q And because the inorganic mercury, according  
21 to the monkey studies, is trapped in the brain, is  
22 that going to create this persistent type of effect?

23 A It would, for as long as the trapped  
24 inorganic mercury remains in a position to block the  
25 uptake of cysteine, and otherwise maintain oxidated

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1 stress in these neurons. Then this enzyme will remain  
2 inhibited, at least the co-factor synthesis in this  
3 slide no. 26 will remain inhibited, and the function  
4 it subserves will remain dysfunctional.

5 Moving on, the next slide allows us to say  
6 if you don't have the methyl B-12 availability, then  
7 one would predict that the enzyme, methionine  
8 synthase, as we've already alluded to, should be  
9 inhibited by concentrations that are relevant here for  
10 exposure to thimerosal.

11 And in the data in the next slide, which now  
12 brings us to slide no. 28, shows our measurements of  
13 methionine synthase activity, in the presence of  
14 either methyl B-12 measured with methyl B-12 as blue  
15 lines in this diagram, or hydroxy B-12 in red line.  
16 And the distinction between using those two co-factors  
17 is that the methyl B-12 is already methyl B-12, and  
18 doesn't require glutathione, whereas the hydroxy B-12  
19 requires glutathione to be made into methyl B-12.

20 So we compared these two co-factor  
21 situations, and we compared them in the lower left-  
22 hand corner.

23 MR. WILLIAMS: Can you blow that up, Scott?  
24 The lower left-hand box?

25 THE WITNESS: The lower left-hand box in

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1 this figure has thimerosal-dose-response relationship.

2 BY MR. WILLIAMS:

3 Q I ask these questions, and I don't know if  
4 I'm always going to get the right answer.

5 A Even though it says "aluminum" at the top,  
6 this is the thimerosal dose response curve here. And  
7 looking at this curve again, we can see potent effects  
8 of thimerosal if we look first at the hydroxy B12  
9 assayed condition, we see that there's essentially a  
10 complete loss of activity of the enzyme with hydroxy  
11 B12 at concentrations as low as 10 to the minus-11.

12 Now, in our previous published study, Waly,  
13 et al, in 2004, we used hydroxy B12 in the assays in  
14 that paper. And as we reported in that paper, the  
15 thimerosal completely eliminates the methionine  
16 synthase activity. And so this is actually a  
17 replication, if you will, of that finding.

18 And we can see that when methyl B12 in blue  
19 is present, however, activity is still maintained at a  
20 higher level, even though it's going down as a  
21 function of thimerosal concentration. As long as the  
22 methyl B12 is provided, then you still have a  
23 significant amount of enzyme activity.

24 So from this comparison we can see that what  
25 thimerosal is doing is interfering primarily with the

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1 conversion of the hydroxy B12 to the methyl B12 that's  
2 needed to sustain enzyme activity.

3 Now, the lower right-hand portion of this  
4 figure is again a measurement of the glutathione  
5 reduction that the thimerosal has caused, the far  
6 right-hand column is thimerosal. And again, you can  
7 see the reduction of approximately two thirds to three  
8 quarters of the glutathione concentration.

9 Now, the remaining figures, starting with  
10 the upper left, are different metal ions rather than  
11 the thimerosal. Again, at different concentrations  
12 for one hour, before measuring the enzyme activity  
13 here. The upper left-hand corner is lead, which is  
14 certainly associated with neurodevelopmental  
15 disorders, and is also recognized as an important  
16 environmental risk factor for ADHD.

17 To the right of the upper panel we have  
18 arsenic, an encountered environmental toxin. And the  
19 second from the top, in the middle panel on the left,  
20 is aluminum, which of course we recognize as a  
21 continuing adjuvant in vaccines, and shows important  
22 effects of aluminum, which aren't as potent, but are  
23 still very potent. Not as potent as thimerosal, but  
24 still very potent effect, sufficiently potent to  
25 inhibit here.

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1           And then finally in the middle panel on the  
2 right is inorganic mercury. And the pattern for  
3 inorganic mercury most closely resembles that of  
4 thimerosal; it's only slightly less potent in the  
5 inhibition of the hydroxy B12 activity.

6           So the methyl, excuse me, the inorganic  
7 mercury and the thimerosal create a similar pattern of  
8 potent inhibitions here.

9           Q     Before you go on --

10          A     Please.

11          Q     -- let me ask a question about this  
12 particular slide. This is a description, slide 28, of  
13 the experiments done in your lab that were reported in  
14 the Waly 2004 article?

15          A     No. These are follow-up not-as-yet  
16 published results. The Waly article that you're  
17 referencing, we showed a similar result to the lower  
18 left-hand portion, but we used only a single  
19 concentration of thimerosal. And we showed a total  
20 loss of activity. The concentration we used was 10 to  
21 the minus-8, to my best recollection. And here in  
22 this more detailed follow-up study we used different  
23 concentrations, and we also used, by comparison, the  
24 methyl B12 as well as the hydroxy B12.

25               SPECIAL MASTER VOWELL: This is unpublished

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1 data from our lab.

2 BY MR. WILLIAMS:

3 Q And let's go back, then, just to clarify in  
4 that regard, beginning with slide 21 through 28.

5 A That's right. Each of --

6 Q All of these are from your latest  
7 unpublished experimentation.

8 A That's correct. The next one that I'll show  
9 next is from Waly, et al, but otherwise the preceding  
10 ones on the EAAT3, on the glutathione level, and the  
11 bar graph with the methyl B12, we have not yet  
12 submitted that for publication, because in fact the  
13 bar graph that I just showed, where I'm awaiting a  
14 particular graduate student's dose-dependent results  
15 on the methyl B12 concentration reduction. We wanted  
16 to show the dose dependence of that effect. And at  
17 this moment in time, that's data that's keeping us  
18 from submitting this for publication. So that's why I  
19 have only a bar graph instead of a dose-dependent  
20 graph.

21 SPECIAL MASTER VOWELL: Dr. Deth, I have  
22 another question while we're on slide 28. And that  
23 has to do with the levels that are measured in the  
24 absence of whatever heavy metal you're testing.

25 There appears to be a significant

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1 variability. If we look at slide E, the upper limit  
2 is 100. If we look at slide C, it's 140. Why is  
3 that? I mean, it would seem to me if we're comparing  
4 effects, we would want to use the same scale.

5 THE WITNESS: I certainly could have used,  
6 maybe even should have used, the same scale. But I  
7 will say that these are not great variations, in my  
8 opinion. They range from let's say a Basal level of  
9 70 to the highest and the lowest, and the highest that  
10 I see is, it looks like 128 to me, in panel C. It's  
11 less than a twofold variation.

12 Even though these are cultured cells, these  
13 experiments aren't done on the same day. They're not  
14 exactly twin studies in that regard. They may be done  
15 a week or two or three later, even if they're done in  
16 succession. And that amount of variation to me is not  
17 surprising, as experiment-to-experiment variability in  
18 the baseline activity.

19 I'd like them to be better, but the truth is  
20 the kind of variation that one encounters in using the  
21 subject cells.

22 SPECIAL MASTER VOWELL: Thank you. Okay.

23 THE WITNESS: So these are indications that  
24 confirm the inhibition of methionine synthase activity  
25 is sensitive to thimerosal. If methionine synthase is

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1 sensitive to thimerosal, then the methylation process  
2 is that its supports should likewise be sensitive.  
3 And the next illustration just showed that  
4 schematically, slide 29.

5 So now we'll look at methylation events, not  
6 of the methionine synthase, but the actual methylation  
7 here. And then slide 30 has some of this. Now, this  
8 would represent published data from Waly, slide 30.  
9 Scott, thank you.

10 So in this data we examine the methylation  
11 of phospholipids again in the same cell system used in  
12 the preceding experiments. We see on the left the  
13 baseline activity. The lower line represents the  
14 activity of phospholipid methylation with nothing  
15 added to the cells. You see a level of approximately  
16 four.

17 When dopamine is added, we see one of those  
18 upper lines. In fact, the upper line that has the  
19 boxes as the symbols, and there's approximately 12 --  
20 excuse me, approximately 13 -- indicating that  
21 dopamine has stimulated phospholipid methylation, as I  
22 described earlier.

23 And now, as thimerosal incubation are taking  
24 place, one hour at these different concentrations, we  
25 see a graded reduction in the baseline level. We can

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1 see that bottom line going down. And the dopamine-  
2 stimulated level likewise decreases, again potently  
3 affected by thimerosal here, reaching a maximum  
4 inhibition at about 10 to the minus-7 concentration.

5 Now, in the same figure is included the  
6 other stimulating agent, IGF1, or insulin-like growth  
7 factor 1. This is an example of a growth factor which  
8 acts similar to other brain growth factors, neuronal  
9 growth factor, brain-derived growth factor, and  
10 stimulates the signaling pathway that activates the  
11 cysteine uptake that I mentioned earlier.

12 And indeed, the IGF1 stimulation of  
13 methylation here is potently inhibited by thimerosal  
14 at the same concentrations that inhibit the dopamine-  
15 stimulated methylation.

16 The final line which I included in this  
17 published figure here was one in which we added  
18 divalent copper ions along with the IGF1. And we did  
19 that because of a paper showing that the signaling  
20 activity of this IGF1 was, in fact, copper-dependent.  
21 And we can see that when copper was added here, it  
22 offset some of the effects of the thimerosal. The  
23 thimerosal is not as effective when this extra  
24 complement of copper was added in the experiment. And  
25 I can just mention here that what the copper is doing

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1 is affecting thiol status in such a way as to counter  
2 the effects of the thimerosal.

3 So in any case, this slide verifies the  
4 potent effects of thimerosal on phospholipid  
5 methylation, including dopamine-stimulated.

6 The next slide no. 31 shows a similar  
7 phospholipid methylation experiment carried out with  
8 lymphoblasts. Instead of using human neuronal cells,  
9 here we're using white blood cells in culture or  
10 lymphoblasts. And similarly, we're adding  
11 concentrations of thimerosal here.

12 And thimerosal again inhibits phospholipid  
13 methylation in these lymphoblasts. But the potency is  
14 somewhat less, perhaps tenfold or more less, than it  
15 is in the neuronal cells. The purpose of concluding  
16 this is to indicate that the higher sensitivity of  
17 thimerosal is associated with human neuronal cells,  
18 compared to even other human cells, in this case human  
19 lymphoblasts in cell cultures.

20 So the upshot of that would be to alert  
21 ourselves to the most vulnerable tissues, most  
22 vulnerable cell types would be the neurons in whom, as  
23 I indicated, the transsulphuration is less efficient.

24 So we recently, even more recently than that  
25 previous data, have had the extraordinary opportunity

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1 to measure the levels of methionine synthase at the  
2 level of its messenger RNA in autopsy-based post-  
3 mortem samples of autistic subjects in age- and sex-  
4 matched control subjects.

5 The next slide just illustrates what I'm  
6 referring to here. Slide 32 shows us that the final  
7 protein, for example at the bottom, methionine  
8 synthase, its availability depends upon its gene in  
9 the DNA, which is transcribed to its MRNA, or  
10 messenger RNA, which then gives rise to the final  
11 protein enzymes.

12 And indeed, regulation of methionine  
13 synthase activity we can understand from this  
14 relationship, regulation of methionine synthase can be  
15 exerted at the protein level. For instance, the  
16 cofactor can be oxidized of B12, it can be exerted at  
17 the level of the messenger RNA, which can be, for  
18 example, determine how much messenger RNA is  
19 translated into protein. Or it can be at the gene  
20 level itself, how much original product from the gene  
21 is made into messenger RNA that is transcription.

22 So we can see that nature can regulate the  
23 activity of methionine synthase in very short  
24 microseconds or millisecond waves, that's a level of  
25 the co-factor, or for days or hours at a time,

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1 depending upon which level of control is chosen.

2 We had the opportunity to use messenger RNA  
3 samples that were provided to us by the Autism Tissue  
4 Program, and maintained in part by Johns Hopkins  
5 Institute. And in fact, the samples that we were able  
6 to obtain and to analyze the messenger RNA from were  
7 the same samples in most types used by Vargas, et al,  
8 in their study, in which they concluded that there was  
9 neuroinflammation present in these post-mortem brain  
10 samples.

11 So essentially what we were able to do is,  
12 using those same samples, and the question is what was  
13 the level of the methionine synthase messenger RNA in  
14 those same brain samples.

15 So the next slide --

16 BY MR. WILLIAMS:

17 Q Let me stop you just for a second.

18 A Excuse me.

19 Q To the extent that the DNA is affected here  
20 by the toxin, we're not talking about genetic damage,  
21 are we? We're talking just about shutting down the  
22 gene operation.

23 A I haven't shown you the results yet.

24 Q Okay.

25 A When we see those results, we could

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1 interpret them in light of the fact that regulation,  
2 rather than mutation, may be taking place. Okay?

3 Q Okay.

4 A I think we're ready to look. Actually, the  
5 next slide just illustrates how we did this  
6 experiment.

7 Q And its slide number?

8 A Excuse me now, it's slide no. 33. And we  
9 carried out a very basic, a very commonly employed  
10 laboratory procedure called PCR, or polymerase chain  
11 reaction, which is used to amplify the available  
12 messenger RNA. And by using comparative samples, one  
13 can estimate the relative amount or abundance of the  
14 messenger RNA for methionine synthase.

15 Usually the PCR reaction is carried out with  
16 one so-called primer set for the entire gene or  
17 messenger RNA. But we recognize that the methionine  
18 synthase has five of those different domains or  
19 regions to it. We devised a method, or very simply  
20 used a method where we had primer sets directed  
21 against each of those domains of the proteins that I  
22 introduced earlier: the pink one, the green one, the  
23 yellow one, the red one, and the blue one.

24 And so we did what we can call primer,  
25 excuse me, domain-specific PCR. And in doing so, we

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1 found, although I won't include those results  
2 explicitly here, we found that that cap domain, the  
3 yellow one that is in the middle, is actually excised  
4 at the level of messenger RNA as a function of age.  
5 And in elderly individuals, it's missing.

6 But we then, using this strategy, analyzed,  
7 as I said, the autism samples versus controls. And  
8 now slide 34 has the first of that dataset. And shown  
9 here on the left, the open bars represent the  
10 abundance of messenger RNA for methionine synthase  
11 using primer sets directed against the cap domain. Or  
12 on the right side of the open and closed bars, the  
13 primer sets directed against the B12 binding cobalamin  
14 domain.

15 So these are two different types of  
16 messenger RNA that we're probing for here. And in  
17 either case, in both cases, we found a significantly  
18 lower amount of the messenger RNA or methionine  
19 synthase in the autism brain sample.

20 Again, if we think of these as samples in  
21 which neuroinflammation could be or was detected, we  
22 can then suggest the possibility that there is a  
23 relationship between lower levels of the messenger RNA  
24 of methionine synthase, and the presence of  
25 inflammation.

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1           Because indeed, if you have less messenger  
2 RNA level, then in fact you would have less of the  
3 enzyme, and more homocysteine would be diverted to  
4 make more glutathione, an appropriate response at that  
5 level of regulation to inflammation or oxidative  
6 stress.

7           The next slide no. is 34; 35 allows me just  
8 to capture the main thoughts from that result. And  
9 that result indicates that the brain levels of  
10 methionine synthase, mRNA, are indeed significantly  
11 lower in autistic subjects, and at that lower level of  
12 mRNA will lead to diversion of homocysteine to more  
13 transsulphuration and glutathione synthesis. And  
14 again, the Vargas study indicates the presence of  
15 neuroinflammation in these very same brain samples,  
16 suggesting that these two outcomes are related to each  
17 other. And we can propose as an end statement that  
18 reduced transcription of methionine synthase may be  
19 viewed as an adaptive response to the presence of  
20 oxidative stress and neuroinflammation.

21           Again, this alerts us to mechanisms that  
22 nature can employ at multiple levels to control the  
23 flow of homocysteine towards transsulphuration or not.

24           Now, in this same dataset, the next slide  
25 no. 36, allowed us to do a paired comparison, because

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1 we had paired samples, age-matched samples and sex-  
2 matched samples. And we were struck by the pattern  
3 that we observed here.

4 On the right-hand side are the  
5 representative members of the pair from the  
6 neurotypical controls, and on the left, the autistic  
7 members of the pair. And we color-coded the samples  
8 here into age groups. That is to say, individuals  
9 that were between the ages of one to five are sort of  
10 a red color; correspondingly, six to 10, orange; 11 to  
11 15, yellow; 16 to 20, green; 21 to 25, blue; and then  
12 finally 26 to 30, the samples that were in purple  
13 here.

14 And in the controls in particular, what you  
15 can see is an age-dependent pattern. You can see that  
16 the youngest individuals in this control group had the  
17 highest levels, and that progressively, as age  
18 increased, there was lower levels across the span of  
19 the ages that we had available to us.

20 And the number of samples is limited here,  
21 thankfully, because these are post-mortem samples.  
22 And the ones that we had available to us in this  
23 limited number however do show this age-dependent  
24 pattern here.

25 On the other hand, the autistic samples,

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1 even at a young age, had a much lower level of  
2 methionine synthase activity. And in fact, the  
3 decrease associated with autism was dramatically  
4 lowered as a function of age.

5 So the implication here is that if you have  
6 oxidative stress and a reduction in methionine  
7 synthase as a compensatory or adaptive response to  
8 that, the impact is greatest when you're young.

9 So I think the slide 37 provides again a  
10 narrative summary. So in the limited samples that we  
11 had, again, the pattern of age dependence to the  
12 reductions in methionine synthase, the messenger RNA,  
13 was apparent. The age dependence was obvious in the  
14 controls, but not obvious in the autism samples. The  
15 MRNA levels in autism don't show an age-dependent  
16 pattern, we'll call it the normal age-dependent  
17 pattern.

18 And the conclusions from that would be that  
19 the inhibition of methionine synthase in this case by  
20 the neuroinflammation and oxidative stress, confirmed  
21 in the same samples by other investigators, is of  
22 greater significance at younger ages.

23 Now, the occurrence of autism is estimated  
24 to be one in 150 individuals, by CDC. And so this  
25 tells us that exposure to thimerosal or other

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1 uniformly exposing agents in our society only affects  
2 a subpopulation of this society.

3 And this has led to the suggestion that the  
4 subpopulation with autism has certain genetic  
5 features. And the genetic features have in part been  
6 investigated. And the next slide no. 38 shows an  
7 illustration of the findings of Dr. Jill James,  
8 published in 2006.

9 And in her study, she particularly focused  
10 on normal polymorphisms; that is, normal variants of  
11 genes that are involved in the pathways that I  
12 reviewed here. Pathways involving methylation and  
13 transsulphuration.

14 The genes that she particularly investigated  
15 in her population were highlighted in pink in this  
16 illustration. For example, on the left, the enzyme  
17 MTHFR, methylene tetrahydrofolate reductase, a gene  
18 that has several, two distinct polymorphisms. And  
19 that enzyme normally makes the methylfolate that the  
20 enzyme methionine synthase depends upon.

21 Next to it we have the RFC, or the reduced  
22 folate carrier gene, RFC-1. As the name implies, this  
23 gene product is the proteins, the carrier that brings  
24 folate into cells. Again, folate is required for  
25 methionine synthase activity.

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1                   Next in the middle we have transcobalamin  
2                   II. And transcobalamin II is the enzyme, the  
3                   transporter that brings B12 into cells. And in doing  
4                   so, it limits the activity of methionine synthase.

5                   On the right-hand side we have catacol  
6                   methyltransferase, COMT, the enzyme that determines  
7                   the duration of dopamine action.

8                   And finally at the bottom, glutathione as  
9                   transferase, particularly the M-1 form. And so Dr.  
10                  James examined these proteins and their genes, because  
11                  the polymorphism that they normally show might or  
12                  might not be more prevalent in a particularly at-risk  
13                  population.

14                  The results that she found, that I'll  
15                  present here because of how they relate to our work,  
16                  in the next slide, which is designated as slide 39,  
17                  the results that she found in this table is an  
18                  association between the risk associated alleles; that  
19                  is, the lower-activity alleles. And she highlighted  
20                  them in bold print in this particular diagram.

21                  And as we can see by the occurrence of bold  
22                  print, these list associated alleles in these  
23                  particular genes are associated with a higher  
24                  frequency in the autism population. That is to say  
25                  that they are at risk of problems with methylation,

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1 problems with methionine synthase, and problems with  
2 dopamine, if they have these alleles.

3 I actually didn't mention the last one on  
4 this list at the bottom. It's methionine synthase  
5 reductase. It's responsible for the activation of the  
6 enzyme. But she also found a significant association  
7 with methionine synthase reductase especially when  
8 compared in combination together. Each of these risk  
9 alleles brings an individual risk. But in the common  
10 pathway, such as we've described, they can be additive  
11 or even synergistic.

12 And the next slide now, no. 40, illustrates  
13 combinations of these alleles to further increase the  
14 odds or ratio of autism. That is to say, when you  
15 have three, four, or more of these common alleles,  
16 then your risk is accordingly higher than if you have  
17 only one or two.

18 So the genetic data especially from Dr.  
19 James's study, which focus on the methylation and  
20 redox cycles, cites a process of identifying the at-  
21 risk population from their genetic features.

22 Q And they are at risk because of an  
23 interference with the redox?

24 A The presence of these polymorphisms  
25 indicates that the enzymes, let's say in the case of

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1 MTHFR for example, that they function at a lower rate  
2 than if that polymorphism was not present.

3 Alone, in the normal circumstances, in a  
4 circumstance or an environment where there was no  
5 extraordinary challenge by stressful factors on the  
6 system, those polymorphisms are not a commitment to  
7 the outcome of autism or any other disorder. In fact,  
8 their occurrence at high frequency in the population  
9 suggests that they may have a favorable role to play  
10 under most environmental conditions.

11 However, in the presence of adverse  
12 environmental conditions, such as perhaps the  
13 introduction of heavy metal toxicity, then these  
14 otherwise latent polymorphisms, or risk factors, can  
15 be activated to in fact be real consequential risk  
16 factors. So it's really reflecting the fact that our  
17 evolution in one environment may not be ideal for a  
18 more hostile alternative environment.

19 So the final slides that I've prepared here,  
20 and it's part of the review article that I published  
21 in The Journal of Neurotoxicology in January of this  
22 year, attempt to summarize the relationship and the  
23 interaction between genetic risk factors identified  
24 here in red, and environmental exposure, a broad term.  
25 Environmental exposure includes things other than in

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1 genetic nature that are, that are the organisms that  
2 we are exposed to during our lives. In this case, in  
3 this proceeding, it's meant to include thimerosal and  
4 the inorganic mercury that it releases in the brain.

5 And such exposures, for reasons that I  
6 outlined, impair sulphur metabolism, especially when  
7 their focused target is sulphur compounds. And  
8 individuals that possess these risk factors in  
9 combination are at high risk.

10 The risk arises because of the importance of  
11 sulphur metabolism for oxidative stress, and in  
12 responding to oxidative stress. I've illustrated that  
13 the enzyme methionine synthase is a particularly  
14 important factor, and that polymorphism affecting  
15 thiamine synthase, directly or indirectly, introduce a  
16 high level of risk.

17 The consequence of inhibition of methionine  
18 synthase are manifested throughout methylation  
19 reactions. There is 100 to 150, 200 such reactions.  
20 They will all be affected. Some of the most important  
21 include DNA methylation, as I specified earlier, whose  
22 consequence will be altered gene expression during  
23 development.

24 So the idea of this mechanism accounting for  
25 developmental disorder is rather direct.

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1 Q Now, I have one other question I wanted to  
2 ask you. It was a question that was put to Dr.  
3 Aposhian this morning by the defense. And that is,  
4 you studied oxidative stress and have been working on  
5 oxidative stress.

6 If chelation is shown or found to be  
7 effective in helping autistic children recover some of  
8 their function, but it doesn't pull inorganic mercury  
9 out of the brain, is there some explanation related to  
10 your work that could explain that phenomena?

11 A The oxidative stress that's actually the  
12 last slide illustrated, and otherwise we've talked  
13 about, in the case of autistic individuals, it is a  
14 whole-body oxidative stress. The fact that you can  
15 draw a plasma sample and find a 40-percent reduction  
16 in circulating blood of glutathiones indicates very  
17 strongly that it's a systemic, not a problem  
18 restricted to the brain.

19 And as such, the mercury effects that I  
20 mentioned and spoke about as a general feature of  
21 sulphur metabolism are affecting peripheral tissues,  
22 like liver, important metabolic organ that it is.

23 And so the chelation of peripheral mercury  
24 can have useful effects by restoring normal metabolism  
25 and normal redox state peripherally, helping

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1 peripheral cells to work better. And as a result, the  
2 beneficial peripheral metabolism can affect brain. A  
3 most explicit example would be, for example, would be  
4 reducing the amount of inflammatory cytokines in the  
5 blood that otherwise could contribute to  
6 neuroinflammation, or the availability of the cysteine  
7 that's ultimately the source of sulphur compounds for  
8 the brain, and for neuronal inflammation.

9 So there are benefits from correcting heavy  
10 metal exposure and toxicity peripherally that can have  
11 benefits for neurological function, even though the  
12 chelating agents don't penetrate the brain and  
13 directly remove the mercury from the brain, in my  
14 opinion.

15 Q So do you have an opinion, then, as to  
16 whether thimerosal exposure and inorganic deposition  
17 in the brain at the levels we've seen in the monkey  
18 studies, can those levels of thimerosal and inorganic  
19 mercury cause interference to the brain that can lead  
20 to autism symptoms?

21 A Based upon both my understanding and reading  
22 of the literature, the results of others that I've  
23 incorporated into my own presentation, as well as the  
24 direct result that we have obtained when we looked --  
25 and the important thing is that we have looked -- and

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1 when we looked, we found basically the return effects  
2 of thimerosal, which suggests that it has the  
3 molecular capability to cause autism, and to account  
4 for the major symptoms of autism, which include  
5 impaired attention, awareness, sociability, and  
6 neuronal synchronization in the gamma range.

7 All these things together lead me to the  
8 unavoidable conclusion that it's involved as a  
9 causative factor in autism.

10 MR. WILLIAMS: Thank you very much. That's  
11 all I have.

12 SPECIAL MASTER VOWELL: It would appear to  
13 be an appropriate time to take our mid-afternoon  
14 break. So let's plan on 15 minutes, or do you need a  
15 little longer?

16 MR. MATANOSKI: May I have a little bit  
17 longer than that?

18 SPECIAL MASTER VOWELL: How much time would  
19 you like?

20 MR. MATANOSKI: May I have until five after?

21 SPECIAL MASTER VOWELL: Certainly.

22 MR. MATANOSKI: Thank you.

23 SPECIAL MASTER VOWELL: So we will reconvene  
24 at five after 4:00.

25 MR. MATANOSKI: Thank you.

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1 (Whereupon, a short recess was taken.)

2 SPECIAL MASTER VOWELL: Please be seated.

3 We're back on the record in the Autism Omnibus

4 Proceeding Theory II in the King and Mead cases.

5 You may proceed, Mr. Matanoski.

6 MR. MATANOSKI: Thank you.

7 CROSS-EXAMINATION

8 BY MR. MATANOSKI:

9 Q I am Vince Matanoski, and I'm representing  
10 the United States. Good afternoon, Doctor.

11 Doctor, could you tell me the strongest  
12 piece of evidence you have to support your hypothesis?

13 A I would say the strongest piece, especially  
14 in the context in which I presented today, is probably  
15 the post-mortem samples showing, in the real brains of  
16 real people with autism, a down-regulation and  
17 alteration in the enzyme methionine synthase, that  
18 serves the role, as I described it, relating to  
19 dopamine receptors, as well as other important  
20 methylation events.

21 Q Do I understand this to be the information  
22 that you were giving us towards the end of your talk  
23 this afternoon, that had to do with work in your own  
24 lab?

25 A That's correct, as I presented it. I took

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1 your question to, I think you had the term as you. So  
2 I'm not saying our work is the most important. I'm  
3 saying that among the work that I presented today of  
4 ours, that's the one piece that I think is most  
5 important in describing, in relating these findings to  
6 autism.

7 Q I'm sorry, anything else?

8 A That was how I took your question. Were you  
9 asking about our work? Or were you asking about work  
10 in general?

11 Q I'm asking what you believe, in forming your  
12 hypothesis, is the strongest piece of evidence to  
13 support that hypothesis.

14 A I must defer to the work of Dr. Jill James,  
15 whose studies involving both measurements of sulphur  
16 metabolites, but also the genetic polymorphisms, which  
17 I presented, I think are clearly the strongest  
18 evidence in favor of that hypothesis.

19 Q Would those be the two studies that you  
20 referenced in your report? In your report you  
21 referenced, and your report being Petitioner's Exhibit  
22 No. 23, I believe you referenced those as 9 and 10?

23 A That's correct.

24 Q Okay. And I was hopefully going to be able  
25 to tell everyone, so that we'd have it for the record,

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1 I believe No. 9 was PNL No. 49, and No. 10 was PNL No.  
2 5, I believe.

3 (Discussion held off the record.)

4 BY MR. MATANOSKI:

5 Q Doctor, we'll turn to your CV. The  
6 memberships that you list there, in terms of these  
7 various memberships, are these memberships -- how does  
8 one join these different organizations? How did you  
9 join them?

10 A Well, the first several are, they invite you  
11 as honor societies; Rho Chi happens to be in the  
12 pharmaceutical area that I'm in.

13 Q I'm sorry, that was pharmaceutical?

14 A Rho Chi is the honor society for  
15 pharmaceutical areas.

16 Q Okay.

17 A The AAAS is just science, and you just  
18 subscribe basically to Science Magazine, and you are a  
19 member of the AAAS.

20 Q So if you buy a subscription to their  
21 magazine, you become a member?

22 A That's my understanding. The Society for  
23 Neuroscience, you have to be, I'm trying to remember  
24 because I've been a member for many years. You have  
25 to have approval of other members who sponsor your

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1 membership, and evidence of your publications.

2 Q Are you still a member of the Society for  
3 Neuroscience?

4 A Yes. You want to check my dues? The date,  
5 or something like that?

6 (Laughter.)

7 Q And once you're invited, you pay dues to  
8 stay in, is that --

9 A That's correct.

10 Q And the American Association of Colleges of  
11 Pharmacy?

12 A That's an education one.

13 Q How did you enter that?

14 A It's, as a faculty member in a school of  
15 pharmacy.

16 Q You enter by, is it dues?

17 A You decide to join.

18 Q So it's by your own decision to join.

19 A Yes. It's not a distinction. I hope  
20 you're, I hope I didn't misrepresent these as points  
21 of distinction or something like that.

22 Q No, I'm just asking. You haven't; I don't  
23 believe you have. I'm just asking on each of these  
24 how one becomes a member of that organization.

25 And the American Society of Pharmacology and

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1 Experimental Therapeutics? Is that by your  
2 voluntary --

3 A You likely have to I think be sponsored.  
4 Again, I've been a member of that for 30-some-odd  
5 years. I probably don't recall the exact criteria.  
6 But I know you have to nowadays be sponsored by  
7 someone who is a member.

8 Q So it's a membership that's voluntary; it's  
9 not an honorary membership.

10 A None of these are honorary memberships.  
11 They are just indications of my affiliation at some  
12 point with these organizations.

13 Q So the last one is also not an honorary  
14 membership.

15 A No.

16 Q Okay. Also in your curriculum vitae, you  
17 mention some grants. And then you have a section  
18 after you talk about the grants where you say "grants  
19 pending."

20 Now, by "pending," did you mean that those  
21 grants had been approved, and you were just awaiting  
22 funding for them?

23 A No. I think the common use of the term  
24 "pending" in these circumstances is that application  
25 has not been acted upon at the time at which this

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1 document was prepared.

2 Q Okay. So these are just grant applications,  
3 then.

4 A That's right.

5 Q They don't necessarily reflect any approved  
6 research by the organization.

7 A That's right. That's what the word  
8 "pending" means.

9 Q And the timeframes that you have there, some  
10 of them extend back to 2005. Does that mean that --

11 A It probably means that this is an out-of-  
12 date CV.

13 Q I see, I see. Well, then, maybe you could  
14 tell me, on the one that you submitted, the grant you  
15 applied for from the Nancy Lurie Marks Foundation, was  
16 that approved?

17 A No, that was not approved.

18 Q And the one that you submitted to NIH, was  
19 that approved?

20 A The one that I submitted to NIH. That one  
21 sticks in my mind, because that one was not approved  
22 with the -- instead of the review of my project, there  
23 was instead a cutting and pasting of a statement from  
24 the FDA indicating that thimerosal does not contribute  
25 to autism. And therefore, that particular grant

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1 should not be funded.

2 So in fact, it was not funded because there  
3 was a sentiment on the part of the primary reviewer  
4 that it was inappropriate to study thimerosal, because  
5 it doesn't cause autism.

6 Q I see. So the conclusion was, so this grant  
7 wasn't --

8 A That's correct.

9 Q Wasn't approved.

10 A That's correct.

11 Q And the conclusion in not approving it was  
12 essentially the money shouldn't be spent there,  
13 because there has not been any verification that  
14 thimerosal causes --

15 A Because the FDA website posted a statement  
16 indicating -- and it was literally cut and pasted --  
17 so it was clear that that was the factor, a factor.

18 Q If you know, when NIH receives a grant, do  
19 they ask for other individuals outside of NIH to  
20 review the grant to determine whether or not it should  
21 be approved?

22 A They constitute a study section. Each grant  
23 is assigned to a study section, which may have  
24 inherently the appropriate expertise to review and  
25 evaluate that application. If not, then the chair of

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1 that study section can opt to bring in additional  
2 reviewers. It's not a necessary part of the process,  
3 but it can occur.

4 Q And the study section, so do I understand  
5 that it is not necessarily NIH employees that review  
6 your grant application, or a grant application?

7 A No, in no case is it really NIH employees.  
8 But there are fixed study sections whose membership  
9 includes people from broad aspects of academia and  
10 non-academia.

11 Q So the study section isn't necessarily the  
12 government, in other words; it's a spectrum of  
13 academia that has an interest in that area, an  
14 expertise in that area.

15 A That's true.

16 Q And that was true in the case of the grant  
17 application you made concerning methionine synthase,  
18 methyl B12 synthesis in autism?

19 A I'm sure it was true then, yes.

20 Q You mentioned you had several book chapters  
21 on autism pending?

22 A That's correct.

23 Q By "pending," do you mean that they are  
24 awaiting publication?

25 A That's correct.

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1 Q Could you describe those book chapters?

2 A One, under the editorship of Dr. Gene Blatt,  
3 Boston University, a chapter which he asked me to  
4 contribute relating to D4 dopamine receptor  
5 methylation mechanism that I described and its  
6 relationship to autism.

7 Second, I'm a co-author of a chapter of a  
8 book focused mainly on nutritional aspects of  
9 childhood diseases in the chapter on autism, co-  
10 authored with Dr. Patricia Cain.

11 Q Are these expected out any time soon?

12 A Books can take most of a year. I wouldn't  
13 expect them any sooner than the end of this year.

14 Q In the D4 -- have you written a chapter?

15 A Excuse me?

16 Q Have you written a chapter that you're  
17 giving to James Blatt?

18 A No, Gene Blatt. Yes, I gave him that  
19 chapter several months ago.

20 Q In that book chapter on D4 dopamine, did you  
21 conclude that there is sufficient evidence to conclude  
22 that thimerosal-containing vaccines cause autism?

23 A This was not a chapter about thimerosal,  
24 although I included a paragraph about environmental  
25 factors including, but not limited to, thimerosal that

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1 can contribute to autism.

2 Q And did you say that it's established that  
3 these environmental factors, such as vaccines, cause  
4 autism?

5 A I don't believe I did, because that wouldn't  
6 reflect the general establishment.

7 Q That wouldn't reflect the -- this is your  
8 book chapter, though. This is your writing.

9 A The term that you used, could you repeat  
10 your question? Then I could --

11 Q Yes. I wasn't understanding, because your  
12 answer doesn't reflect the establishment.

13 A I asked what your question was. I wanted to  
14 clarify my answer, if I could have your question.

15 Q Why would you write something different in  
16 that chapter than what you're testifying to here?  
17 That ought to be an easier way to ask it.

18 A The chapter was about, was not about  
19 thimerosal. And in fact, I wanted to not make  
20 thimerosal the focus of the chapter. I wanted, as I  
21 was requested, to make the D4 dopamine receptor the  
22 focus of the chapter.

23 Q I'm sorry, I wasn't clear enough. I did say  
24 the chapter, and I should have said the paragraph that  
25 dealt with environmental factors. As I understand --

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1 A And your question was?

2 Q I understand your answer to my previous  
3 question, that you didn't put in there that you  
4 believe there is sufficient evidence to conclude that  
5 thimerosal causes autism. And then your answer to  
6 that, to subsequent questions, had something to do  
7 with the establishment. And I was trying to  
8 understand what you meant by that.

9 A I was answering your answer to me. I'm not  
10 sure we have a transcript here, but you asked, you  
11 said something to me about established -- what did you  
12 ask me? I was responding to what you said.

13 Q Maybe we should start again.

14 A I think we should. So if you'll ask your  
15 question, I will respond.

16 Q Well, I had one.

17 A If you ask it again, I'll respond again.

18 Q What does your paragraph concerning  
19 environmental factors say in the book chapter that you  
20 submitted?

21 A I included a paragraph about environmental  
22 factors, including, but not limited to, thimerosal as  
23 possible causative factors interacting with the D4  
24 receptor causing oxidative stress, and contributing to  
25 the causation of autism.

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1 Q So there you used the term "possible."

2 A I used the term "possible," that's right.

3 Referencing, of course, the range of factors. Because  
4 the probability of each of them, and the probability  
5 of exposure of large numbers of children across the  
6 country to individual agents is not as predictable for  
7 each of these possible agents. So the term "possible"  
8 certainly applies to a group of agents with differing  
9 possibilities of exposure and contribution.

10 Q So your conclusion there is that it's only  
11 possible; you didn't say it's established.

12 A I don't have it in front of me, and at this  
13 point in this inquiry, thinking that I would have to  
14 refer to that which I don't have in front of me. If  
15 you would like precise language, I'd have to have  
16 access to that.

17 Q Your recollection is --

18 A My recollection is?

19 Q -- on this, that you said "possible," but  
20 not that you said that it was established.

21 A The precision that you're looking for I  
22 don't have available to me, because I don't have the  
23 chapter available to me.

24 Q So you don't know.

25 A I don't know? I don't have the chapter

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1 available to me. If it means I don't know or it means  
2 something different.

3 Q Well, let me ask you this about that  
4 particular point. Would you be more cautious in what  
5 you say in a book chapter than what you say in the  
6 courtroom about what you're willing to conclude?

7 A There's no reason to be differentially  
8 cautious. The theme of a chapter might be different  
9 than the theme of a courtroom proceeding, in which  
10 case different questions, different facts, different  
11 specifications would apply.

12 Q So what you write for the scientific  
13 community in general would reflect your true beliefs  
14 about a subject.

15 A I would hope so.

16 Q Now, funding for your research in general,  
17 what's your research budget, say on an annualized  
18 basis, for this year? How much money do you have for  
19 research in your lab?

20 A Not much, but I can be specific. My lab,  
21 for the past year -- I'll use as reference my past  
22 year -- I've had a post-doctoral fellow, Dr. Musafa  
23 Waly. I've had two doctoral graduate students and a  
24 number of Master's students and undergraduates.

25 The post-doctoral fellow pay at the rate of

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1 \$40,000 annually, plus fringe benefits of 25 percent,  
2 would bring it to \$50,000, and the graduate students  
3 and supplies and things like that probably add \$30,000  
4 to \$40,000.

5 So I suppose at a minimum, somewhere at  
6 \$80,000 to \$90,000 for that year. Now, because I  
7 don't have the money to pay him going forward, he'll  
8 be terminated June 13.

9 Q So the past year you figure your research  
10 budget was about \$90,000.

11 A That's a reasonable estimate.

12 Q What are your sources of funding for your  
13 research budget?

14 A Over the past five years, they have been  
15 largely organizations that have an interest in autism,  
16 typically parent-supported organizations, including  
17 Cure Autism Now, which later merged with Autism  
18 Speaks. The Safe Minds, the National Autism  
19 Association, and the Autism Research Institute. These  
20 are the primary sources.

21 Q For your last year, since we are talking  
22 about \$90,000, do you know how much of that would come  
23 from the various organizations? Do you know how much,  
24 let's say, came from Safe Minds?

25 A This past year I had a 50/50 shared grant

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1 with the National Autism Association and Safe Minds.  
2 My recollection is it amounted to \$43,000. So Safe  
3 Minds would have been half of that.

4 Q I'm sorry, so half of \$43,000 was the  
5 contribution from Safe Minds, and then the other half  
6 was from another one?

7 A National Autism Association, NAA.

8 Q And the balance of that would be made up  
9 from Autism Research Institute and Cure Autism Now?

10 A I had two grants during that time period,  
11 from Autism Research Institute. The Cure Autism Now,  
12 I remember, I don't know whether this was this past  
13 year. They funded me for a two-year period. I'd have  
14 to be more precise about whether it overlapped with  
15 the past calendar year.

16 During the past calendar year I had two  
17 separate grants from Autism Research Institute, one to  
18 investigate the importance of methyl B12 in methionine  
19 synthase activity in the brain and the neuronal cells.  
20 And also another one to investigate the methods for  
21 measuring homocysteine thiolactone.

22 Q So do you know roughly in the last year,  
23 since we're using that as our example, how much came  
24 from Autism Research Institute? How much of that  
25 \$90,000 would represent money from Autism Research

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1 Institute?

2 A Let's see. The thiolactone study I  
3 referenced was for \$35,000. Although that is still  
4 ongoing, so only a portion of that would be  
5 attributable to the previous 12-month interval. The  
6 other one would -- so I would apportion \$10,000 into  
7 that, if you like. Thirty-five thousand for another  
8 one, maybe \$40,000, something like that.

9 I didn't come prepared with the numbers.

10 Q I was just asking for your rough estimate.  
11 Doctor, doesn't at least Safe Minds at least have an  
12 explicit research agenda to find a credible, as they  
13 call it, credible findings to support the mercury  
14 autism hypothesis is true?

15 A Quite frankly, I don't know explicitly what  
16 their, what their website is. I guess we're about to  
17 find out what it says.

18 Q And they funded that particular study of  
19 yours. Is that the one you were referencing, or was  
20 that a different one?

21 A That's an earlier one.

22 Q So they funded other work that you'd been  
23 doing, as well.

24 A Right, before this calendar year.

25 Q In all, how many studies did they fund for

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1 you?

2 A Two. The one that we see here on the  
3 screen, and the more recent one that I mentioned was  
4 co-funded with the National Autism Association.

5 Q Thank you. How many publications do you  
6 have that directly deal with oxidative stress?

7 A Well, since we only recognized the role of  
8 oxidative stress subsequent to the Waly paper that I  
9 mentioned earlier today, which was published in 2004,  
10 it only really, it wasn't immediately after that paper  
11 that we uncovered, I guess, the role of oxidative  
12 stress in regulating methionine synthase.

13 And so we've researched on that in the  
14 interval of I would say 2005 now until current times,  
15 and have only published a review paper during that  
16 interval that is directly about oxidative stress.

17 Q A review paper? That's the --

18 A A review paper.

19 Q -- only publication that you have on  
20 oxidative stress?

21 A Yes, that's what I said.

22 Q So there's no publication that you have  
23 that's direct research that you've done into oxidative  
24 stress.

25 A Not at this time.

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1 Q How many years did you work in  
2 cardiovascular diseases?

3 A My PhD work began in that area, and it began  
4 roughly 1972, and then through 1996. So you're  
5 talking about 24, 25 years.

6 Q And how many years have you researched  
7 mercury?

8 A Well, I don't actually -- we have done  
9 research on mercury. But again, as an offshoot of our  
10 interests in this D4 dopamine receptor, and the  
11 mercury aspect only came in I suppose 2003, I believe.  
12 Wait a minute, let's see. I believe 2002 or 2003  
13 would be my estimate of when we first did our first  
14 studies with thimerosal and mercury.

15 Q So five or six --

16 A Leading to the publication that was Waly, et  
17 al, which was 2004.

18 Q So for five or six years, you have had some  
19 research interest in mercury.

20 A Four or five.

21 Q Four or five years. And is the 2004  
22 publication, Waly, et al, that you referred to, is  
23 that your only publication on mercury?

24 A Let's see. Actually, in my monograph there  
25 was a figure involving using effects of thimerosal

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1 that preceded actually the Waly paper. Then I believe  
2 that is the only, those two would represent the only  
3 two.

4 Q There's one before the 2004 Waly, et al  
5 paper?

6 A The book that I wrote the monograph I wrote,  
7 I believe had a figure in it. Obviously the book was  
8 not about thimerosal or mercury. But my recollection  
9 is the chapter on autism in that book included a  
10 figure, and that was something. The book was sent to  
11 the publisher in 2002 or something like that.

12 Q Is that book a peer-reviewed book?

13 A Not really, no.

14 Q It was written by you, it wasn't submitted  
15 to an editor?

16 A It's not a peer-reviewed, it's, it would be  
17 a monograph that I wrote.

18 Q So there was no scrutinizing what you had  
19 worked to determine whether it reflects --

20 A It wasn't the nature of that publication  
21 that it would be scrutinized.

22 Q What was the nature of that publication?

23 A Let me put it into context. We had made  
24 what seemed like an unusual finding, where a  
25 neurotransmitter receptor, the neurotransmitter being

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1 dopamine, which was linked to dopamine being linked to  
2 schizophrenia being linked to ADHD, other disorders  
3 seemed like finding a new action of that  
4 neurotransmitter and its receptor, the D4 receptor,  
5 might be worthy of pause and worthy of analysis in  
6 terms of what role it might play.

7           So I took a sabbatical year, and used that  
8 sabbatical year to do that; to look into the  
9 literature not only about methylation and lipid  
10 events, but neural network and theories of attention  
11 and cognition and neurosynchronization, as well as  
12 look into the biochemical foundations for various  
13 neurological disorders. Asking myself, but at the  
14 same time using the opportunity to express what I  
15 found in a monograph. And so that resulted in the  
16 publication of that book.

17           Q     Did you take any parts of what you were  
18 writing, and attempt to put them into a paper and have  
19 a published, peer-reviewed paper?

20           A     Well, the thimerosal figure that I mentioned  
21 before appears in the Waly article, so I suppose that  
22 would be an example of that. But it wasn't the  
23 purpose of the book to somehow use it as a stepping  
24 stone for publishing the same information in the form  
25 of papers. I thought the book was sort of an end

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1 point in itself, and it wasn't on my mind at least to  
2 somehow create papers.

3 Really, the book represented an opportunity  
4 to synthesize bodies of information and integrate  
5 them. And it's really provided me with a very useful  
6 framework from which to go forward to do research.  
7 But that research is not necessarily already in the  
8 book.

9 Q Do you receive, did you receive payment for  
10 your work, this monograph? Did you get paid for this?

11 A I think it's like two percent of the, I'm  
12 not sure whether it's two percent of the total. But I  
13 think it amounted to a total of \$500 over a period of  
14 five years, or something like that. Maybe even less.

15 The other day I think I sold five copies of  
16 it. We're not talking about a bestseller here. And  
17 so I think, I don't even think they bothered to put a  
18 check in, as a matter of fact, for the possible  
19 royalties. It might have been Starbucks kind of  
20 money.

21 Q So you didn't have to pay to get this  
22 published, did you?

23 A No. Not quite.

24 Q Okay. But it really hasn't generated a lot  
25 of sales.

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1           A     Let's see. Have you checked the price of  
2     this book?

3           Q     No.

4           A     No, okay. One of the unfortunate things I  
5     learned, besides the science that I gathered from my  
6     book, was to be a little more careful in choosing --  
7     not that I had that much choice -- your publisher and  
8     the arrangements. Because the book, the last time I  
9     checked, was \$180 for a 200-page, rather small, modest  
10    book, or something like that. It was designed to not  
11    sell, from a financial standpoint.

12                   (Laughter.)

13          A     And I was disappointed, because I think the  
14    information in that book, as relative to the testimony  
15    I gave today, is actually very worthwhile. And it was  
16    a heartfelt effort on my part to write it. So it was  
17    worthwhile doing it, but it certainly was never really  
18    one for monetary gain; and in fact, it never resulted  
19    in monetary gain.

20          Q     Publishers don't price their books not to  
21    sell, though, do they? I mean, they go out of  
22    business if they try to publish a book that's not  
23    going to sell.

24          A     We're way off base in terms of why I'm here.  
25    But otherwise, publishers sell books to libraries at

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1 whatever price libraries will pay, and it's not  
2 necessarily the consumer market that they have first  
3 on their minds. They may be just looking to have  
4 something available for institutions to buy for their  
5 libraries.

6 Q Doctor, I've looked at some of your  
7 presentations at Defeat Autism Now conferences, and  
8 actually some other works that you've put out that are  
9 on the public sphere. And I think every time I've  
10 seen you reference articles written by Mark Geier as  
11 support for your hypothesis. Is that right? Do you  
12 usually cite Mark Geier as support for your  
13 hypothesis?

14 A Am I aware of their work? Is that what  
15 you're asking?

16 Q No. I'm wondering with your presentations,  
17 for example at Defeat Autism Now conferences, you cite  
18 Mark Geier.

19 A I am aware of the Geiers, I am aware of  
20 their work, and on occasion I have cited their work.

21 Q I didn't see it as one of the references in  
22 your opinion here, and I was wondering why that was.

23 A The citations that I gave here support the  
24 work that I included in my remarks.

25 Q In your 2007 review paper, did you cite Dr.

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1 Geier there?

2 A To which paper are you referring to?

3 Q I think you were talking about a review  
4 paper that you just, that you had come out.

5 A In 2008? I thought you said 2002.

6 Q Oh, 2008. I'm sorry, 2008.

7 A I may have. Some of their work is very  
8 interesting, and they are very active clinicians and  
9 investigators in the autism area.

10 Q So you've relied on their work?

11 A I rely on their findings within the context  
12 to which it's presented.

13 Q So then I take it since you didn't cite it  
14 here, it doesn't support you, you don't find it to  
15 have value in the context of the hypothesis you're  
16 giving us today?

17 A I wouldn't necessarily draw that conclusion.

18 Q Oxidative stress, would it be fair to say  
19 that that describes a very general mechanism of  
20 injury?

21 A Oxidative stress status, or redox status, is  
22 fundamental to cellular function for many different  
23 cells. As such, it represents a very general  
24 mechanism that could express itself as, and does  
25 express itself as different diseases in a general way.

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1 The question is a bit vague, and I'm not sure if  
2 that's an adequate answer.

3 Q I think that is. In other words, it plays a  
4 role, or is thought to play a role in a wide variety  
5 of diseases, correct?

6 A That's correct.

7 Q And isn't it thought to be caused by a wide  
8 variety of events?

9 A That's a reasonable statement.

10 Q For example, exposure to infectious agent?  
11 Is that right? Would that cause oxidative stress, or  
12 could it cause oxidative stress?

13 A It could. We recognize that part of the  
14 innate immune system, the resistance is mounted  
15 against an infectious organism. Includes an important  
16 role for oxidative events.

17 Q Let's say I went out for a jog. Will that  
18 create an oxidative stress state in my body?

19 A While I'm not expert in exercise physiology,  
20 I wouldn't expect that it would. So there are  
21 limitations to what I know about oxidative stress  
22 during exercise. I wouldn't define the experience of  
23 exercise as oxidative stress, although it's such as  
24 dynamic and moment-to-moment.

25 So the response system that I suppose that

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1 mitochondrial activity being heightened during  
2 exercise might change, even increase the generation of  
3 oxygen species. So there might be a dynamic change in  
4 the redox systems. But it's certainly beyond my  
5 expert knowledge to say more than that.

6 Q So, okay. So you don't know anything more  
7 than what you've stated just now, in terms of --

8 A About exercise and oxidative stress?

9 Q Yes.

10 A That's probably a reasonable statement.

11 Q Now, your mechanism of thimerosal triggering  
12 oxidative stress then would potentially implicate a  
13 wide variety of diseases as a possible outcome. Is  
14 that right?

15 A Potentially, it could.

16 Q I believe you were talking a little earlier  
17 about Parkinson's disease?

18 A Parkinson's disease is another oxidative  
19 stress-related neurodegenerative disease.

20 Q Alzheimer's?

21 A Too.

22 Q Do you believe that either of those diseases  
23 are caused by exposure to thimerosal?

24 A I don't. I would recognize that those are  
25 diseases of advanced age. And our work that I alluded

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1 to in the background is consistent with the idea that  
2 the ability to tolerate oxidative stressors decreases  
3 with age, because aging itself is considered an  
4 advancing oxidative state. And with thimerosal  
5 exposure that we're concerned with here being  
6 restricted to younger individuals, it's unlikely that  
7 it contributed to the lives of those old enough to  
8 suffer these degenerative diseases of old age.

9 Q So younger individuals are better able to  
10 tolerate oxidative stress.

11 A That's consistent with what I know.  
12 However, let me qualify that. By tolerating, it means  
13 surviving it. And when you survive an insult, it  
14 doesn't mean that you don't carry the scars, or  
15 otherwise the consequences of that even temporary  
16 episode that you survived.

17 And so one might consider certain conditions  
18 to reflect the influence of oxidative stress, but not  
19 to the catastrophic end that autism can represent.

20 Q And you have hypothesized that thimerosal,  
21 through this mechanism of oxidative stress, can lead  
22 to obesity?

23 A I've noted at a recent conference that a  
24 paper was published, perhaps six months ago now, by  
25 researchers in Italy. And I found that paper of

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1 interest. It popped up on a search mechanism that I  
2 use to follow methionine synthase-related literature.

3 Because what these researchers found was  
4 that some of the same genes that I referred to from  
5 Dr. Jill James's study, explicitly methionine synthase  
6 itself, methionine synthase reductase, and I believe  
7 MTHFR, methylfolate synthesizing enzyme, that the  
8 polymorphisms of those enzymes, according to their  
9 study carried out in Italy, were highly associated  
10 with obesity. And that is, in combination, they found  
11 up to a 16-fold increase in obesity risk, odds of  
12 ratio for obesity, with the same genes that I have, or  
13 I have been paying attention to, and Dr. James has  
14 associated with autism.

15 And at least it caused me to entertain the  
16 hypothesis, which I publicly passed along, the  
17 hypothesis that, in fact, other conditions that we  
18 perhaps are experiencing epidemic outcomes of, might  
19 also be related to shared mechanisms.

20 Q Under your hypothesis or mechanism of  
21 thimerosal causing autism, what's going to happen to  
22 neurons?

23 A The consequences would, at the level of  
24 function, be a loss of methylation related, or  
25 reduction methylated related activities. Most

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1 important of those for our laboratory interests are  
2 the D4 dopamine receptor function would be  
3 compromised. And whatever role that does play, and  
4 there is reason to think that the D4 receptor has a  
5 unique role to play in the ability of neuronetworks to  
6 synchronize their firing activity to a particular  
7 frequency, gamma frequency, during attention, that I  
8 would suppose that a consequence would be impaired  
9 gamma frequency synchronization during attention.

10 And as I alluded to, there's many other  
11 methylation reactions, each one of which, although not  
12 necessarily to the same extent, but each one of which  
13 would likely be reduced in its efficiency as a result  
14 of inhibition of a thioneine synthase consequent to  
15 oxidative stress.

16 Q Are the neurons going to die? Or are they  
17 going to be spared? Are they going to look any  
18 differently than they look before the oxidative stress  
19 that you hypothesized results in autism?

20 A At doses which are within the range of  
21 typical exposures that we've discussed here, I would  
22 not expect death of neurons. At higher  
23 concentrations, as demonstrated in a number of  
24 studies, thimerosal and certainly mercury can cause  
25 neurons to die and cells to die.

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1           But I think my expectation of the  
2           concentration ranges that we're talking about here, by  
3           that I specifically mean 100 nanomolar or less, those  
4           concentration ranges, rather than causing the cells  
5           and neurons to die, or even to show overt anatomic  
6           differences, might rather instead of that cause a loss  
7           of function or impaired function.

8           Q     In your studies that you've done in your  
9           lab, published in 2004, and then I believe you spoke  
10          about some other studies being done currently in your  
11          lab, what happened to the neurons there?

12          A     The neurons did not die. In fact, there was  
13          a discernible change in the cell shape while they were  
14          exposed to thimerosal. They rounded up and lost their  
15          processes; that is, they became more spherical. And  
16          this was reversible.

17                 And so recovery under these concentrations,  
18          and the concentrations that we used, as I showed,  
19          these were actually 10 to the minus-7; again, not  
20          necessarily extremely high concentrations, but lower  
21          concentrations.

22                 And it was clear to us that the cells had  
23          changed over an influence, but they had not been  
24          killed. This is actually a point of encouragement, I  
25          hope, and I take for the possibility that recovery

DETH - CROSS

612

1 from damage or oxidative stress conditions,  
2 neuroinflammation might be reversible. And there is  
3 encouragement along those lines in the treatment of  
4 autistic children, including the administration of  
5 methyl B12 and folinic acid supplements, which not  
6 only improve their metabolic characteristics, but  
7 also, as reported recently, improve their neurologic  
8 function.

9 And so this is consistent with the idea that  
10 the underlying cellular components are still there,  
11 and in a significant number. But alas, not all  
12 children can be improved significantly, if not fully  
13 recovered. So it's an important distinction to say  
14 that we're not killing, not proposing the death of  
15 neurons as an explicit part of autism.

16 Q And you said when you looked at these cells,  
17 when they were under these conditions you had put them  
18 under, they actually looked different than they did  
19 prior to your treatments.

20 A That's correct. These are SY5Y cells.

21 Q So the treatment actually changed the  
22 physical appearance of the cells.

23 A They were more round.

24 Q And is that because of the --

25 A Let me make it clear that these are again

DETH - CROSS

613

1 cells in cell-culture petri dishes that have a typical  
2 morphology of having some processes or extensions,  
3 pointy features. And it was those features that were  
4 not maintained as well in the presence of  
5 concentrations of thimerosal of 10 to the minus-7, in  
6 that range.

7 Q In your report, you stated that thimerosal  
8 is toxic to human cortical neurons and neuronal cells  
9 grown in culture. Thimerosal caused 50 percent of the  
10 cells to die after 48 hours. Concentrations between  
11 five and 100 nanomolars.

12 So in those instances, the --

13 A I would like for you to reference which  
14 page?

15 Q Page 3. So thimerosal caused neuronal death  
16 as reported in those references I gave you?

17 A You're not talking about my lab work now, I  
18 don't believe.

19 Q No, no, I'm not.

20 A Thank you.

21 Q So it caused neuronal death.

22 A Uh-huh.

23 SPECIAL MASTER VOWELL: Is that a yes?

24 THE WITNESS: That's what the report says,  
25 and that was reference no. 5? Oh, is that a -- I hope

DETH - CROSS

614

1 that wasn't a typo. Is that where we're headed here?

2 Because if that --

3 BY MR. MATANOSKI:

4 Q You don't need to anticipate where I'm  
5 heading, Doctor.

6 A I think I --

7 Q I hope you'll hear my question, so you'll  
8 know exactly what I'm asking you.

9 A Okay, good. Because I am noticing that's  
10 what it says, and that was reference 5 here. But on  
11 my personal reflection, I'm thinking oh, that's an  
12 impressively low concentration for causing cell death.

13 Q Doctor, doesn't the body have numerous  
14 compensatory processes for coping with oxidative  
15 stress?

16 A Yes.

17 Q Doesn't your hypothesis -- I'm sorry. Does  
18 your hypothesis apply only to regressive autism?

19 A No.

20 Q Doctor, do you believe there's an epidemic  
21 of autism directly tied to the use of thimerosal in  
22 vaccines?

23 A I do.

24 Q Do you believe that the incidence of  
25 autism -- never mind, strike that.

DETH - CROSS

615

1 Do you believe that there is also a rise in  
2 the, in obesity in children linked to thimerosal?

3 A I don't believe that with anywhere near the  
4 same certainty that the relationship to autism is both  
5 believed and supported by my work and others. Because  
6 in fact, I haven't done a parallel investigation of  
7 that. I raised it as a hypothesis.

8 Because the exposure of the public as a  
9 whole, our population as a whole, to an agent that  
10 induces oxidative stress and impaired methylation,  
11 might -- and hypothetically here, might -- result in  
12 more than one consequence.

13 If we generalize what I presented, and we  
14 got autism, it's those who have a certain number of  
15 polymorphism or risk genes, and are exposed to  
16 thimerosal; have a high risk of having a neurological  
17 condition, in which impaired methylation of methionine  
18 synthase activity plays a role. We might imagine that  
19 people with another set of risk genes, perhaps  
20 involving instead of neurological functions, perhaps  
21 metabolic functions more closely aligned to, with the  
22 metabolism VLDL formation, might manifest a different  
23 set of symptoms.

24 And if one hypothesis is true, then the  
25 other should be looked for. And that's why I was

DETH - CROSS

616

1 struck by the finding that there was an association of  
2 obesity with some of the same genes.

3 Q And you've publicly spoken to imply that the  
4 two epidemics, that is in your view two epidemics,  
5 autism and obesity could be linked to thimerosal.

6 A The way I presented it was an interesting  
7 finding, which in fact it is. And I presented that,  
8 because I think the public, who at some level our  
9 information serves, should be aware of the  
10 possibilities that different disorders, for whom an  
11 explanation is frequently not directly available,  
12 might have something in common with another disorder.

13 Q In 2003 you authored the paper for a Defeat  
14 Autism Now conference. And in that, you essentially  
15 said that it would be interesting to see, since  
16 thimerosal had been virtually removed from vaccines in  
17 the U.S., to observe whether the incidence of autism  
18 decreases in the next three to five years.

19 Do you recall making that statement?

20 A I can easily, it sounds correct. It sounds  
21 certainly as a thought that I have held, so I can  
22 acknowledge that.

23 Q And are you familiar with the information  
24 that was recently published about the incidence of  
25 autism in California?

DETH - CROSS

617

1 A I am.

2 Q And that information showed an increase, a  
3 continued increase in the rate of autism, is that  
4 right?

5 A That's correct. It's certainly a troubling  
6 finding.

7 Q I agree. And your observation in 2003 where  
8 you, you didn't say which way you expected it to go;  
9 you say it would be interesting to observe whether the  
10 incidence of autism -- I'm sorry, you said it would be  
11 interesting to see whether it decreases in the next  
12 three to five years.

13 By that, did you mean your expectation was  
14 that with the removal of thimerosal, it would  
15 decrease?

16 A I think those words are clear on their own  
17 merit, that what I meant is exactly what they say. I  
18 don't, I didn't want to, and I don't want to take them  
19 in any one direction or another any further than what  
20 they say.

21 Q Well, casting your mind back to 2003, I just  
22 want to make sure I'm --

23 A Is there a particular day you had in mind?

24 Q At the time you wrote this statement, was  
25 your expectation that with the virtual elimination of

DETH - CROSS

618

1 thimerosal in vaccines, the incidence of autism would  
2 decrease?

3 A I was hopeful it would.

4 Q Was that your expectation?

5 A I was hopeful that it would.

6 Q Based on your hypothesis, was that your  
7 expectation?

8 A Because of my hypothesis, I was hopeful that  
9 it would.

10 Q And it did not.

11 A The data in California does not show a  
12 decrease.

13 Q What percentage of individuals are  
14 genetically predisposed to react to thimerosal-  
15 containing vaccine?

16 A I don't have an absolute answer. That's  
17 obviously a question for which the data is not  
18 available to answer it, not only by myself or anyone  
19 else. If I said it, perhaps one in 150, it would be  
20 just on the basis of the fact that rate might indicate  
21 we're experiencing that percentage of sensitive  
22 individuals.

23 Q You mentioned polymorphism in the  
24 population.

25 A Uh-huh.

DETH - CROSS

619

1 Q That you were interested in. Do those, are  
2 those polymorphisms shared by more than one percent of  
3 the population?

4 A Yes.

5 Q Are they shared by more than five percent?

6 A One cannot generalize, because a  
7 polymorphism of more than one percent might be five  
8 percent for one example, or 50 percent for another.

9 Q So these polymorphisms you are talking about  
10 could cover broad areas of the population.

11 A They do cover broad areas of the population,  
12 because they're normal. They are not mutations in the  
13 sense we might think of an aberrant feature of the  
14 DNA, but they are, in many cases, risk-inducing,  
15 especially under changes in the environment. Under  
16 circumstances which their otherwise potentially useful  
17 role is, in fact, reversed to be a risk-inducing role.

18 Q So these, again, these polymorphisms are  
19 normal, and shared by a large percentage of the  
20 population. Is that right?

21 A Again, the percentage varies. It can be as  
22 high as 50 percent. Or otherwise it's, if you're  
23 talking in general about polymorphism, polymorphisms  
24 are shared by all of us.

25 Q I was talking about the polymorphisms that

DETH - CROSS

620

1 you were identifying as potential risk factors.

2 A Right.

3 Q Do these fit these general -- are they  
4 shared generally amongst the population?

5 A Yes.

6 Q In the manner you just described?

7 A Yes.

8 Q Do you believe, under your hypothesis, that  
9 it's thimerosal, ethyl mercury, or inorganic mercury  
10 that is responsible for oxidative stress?

11 A They each take their turn, don't they?  
12 There was no thimerosal administration, then in fact  
13 the risk would be rather low. And so that thimerosal  
14 has its role to play, as the original molecule and the  
15 ethyl mercury had its role to play as the facilitator  
16 of trans-blood-brain barrier movements.

17 But ultimately, the final and longest-  
18 residing form of toxicity can be assigned to the  
19 inorganic mercury within the brain.

20 Q So is it the inorganic mercury in the brain  
21 that is the mercury of interest, in terms of your  
22 hypothesis?

23 A Yes, as far as the neurological  
24 manifestations of the disease, that's correct.

25 Q With your hypothesized mechanism, will the

DETH - CROSS

621

1 same effect be seen after exposure to methyl mercury?

2 A Are you talking about the same dose of  
3 methyl mercury? The same rate of administration? The  
4 same route of administration?

5 Q It's a very general question.

6 A It can't be a general answer, then. Because  
7 the thimerosal as administered as a bolus dose, it is  
8 relatively quickly absorbed within a matter of hours.  
9 It is in fact available faster than a tuna sandwich  
10 delivers methyl mercury, over a period of a week or  
11 two. So these things can make a very big difference  
12 in terms of what the same amount of these different  
13 materials will do. Because a proportion of  
14 elimination, the proportion that crosses the blood-  
15 brain barrier are driven by the concentrations. And  
16 the concentrations achieved by a bolus dose are much  
17 higher than by the dribbling in of small amounts, for  
18 whom the excretory pathway, detoxification pathways  
19 maintain a very low concentration.

20 So this makes it difficult to answer your  
21 question.

22 Q How much -- I just need to know whether you  
23 believe that the amount of thimerosal was important.  
24 Now that we've established that that is important to  
25 you, as well as other factors, start with how much

DETH - CROSS

622

1 thimerosal would one need. I'm sorry, how much  
2 inorganic mercury would one need to have the effect  
3 that you hypothesize results in autism?

4 A How much inorganic mercury would be needed  
5 where? Behind the blood-brain barrier in the brain?

6 Q Wherever it's important for your hypothesis.  
7 Is it in the brain?

8 A It's important --

9 Q It doesn't matter if it's elsewhere for your  
10 hypothesis?

11 A Uh-huh.

12 Q I'm sorry, you'll have to say yes or no.

13 A You're changing it. I'm not sure, you're  
14 asking me several questions.

15 Q No, I'm trying to get to where you can  
16 answer the question.

17 A Let's both be on the same wavelength. I  
18 think you're asking me how much you need in the brain.

19 Q Let me step back. Where does the inorganic  
20 mercury need to be in your hypothesis for it to have  
21 an effect that you see autism?

22 A For the neurological symptoms of autism,  
23 which my work reflects most closely on, it is in the  
24 brain. And so therefore, it's the concentration in  
25 the brain that's most relevant.

DETH - CROSS

623

1 Q How much inorganic mercury would be  
2 necessary in the brain to see the neurologic effects  
3 that you, in your hypothesis, that you say are  
4 consistent with autism?

5 A Okay. I obviously went out of my way to  
6 emphasize the concentration-dependent effects on the  
7 various contributors to disturbed sulphur metabolism,  
8 which let's call my hypothesis here. And as we  
9 reflect, I saw concentration-dependent effects at very  
10 low concentrations, concentrations that are sub-  
11 nanomolar, and in fact concentrations that are in that  
12 range of nanomolar and above would likely cause graded  
13 levels of interference with sulphur metabolism.

14 Now, if you'd care to get into more detail,  
15 which if we want to be more sophisticated, would you  
16 like to?

17 Q I just want to know, sir, I'm just looking  
18 for a number. How much?

19 A I'm not going to share a simplistic view  
20 here. Because a certain concentration at moment zero,  
21 let's say, will result in adaptive responses such as I  
22 outlined. And it's possible that you will get little  
23 effects from a one-nanomolar concentration, because  
24 the cell can handle that. It can adapt to that  
25 without any consequential loss of function.

DETH - CROSS

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1           But there will be a threshold concentration.  
2           I think that's really what your question is getting  
3           at. Is there a threshold concentration at which loss  
4           of function occurs because cells can no longer  
5           compensate for the presence of toxic substances like  
6           inorganic mercury.

7           Q       What is that threshold concentration?

8           A       Again, I don't know what that threshold  
9           concentration is in the intact brain. But the studies  
10          which show concentrations after vaccination of  
11          monkeys, I guess it would be the administration of  
12          equivalent concentrations that produce 30 nanomolar,  
13          estimates of human autism, excuse me, human brain  
14          levels are in that same range. I'm drawn to that  
15          range as saying well, I guess at those concentrations,  
16          if autism symptoms do occur, then that might be -- and  
17          I can only say might, I'm trying to help your interest  
18          in finding an estimable number. I'm not dealing with  
19          facts here.

20          But I would guess that in the range of 10 to  
21          100 nanomolar, in that range, would be sufficient to  
22          cause a loss of function. But I have to qualify that  
23          by saying it's really just my efforts to focus on a  
24          number in response to your question. It's not based  
25          on an experimental measurement.

DETH - CROSS

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1 Q So there is no experimental measurement that  
2 you know of that would give us that threshold  
3 concentration.

4 A There is none at hand. And if we're talking  
5 about which concentrations would cause autism, you can  
6 imagine that the subjects for such a study would be  
7 prohibited, and such a study would be prohibited. And  
8 so we're at a difficult situation of extrapolation  
9 here from other experiments that we can do.

10 Q Are you willing to extrapolate from your in  
11 vitro studies as to what the threshold dose would be?

12 A No, I'm not. We should also recognize that  
13 the free concentration -- when I carried out our  
14 studies, we have a concentration in the bathing medium  
15 for cells. And that represents, at the time we added  
16 the free concentration, whereas a concentration in  
17 brain tissue and the extrapolation from the amounts in  
18 microgram or milligram quantities, or parts per  
19 billion, probably represent bound forms, not free  
20 forms.

21 I can, with great confidence, say that there  
22 are probably very marginally small free concentrations  
23 of inorganic mercury in, say, the Burbacher primate  
24 studies, or in humans as we estimate that. It's  
25 bound. It's bound to some sulphhydryl-containing

DETH - CROSS

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1 enzymes. So our concentrations in free form are sort  
2 of a different experimental system.

3 Q In free form, there is more of it available  
4 to react with the cell, than in the human body?

5 A The amount available is, for  
6 concentration -- well, the amount available, if we're  
7 now trying to convert concentration into amounts, is  
8 that the nature of your question?

9 Q My question started with, from your cell  
10 studies, do you feel comfortable calculating a  
11 threshold concentration for which, under your  
12 hypothesis, you would see this neurologic reaction?

13 A No. Our studies, as I presented them,  
14 indicate that when certain concentrations, as free  
15 concentrations, are presented to human neuronal cells,  
16 they inhibit these processes at the stated level. And  
17 so that it's different, it's a different system than  
18 saying that the amount or the concentration in an  
19 intact animal's brain, which is not a free  
20 concentration, but rather a net amount that is  
21 normalized to the weight of the tissue and so forth.

22 So it's really difficult for me to  
23 extrapolate one to the other. I'd like to do that;  
24 it's important to do that. And we all need to do  
25 that. But we have to sort of temper that by the

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1 recognition that those are two different  
2 circumstances. And the truth is, we don't know the  
3 free concentration in the brain, and it's likely to be  
4 very low in the case of the brain studies.

5 Q In other words, in the brain there would be  
6 less freely available to be presented to the cells.

7 A It's going to be bound to an extremely high  
8 percentage, especially at a given time. You can  
9 imagine presenting even within the brain a free  
10 concentration, and then over time a greater and  
11 greater proportion of that will be in a bound form, as  
12 it finds its targets and binds so strongly that it  
13 doesn't come off of those targets. It's going to be  
14 bound.

15 Q Can you extrapolate from any other research  
16 work that you know of, besides your own, to tell us  
17 what the threshold concentration might be under your  
18 hypothesis, through which you would see this  
19 neurologic event?

20 A No.

21 Q So I take it then you have no opinion as to  
22 whether one vaccination with, say, hepatitis B vaccine  
23 would be enough to create this neurologic effect.

24 A The extrapolation, I think I didn't indicate  
25 I have no opinion. I think your question was do I

DETH - CROSS

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1 have any additional knowledge. I assume, therefore,  
2 the facts that we at most discussed prior to that  
3 final question are not erased. There are reasons to  
4 think that individual doses create individual  
5 concentrations in the brain that can summate over  
6 time, especially with inorganic mercury.

7 Q For your hypothesis, do you need to have an  
8 efflux disorder for the effect you hypothesized?

9 A The efflux disorder, which is a reasonable  
10 way to describe the impairment in glutathione-based,  
11 especially in glutathione-based detoxification,  
12 although there are other efflux pathways. But the  
13 term "efflux" is really one way to think about the  
14 reduced clearance of mercury and its various forms,  
15 when you don't have enough glutathione.

16 For example, if you're autistic and you have  
17 40 percent less glutathione, we could think of that as  
18 a biochemical cause of an efflux disorder.

19 Of course, from dosage of mercury or ethyl  
20 mercury, whether you have a normal efflux capacity --  
21 i.e., normal glutathione -- or not, you'll suffer  
22 consequences and have an overwhelming effect of that  
23 high concentration. It's really a titration issue.

24 We can even view the tolerance for mercury  
25 exposures, but in truth, other heavy metals as well,

DETH - CROSS

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1 as a titration issue, as saying how much can you clear  
2 per day. And are we all equal in our ability to clear  
3 that amount. And if some among us are not, then those  
4 individuals will tolerate less.

5 So given a standard rate of administration  
6 shared by a heterogenous population, we can and should  
7 anticipate that some individuals will be less able to  
8 clear and efflux that mercury, even at the levels that  
9 vaccination provides, albeit seemingly modest levels.  
10 There may be individuals for whom even that modest  
11 level is not excreted, and therefore causes a problem.

12 Q Is it important to your theory that this be  
13 shown in an individual? Or does your hypothesis stand  
14 independent of an efflux disorder?

15 A It's certainly important to that individual.

16 Q Is your hypothesis independent of the  
17 existence of an efflux disorder? Or do you also rely  
18 on that in forming your opinion?

19 A Especially when one considers the role of  
20 glutathione in efflux, and the role of glutathione in  
21 controlling methylation, it's hard to separate those  
22 two. And I have a hard time, under those conditions,  
23 imagining somebody who had, let's say, low glutathione  
24 peripherally, and therefore has an efflux problem, but  
25 has normal glutathione centrally. So it's really, to

DETH - CROSS

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1 me, likely that you would find an efflux problem when  
2 you have a redox problem.

3 And so I think these two are sort of  
4 inextricably part of the central role of glutathione.

5 Q In the work in your lab that you described  
6 in the 2004 paper that was published, and the  
7 unpublished work that you described today, the cells  
8 that you were using were not cells from a human brain,  
9 were they?

10 A No. The SY5Y cells, described as  
11 neuroblastoma cells -- the "oma" indicates that in  
12 fact they were originally isolated from a tumor of  
13 neural origin, but not necessarily brain origin. In  
14 fact, this is a tumor which originally was of  
15 peripheral origin.

16 Nonetheless, they are human. Nonetheless,  
17 they are neuronal. And in fact, the cells that we  
18 chose here to use are by far the most common cultured  
19 cell, neuronal cultured cell model used in, by medical  
20 science. And there's upwards of 3,000 papers  
21 published using these cells.

22 And it's been our experience that the things  
23 that we learn from these cultured human neuronal  
24 cells, albeit non-brain-derived, have a high  
25 predictive value for brain functions in animals, as

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1 well as in humans. And the fact that we found, as we  
2 did, abnormal levels of methionine synthase,  
3 especially among young subjects, in human brains, our  
4 motivation for looking for that in the first place  
5 came from cultured cell studies.

6 So it's a very good example of what you get  
7 from using these cultured human cells. You get ideas  
8 that you can then go ahead and test as best you can in  
9 the more satisfactory systems and materials, as they  
10 are available.

11 Q So Doctor, from your answer I take it these  
12 are cancer cells?

13 A Tumor cells.

14 Q While they're neuronal, they're not from  
15 either the brain or even the central nervous system,  
16 is that right?

17 A I think that's what I specified.

18 Q In your 2004 study that was published,  
19 didn't you find that -- you used both thimerosal and  
20 inorganic mercury, amongst other agents, in testing,  
21 in the testing that you did, is that right?

22 A That's correct.

23 Q And didn't you find that -- and as I  
24 understand it, inorganic mercury now is the focus of  
25 your attention, which you believe we should be looking

DETH - CROSS

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1 at in terms of what might be the mercury species in  
2 the brain that's of interest, at least under your  
3 hypothesis, is that right?

4 A That's correct.

5 Q In that 2004 paper, you found that inorganic  
6 mercury didn't lower glutathione as great as the  
7 thimerosal did, isn't that right?

8 A We didn't measure glutathione in that paper.

9 Q The ability --

10 A It took us a while. That paper showed an  
11 inhibition of methionine synthase, and inhibition of  
12 phospholipid methylation. But it was really, as a  
13 result of our trying to find out more about why that  
14 occurred, that led us to this other series of more  
15 deeper investigations, including glutathione  
16 measurements.

17 Q Let me put it in perhaps a more simplistic  
18 way, because that's where my level of understanding  
19 is.

20 The thimerosal and the inorganic mercury  
21 ability to go across and attack cells was not the same  
22 in your experiment, is that right?

23 A It never would be. Assuming that the ethyl  
24 group was on top of the mercury, it should facilitate  
25 its transfer across the cell membrane in the case of

DETH - CROSS

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1 cultured cells, roughly analogous to the blood-brain  
2 barrier.

3 Q So the inorganic mercury, the cell was  
4 actually better protected against inorganic mercury in  
5 your experiment.

6 A It critically depends upon where the target  
7 is. The target need not be intracellular, but might  
8 well be considered to be intracellular. If it was  
9 intracellular, and if time was a factor, then the rate  
10 at which the ethyl mercury would enter the cell would  
11 be faster facilitated.

12 However, if inside of the cell, the target  
13 preferred, you know, organic mercury, or was more  
14 affected by that than the ethyl, then you'd have sort  
15 of a confounding issue about both the target and the  
16 transports to the inside of the cell where the target  
17 is located. And not to mention there might be more  
18 than one target.

19 So all these factors in the end give you  
20 what you get. When you do the experiment, you get the  
21 result.

22 Q I turn your attention a moment to the  
23 article, the Charleston article that's listed as PML-  
24 32.

25 A Uh-huh.

DETH - CROSS

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1 Q This article, you've referenced it, and you  
2 say in your reference ethyl mercury. Is this article  
3 about ethyl mercury?

4 A The Charleston article, that was about the  
5 middle, you know, that was an earlier paper. It was a  
6 microglial paper I guess. Is that the one where  
7 Charleston was writing that? Okay, methyl.

8 Q Okay. So when you cited this as an article  
9 about ethyl mercury, that was just --

10 A I guess, could you reference on my report  
11 which particular page you're --

12 Q I believe, I'm not sure which reference it  
13 was. I can find that. I just wanted to know whether  
14 you believe that that article was about ethyl or  
15 methyl mercury, because you cited it as ethyl.

16 A Okay. I just wanted to verify that citation  
17 that you're alluding to. It's possible it could be an  
18 error, or not. Okay.

19 Q Actually, Doctor, it's not important about  
20 whether you made an error in citing it or not. I just  
21 wanted to know, because I've seen this cited by you a  
22 number of times in other presentations, and it always  
23 says "ethyl mercury." And I wanted to know whether  
24 that was what you were believing this article was  
25 about.

DETH - CROSS

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1 I'm sorry. To speed us up, you believe the  
2 article is about methyl mercury.

3 A I don't need to be speeded up, I need to  
4 find the reference here, and I'm looking for it here.  
5 So monkeys with thimerosal --

6 MR. WILLIAMS: Page 4.

7 THE WITNESS: Uh-huh. It's page, and it's  
8 reference 20?

9 MR. WILLIAMS: Reference 20.

10 THE WITNESS: Okay.

11 BY MR. MATANOSKI:

12 Q Doctor, actually, all I want to know is when  
13 you were discussing it, whether you thought this study  
14 was about ethyl or methyl. And you've answered that  
15 you do understand that this study is about methyl.

16 A Actually, I'm sort of shocked. I'm looking  
17 at the reference which says "ethyl" in the title. Is  
18 there an M missing in that title?

19 Q Yes, but in discussing this, in discussing  
20 it, it's not --

21 A It's probably not going to make a difference  
22 when we're done figuring this out, because ethyl and  
23 methyl will result in the same trans-blood-brain  
24 barrier potential, and a similar release of inorganic  
25 mercury. But it will be important to make sure we

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1 have either the M or -- so it is, if I'm looking at  
2 the title here, it should be methyl, not ethyl.

3 Q Okay. And as you just said, it's not  
4 important because, in terms of the differences as far  
5 as you're concerned, because both methyl and ethyl  
6 will eventually become inorganic, which, as you're  
7 saying now for your hypothesis, that's the target  
8 species of mercury that's important.

9 A Yes, the long-term source of toxicity is the  
10 inorganic mercury.

11 Q And we know that methyl mercury is available  
12 from a variety of sources that are not vaccine,  
13 obviously actually isn't available through the vaccine  
14 agent.

15 A True.

16 Q So there are a number of environmental  
17 sources of methyl mercury which will eventually end up  
18 as inorganic mercury in your brain.

19 A True. Especially with advancing years, as  
20 it accumulates. Probably not common in younger  
21 children.

22 Q Do you know how, in the Charleston article  
23 we were just talking about, do you know how many  
24 micrograms of mercury per kilogram per day these  
25 squirrel monkeys were receiving?

DETH - CROSS

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1 A No.

2 Q I asked you earlier what your strongest  
3 evidence was. And you said the two James articles?

4 A My strongest evidence?

5 Q For your hypothesis.

6 A That's right, the strongest. Not mine, but  
7 the --

8 Q I'm sorry.

9 A -- strongest evidence for a role of impaired  
10 methylation and oxidative stress I believe comes from  
11 those two papers in particular.

12 Q And the first one that you cited in your  
13 report was cited as no. 9. And it's PML No. 49.

14 Did Dr. James ever directly measure the  
15 activity or level in the methionine synthase in this  
16 study?

17 A No.

18 Q Did she ever measure thimerosal, ethyl  
19 mercury, or inorganic mercury in this study? I'm  
20 sorry, we'll need an audible response.

21 A No. I'm just trying to understand why you  
22 might expect that she would. The study was not aimed  
23 at doing that. I mean, it had nothing to do with  
24 mercury administration, it had nothing to do with  
25 specifically measuring methionine synthase. It did

DETH - CROSS

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1 what it did, it measured what it planned to.

2 But if you want me to answer, I'll just say  
3 no.

4 Q And did Dr. James provide any information on  
5 caloric intake and diet in these studies?

6 A Not to my recollection.

7 Q Can GSH levels change depending on diet?

8 A They can.

9 Q And are you aware that in this study, the  
10 authors state that -- we'll bring this up for you in a  
11 moment. Our attempts to interpret these preliminary  
12 metabolic findings are clearly speculative, and a  
13 better understanding of the abnormal one-carbon  
14 metabolism in these children will require additional  
15 research efforts.

16 A Uh-huh.

17 Q Let's turn for a moment to the other James  
18 study. Can you pull that up?

19 Are you aware what Dr. James stated in that  
20 study?

21 (Discussion held off the record.)

22 Q "Clearly these new findings should be  
23 considered preliminary until confirmed in larger  
24 population-based studies." Have such studies been  
25 conducted and published?

DETH - CROSS

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1           A     Following up on her studies in larger  
2     populations? I don't believe anybody has, to my  
3     knowledge.

4           Q     You were asked a question about chelation,  
5     and you talked about oxidative stress to the body, of  
6     areas of the body besides the brain. Does oxidative  
7     stress in these other areas of the body affect  
8     neuroinflammation in the brain?

9           A     There is metabolic relationships between the  
10    rest of the body and the brain. I particularly focus  
11    on the liver, important metabolic organ that it is.  
12    And ultimately the sulphur material in our diet  
13    processed through the liver, put into the bloodstream,  
14    and eventually transferring out of the bloodstream and  
15    across the blood-brain barrier represents the source  
16    of sulphur resources to the brain.

17          Q     Will decreasing oxidative stress in these  
18    other areas of the body affect neuroinflammation in  
19    the brain?

20          A     Not -- well, let's make sure what the limits  
21    of direct and indirect are. Indirectly, yes. By  
22    making resources available, antioxidant resources  
23    available, not utilized preferentially in the  
24    periphery. They have a better chance of being  
25    available for use in the brain.

DETH - CROSS

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1           And there's a lot of resources to consider  
2 here. For example, when one wants to consider what  
3 keeps glutathione reduced. I had made this sort of  
4 visual analogy between oxidized and reduced  
5 glutathione. The enzyme that does that requires  
6 NADPH. NADPH arises from glucose metabolism. And the  
7 reduced NADPH ultimately becomes available, as well as  
8 even the glucose that becomes available to the brain,  
9 you know. It depends in part of peripheral  
10 metabolisms, as well.

11           And these two, they don't operate in  
12 isolation from each other. And so if you have  
13 oxidative stress in the periphery of your body, you  
14 will have consequences in the brain. Not even to  
15 mention the cytokines and inflammatory remediator  
16 substances produced by activated lymphocytes in the  
17 periphery finding their way to the brain, otherwise  
18 causing inflammation.

19           Q     So it will affect neuroinflammation in the  
20 brain if you reduce or affect the levels of oxidative  
21 stress in other areas of the body.

22           A     Peripherally, that's right. Another area,  
23 if you care to pursue it, would be the intestines, the  
24 gut, if we consider that part of the periphery. The  
25 ability of the intestine to extract, transport in a

DETH - CROSS

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1 normal manner, nutrients necessary for the brain. It  
2 might depend on whether the gut is inflamed.

3 MR. MATANOSKI: Now, if I could ask counsel,  
4 opposing counsel if they could put up the slide  
5 presentation. Can we switch back then over to the  
6 presentation? Now if you can move it forward to slide  
7 no. 7.

8 BY MR. MATANOSKI:

9 Q I'm going to ask you a series of questions,  
10 Doctor, hopefully moving through this very rapidly.  
11 I've seen some of these slides before in presentations  
12 you've given in other, in other --

13 A I gathered that.

14 Q Yes. But I'm not sure which ones in all  
15 I've seen elsewhere. And I wanted to take you through  
16 some of these slides and ask you what is different  
17 about this slide, if anything, from what you prepared  
18 before and what you have here today?

19 Now, let's start with 7. Can you tell me on  
20 that slide if you, if it's one that you've used  
21 before, and if you altered it in some way for the  
22 presentation today? And what that alteration, if any,  
23 was, or alterations, if any, were.

24 A Sure. The basics of the slide are the same,  
25 and you recognize that, as well. The genetic risk

DETH - CROSS

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1 factors used to be on the right side, and I moved it  
2 over to the left, and I added on the upper right,  
3 mitochondrial dysfunction and neuroinflammation in  
4 recognition of the fact that this terminology,  
5 neuroinflammation, was going to be central to the  
6 proceedings here.

7 I wanted to make it clear that  
8 neuroinflammation was in fact associated with an  
9 increase in oxygen radical numbers, and also  
10 recognizing that because of the Poling decision and  
11 related events, that the role of mitochondria as a  
12 source of those oxygen radicals was worth adding to  
13 this slide.

14 Q So prior to this litigation, when you were  
15 discussing this theory and explaining it, you never  
16 talked, or at least you never used neuroinflammation  
17 and mitochondrial dysfunction in explaining your  
18 hypothesis.

19 A On this slide? On this slide.

20 Q Right.

21 A On this slide, right? That would be  
22 incorrect.

23 Q The part, the part of your hypothesis that  
24 you use in this slide to explain, you had never  
25 previously discussed mitochondrial dysfunction or

DETH - CROSS

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1 neuroinflammation.

2 A I actually can't really say that. Even  
3 though we're nitpicking here, I frequently include  
4 neuroinflammation and mitochondria as a source of  
5 oxygen radicals in my talks.

6 And so you're asking me now what the verbal  
7 accompaniment was to this slide; did I ever talk about  
8 where the oxygen radicals came from? It wouldn't be  
9 unlikely that I'd mention that they come from  
10 mitochondria.

11 And here what I'm really doing is just sort  
12 of bringing that to a visual form, rather than  
13 thinking it. Again, I don't think that's a big point.

14 Q So you didn't feel that it was important  
15 enough to include on your visual depiction of the  
16 process you were describing.

17 A It was always a balance of how much  
18 information to put on a slide. One has to be careful  
19 not to clutter it. And for the most naive reasons one  
20 can imagine, I decided to add that here. I think --

21 Q Not only add it, but discuss it here,  
22 correct?

23 A Well, if it was there, I felt an obligation  
24 to discuss it.

25 Q Can we move to slide 18? Have you used this

DETH - CROSS

644

1 slide before?

2 A Maybe. Let's see. Not in the precise form.

3 Q Was it altered in some way for this  
4 presentation today?

5 A I added glutamate to the EAAT-3 to indicate  
6 that glutamate can be alternatively transported.  
7 Whenever I give this talk, I say that it's excitatory  
8 amino acid transporter 3, and the excitatory amino  
9 acid is glutamate. But having explicitly presented  
10 that here, it makes it easier for the viewer to grasp  
11 what I'm communicating or saying.

12 Q Any other alterations to this slide?

13 A Well, I added the hydroxocobalamin over  
14 there in green. And let's see, did I say, did I  
15 change glial cells to healthy, and in parentheses  
16 astrocytes? I have a suspicion that you know better  
17 than I about that.

18 Q I'm just trying to find out what you --

19 A Again, I don't remember at what point I  
20 changed that. It may be that I didn't use that in  
21 prior presentation, but I can't remember. I make  
22 presentations regularly.

23 Q So from your recollection right now, you  
24 altered this slide to add glutamate, and perhaps glial  
25 cells.

DETH - CROSS

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1 A The hydroxocobalamin, I now I added that.

2 Q And the hydroxocobalamin.

3 A And I'm not sure about that last part, the  
4 healthy glial cells. It was meant to illustrate yes,  
5 that when they're healthy they're putting out  
6 glutathione. Whereas if they weren't healthy,  
7 otherwise they were oxidatively stressed themselves,  
8 they wouldn't be putting out the glutathione.

9 Q Will you turn to slide 20? Take a look at  
10 this. Have you used this slide before?

11 A No.

12 Q This is, I see this is essentially --

13 A Custom for this occasion.

14 Q Well, it looks like it's a repeat of the  
15 slide that you had before.

16 A If you're going to ask me about whether it's  
17 the same one, it's obviously not the same one because  
18 it's got thimerosal on it, and the others didn't.  
19 Don't.

20 Q Are you sure this isn't just taking the  
21 slide that you had in 18 and changing it? If you look  
22 at the slide in 18, and then you look at the --

23 A They're all based on, they're all based on  
24 some original slide. And I'm sure 18 is not equal to  
25 20. What are you -- I'm not sure. Are we on the same

DETH - CROSS

646

1 wavelength about what your question is?

2 Q I'm sorry, but you can't have them side by  
3 side the way it's set up here. Do you have the  
4 presentation in front of you?

5 A Okay, let me do that here. So what is the  
6 question? Is this the same, is 20 the same as 18?

7 Q Eighteen you believe you used before, and  
8 made some alterations to it for this hearing.

9 A Uh-huh. And here --

10 Q And if you look at it side by side with 20,  
11 it looks like it's largely the same slide, with a few  
12 changes to it. You're working off of the same slide  
13 that you originally used previously, and making  
14 additional changes to it here.

15 I think, I'm sorry. If you could just --

16 A I wish we were helping autism by doing this,  
17 but I don't think we are. I can't understand at all  
18 what's --

19 Q Take a look at the two side by side.

20 A Yes?

21 Q Are you saying you started from scratch on  
22 slide 20?

23 A I didn't say I started from scratch. No,  
24 these are all a template. It takes a certain effort  
25 to do that, so I'll use the same, the players are the

DETH - CROSS

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1 same, they're always there. It's a question of  
2 whether there's more or less of one of them. I'm  
3 trying to depict that by making either arrows or  
4 something like that different between them? Perhaps  
5 I've erred in some manner here, but this is the way  
6 that slides are made.

7 Q No, I just -- and this one, working from the  
8 template that you've used previously, glutamate and  
9 perhaps thimerosal, is that it?

10 A Of course it is. That's what the purpose of  
11 this slide is, to show that thimerosal in slide 20 is  
12 illustrated as inhibiting EAAT-3, because the data  
13 coming up in slide 21 shows that.

14 Q So when you previously -- moving back to 18,  
15 then. When you previously gave this, glutamate and  
16 these other things, additions didn't appear on this  
17 slide. They weren't important for your explanation at  
18 that time.

19 A I added glutamate because I got tired of, I  
20 did a better job. Because usually I'd talk about the  
21 fact that glutamate can also be transported there.  
22 But instead of having to remember to do that, if it is  
23 on the slides, no one can then otherwise ignore the  
24 fact that this transporter, named for glutamate, and  
25 otherwise can alternatively turn towards glutamate.

DETH - CROSS

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1 Which is an important function that it plays.

2 Q Doctor, I'm going to move on, then, to --

3 SPECIAL MASTER VOWELL: Mr. Matanoski, how  
4 much longer do you think this will take?

5 MR. MATANOSKI: I'm very close to the end.

6 SPECIAL MASTER VOWELL: Mr. Williams, do you  
7 anticipate redirect?

8 MR. WILLIAMS: About two minutes' worth.

9 SPECIAL MASTER VOWELL: Okay. We are just  
10 approaching what we said was our 6:00 p.m. stop time,  
11 and I wanted to make sure that we weren't -- it  
12 complicates getting people out of the building.

13 MR. MATANOSKI: Yes, ma'am.

14 SPECIAL MASTER VOWELL: Okay. Please  
15 proceed.

16 BY MR. MATANOSKI:

17 Q Slide 21, is this published data?

18 A No.

19 Q And slide 24, is this published data?

20 A As I indicated during my testimony, these  
21 experiments are not published yet. They are  
22 experiments that were undertaken to follow up on the  
23 Waly, et al published results, showing that methionine  
24 synthase was inhibited. And we wanted to know why was  
25 it inhibited. Why could it be zero activity after

DETH - CROSS

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1 thimerosal, for example, but also after other  
2 interventions. Because inhibitors don't normally go  
3 to zero. They may have partial effects.

4 And so we were certainly trying to  
5 understand in more detail what was going on. And when  
6 we did, we found that the zero activity was because  
7 the methyl B12 was not available, and wasn't required  
8 by the enzyme. So we undertook these series of  
9 additional, but not-yet-published, studies to flesh  
10 out the details of why methionine synthase was being  
11 inhibited.

12 Q When did you complete the work in this  
13 study?

14 A Which one are you referring to here?

15 Q Twenty-one.

16 A Twenty-one. I'm thinking that that was  
17 November, November of 2007.

18 Q This isn't discussed in your expert report,  
19 then.

20 A Not explicitly, no. Actually, I think, did  
21 I reference the general idea that cysteine  
22 availability was limiting? And I may have also, and  
23 I'm trying to refresh my memory, mentioned that  
24 cystine uptake was important, as well, but not this  
25 exact result, because we hadn't obtained it at that

DETH - CROSS

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1 time.

2 Q And slide 24, that's new. And when did you  
3 finish that?

4 A Slide 24?

5 Q Slide 24. That's new, isn't it?

6 A Yes. Actually, that was obtained somewhat  
7 earlier, I believe, perhaps even over the summer, or  
8 even slightly before that.

9 Q And slide 26, is that new? Unpublished  
10 material?

11 A That was last April, I believe. April,  
12 perhaps March, the time period of I would say March of  
13 2007.

14 Q Slide 28. That's not published. When was  
15 that available? Because that's not published,  
16 correct?

17 A That's correct. And --

18 Q When was that available?

19 A When was it performed? Performed, I guess  
20 available to me?

21 Q Yes.

22 A Again, I estimate this is probably February  
23 of 2007.

24 Q And slide 30, same question. Is that new?

25 A No, that's published.

DETH - CROSS

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1 Q I'm sorry, I'm sorry, you're right. Slide  
2 31? Was that published?

3 A We've had that one for a while, so that then  
4 is probably some time in 2006, maybe September of  
5 2006.

6 Q And you said that's not published?

7 A Correct.

8 Q Slide 34. When was that available? Is that  
9 unpublished?

10 A It is unpublished, and that was, let's see.  
11 I think it was early summer of last year. So, let's  
12 see. I guess it would be over the summer of 2007,  
13 when the experiments were done. The analysis took us  
14 a little longer to do.

15 Q Now, I think the rest of this is that same  
16 study, the rest of these slides, 35, 36, 37 all are  
17 descriptions taken from that study that you had the  
18 data in summer --

19 A Well, 36 was just available to me actually  
20 only a matter of a few weeks ago.

21 Q Okay. And I'm sorry, 36 did you say was  
22 only available to you a matter of a few weeks ago?

23 A Uh-huh.

24 Q The other two slides, that information was  
25 available before? Is that --

DETH - CROSS

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1 A Correct.

2 Q And that would have been summer of 2007 on  
3 those?

4 A Correct. Correct.

5 Q And slide 41, this represents your -- as I  
6 took it, the way the presentation went, this  
7 represents the hypothesis that you laid out today. Is  
8 this --

9 A This is published. I didn't put the  
10 reference here. This is, with the exception of the  
11 addition of the word "neuroinflammation," it was  
12 published in that review article on neurotoxicology.

13 Q So this is the, with the exception of the  
14 addition here of "neuroinflammation," this is  
15 essentially -- well, put the neuroinflammation aside.  
16 This represents the pictorial representation of what  
17 you described to us as your hypothesis.

18 A Yes, that's a reasonable description.

19 Q And this was put in a publication that came  
20 out in 2008, you said?

21 A Correct.

22 Q And the only change is that you've added  
23 neuroinflammation.

24 A Yes, I believe that's the only change. Yes.

25 Q Does the representation here, even with

DETH - CROSS

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1 neuroinflammation, does that represent the same  
2 understanding or the same idea that you were trying to  
3 express when you made the publication in 2008?

4 Has your, has your hypothesis changed  
5 because you're added neuroinflammation.

6 A No. The word "neuroinflammation" was just  
7 added for the change in here so that we could make it  
8 clear that neuroinflammation and oxidative stress are  
9 closely related principles.

10 Q So the hypothesis is the same one that you  
11 published, in other words.

12 A That's correct. Yes.

13 Q And in that publication you discussed the  
14 role of neuroinflammation as far as your overall  
15 hypothesis, is that right?

16 A I included neuroinflammation, a discussion  
17 of that.

18 Q Let me bring that up. This is your 2008  
19 paper, as you pointed out. I think I might have the,  
20 that was one of the recently submitted articles by the  
21 PSC. I'm trying to find the Petitioner's Master List  
22 Number for that, and I don't seem to have it here. I  
23 apologize.

24 MR. WILLIAMS: 563.

25 MR. MATANOSKI: Thank you, 563.

DETH - REDIRECT

654

1 BY MR. MATANOSKI:

2 Q In that, you said elevated levels of  
3 inflammatory cytokines and evidence of microglial  
4 activation -- oh, there's a typo there, you use it  
5 twice -- was observed in post-mortem brain sections,  
6 including the presence of neuronal inflammation.

7 I don't want to read to you, Doctor. This  
8 lays out your hypothesis, as far as the  
9 neuroinflammation does. This is how it fits in  
10 overall with your theory?

11 A This is certainly a component of it.

12 Q This, though, is meant to express the role  
13 of neuroinflammation as you've discussed it here  
14 today?

15 A In this paper, it served the purpose that it  
16 served now, today? I'm not, I don't expect it as a  
17 conflict between us. If I were going to buy one, then  
18 I'd like to know about it. But otherwise, hopefully  
19 I'm consistent in saying that neuroinflammation  
20 includes oxidative stress, and that certain studies  
21 have revealed neuroinflammation in the brains of  
22 autistic subjects or biomarkers indicating oxidative  
23 stress. And that these are terms that interdigitate  
24 with each other.

25 Q So is it fair to say that the hypothesis

DETH - REDIRECT

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1 that you've described in this paper is the same one  
2 that you gave here today?

3 A In general terms, yes.

4 Q And in that you stated that -- move to the  
5 quote about the starting point.

6 You describe this hypothesis that is "may  
7 serve as a useful starting point that can be  
8 critically tested, accordingly revised, and even  
9 discarded?"

10 A Yes.

11 Q So the hypothesis you presented to the Court  
12 today still awaits critical testing?

13 A There are many ways to test it, and we are  
14 in the middle of continuing to do that, yes.

15 MR. MATANOSKI: I have no further questions.

16 SPECIAL MASTER VOWELL: Go ahead, Mr.

17 Williams.

18 REDIRECT EXAMINATION

19 BY MR. WILLIAMS:

20 Q I just have one quick topic. There was a  
21 question about your source of funding, and Mr.  
22 Matanoski pulled a web page out of Safe Minds to imply  
23 that there was motivation of that organization to  
24 prove the thimerosal-autism connection.

25 There was also a question to you about why

DETH - REDIRECT

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1 the NIH had turned down your application for funding.  
2 And I just want to show you a quote from the former  
3 head of the NIH, and then ask you about that for a  
4 second.

5 We can put it up on the screen. This is  
6 from the website of CBS News from yesterday. And  
7 let's just look at what she said. Could you read  
8 that, please, Doctor?

9 A Starting at the top?

10 Q Yes, just start at the top.

11 A "Dr. Bernadine Healy is the former head of  
12 the National Institutes of Health, and the most well-  
13 known medical voice yet to break with her colleagues  
14 on the vaccine autism question.

15 "In an exclusive interview with CBS News,  
16 Healy said the question is still open. 'I think the  
17 public health officials have been too quick to dismiss  
18 the hypothesis as irrational,' Healy says. But public  
19 health officials have been saying they know they've  
20 been implying to the public there's enough evidence,  
21 and they know it's not causal, Atkinson said.

22 "'I think you can say that,' Healy said."  
23 You can't say that. I mean, this is out of context,  
24 and I really have a hard time.

25 Q There's more coming that will help put it in

DETH - REDIRECT

657

1 context. Okay.

2 SPECIAL MASTER VOWELL: Mr. Williams?

3 MR. WILLIAMS: Yes?

4 SPECIAL MASTER VOWELL: Suppose you get to a  
5 question here? Because having witnesses read  
6 documents that you may introduce is not helpful to me.  
7 I don't know about my colleagues.

8 MR. WILLIAMS: Okay. I thought I was doing  
9 exactly what Mr. Matanoski did, which was reading off  
10 a website and asking him what he thought of it.

11 SPECIAL MASTER VOWELL: Well, that's why I  
12 asked if you were going to get to a question.

13 MR. WILLIAMS: All right.

14 BY MR. WILLIAMS:

15 Q I'll read this statement from Dr. Healy, and  
16 then ask you whether you agree with it.

17 She goes on to say that public health  
18 officials have intentionally avoided researching  
19 whether subsets of children are susceptible to vaccine  
20 side effects, afraid the answer will scare the public.  
21 And then she says there is completely expressed  
22 concern that they don't want to pursue a hypothesis,  
23 because that hypothesis could be damaging to the  
24 public health community-at-large by scaring people.

25 Now, my question to you is, do you have any

DETH - REDIRECT

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1 reason to think that the NIH turned down your grant  
2 for these reasons?

3 A I do. I expressed before the fact that  
4 reviewers, primary reviewers in the very first  
5 paragraphs of their supposed review instead took a  
6 government statement indicating that thimerosal does  
7 not cause autism; and on the basis of that, indicated  
8 it was therefore not appropriate to study thimerosal.  
9 This is, as I'm saying, unfortunately not restricted  
10 to government agencies. I've had the same response  
11 from reviewers, you know, in the private sector,  
12 foundations.

13 And so it's unfortunate. And I understand  
14 the importance of preserving public confidence in  
15 vaccines. I think the most, the best way to gain that  
16 confidence is by scientific validated studies of their  
17 safety and their components' safety. But nonetheless,  
18 it's frustrating to not be able to pursue important  
19 questions because of lack of funding.

20 MR. WILLIAMS: Thank you. That's all I  
21 have.

22 SPECIAL MASTER VOWELL: Mr. Matanoski?

23 MR. MATANOSKI: Briefly.

24 //

25 //

DETH - RE-CROSS

659

1 RE-CROSS-EXAMINATION

2 BY MR. MATANOSKI:

3 Q Doctor, just to be clear, your particular  
4 study was denied by your colleagues in academia, is  
5 that correct?

6 A I don't remember. Because it's blinded, I'm  
7 not allowed to know who the reviewer was who took that  
8 action. I can assume it was the panel; I don't  
9 believe it was exclusively from academia.

10 Q It was not governmental officials involved  
11 in that decision.

12 A Again, the people on these panels are not  
13 government officials, though they may have government  
14 positions. They could be scientists at government  
15 locations. They could be in the private sector that  
16 are probably likely to be academicians. But that is,  
17 I really don't know. I don't know who that person was  
18 who chose to do that.

19 Q And you just stated that you've had other  
20 grants turned down by private foundations.

21 A This is a general issue. The general issue  
22 is will agencies, will reviewers allow studies of this  
23 issue, or not. Will they fund studies of this issue  
24 or not? And let's be honest. The truth is there has  
25 been restricted funding. And while the parent

DETH - RE-CROSS

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1 supporting groups have taken on the necessity of  
2 funding those, their resources are limited; and as a  
3 result, there probably isn't the finding in terms of  
4 how broad the question is explored.

5 Q So is it your personal belief that it didn't  
6 have anything to do with the merits of the grant that  
7 you put in?

8 A I can't be confident it had nothing. But  
9 just the actual cutting and pasting of an official  
10 position has no real role, in my opinion, in the  
11 evaluation of the scientific validity of the research  
12 proposal.

13 MR. MATANOSKI: I have no further questions.

14 SPECIAL MASTER VOWELL: I take it we are  
15 concluded for today, and we can excuse Dr. Deth.

16 (Witness excused.)

17 SPECIAL MASTER VOWELL: All right. We will  
18 reconvene at 9:00 a.m. tomorrow morning.

19 (Whereupon, at 6:12 p.m., the hearing in the  
20 above-entitled matter was recessed, to reconvene at  
21 9:00 a.m. the following day, Wednesday, May 14, 2008.)

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23 //

24 //

25 //

661/760

REPORTER'S CERTIFICATE

DOCKET NO.: 03-584V; 03-215V  
CASE TITLE: King and Mead v. U.S.  
HEARING DATE: May 13, 2008  
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 United States Court of Federal Claims.

Date: May 13, 2008

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