

UNITED STATES
COURT OF FEDERAL CLAIMS

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. MEAN,)
A MINOR,)

Petitioners,)

v.)

Docket No.: 03-215V

SECRETARY OF HEALTH AND)
HUMAN SERVICES,)

Respondent.)

Pages: 1 through 286/350

Place: Washington, D.C.

Date: May 12, 2008

HERITAGE REPORTING CORPORATION

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1220 L Street, N.W., Suite 600
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IN THE UNITED STATES COURT OF FEDERAL CLAIMS

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

Monday,
May 12, 2008

The parties met, pursuant to notice of the
Court, at 10:00 a.m.

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

APPEARANCES:

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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>VOIR DIRE</u>
<u>For the Petitioners:</u>					
Sander Greenland	69	119	--	--	--
Vasken Aposhian	136	242	--	--	--

E X H I B I T S

PETITIONERS'

<u>EXHIBITS:</u>	<u>IDENTIFIED</u>	<u>RECEIVED</u>	<u>DESCRIPTION</u>
1	72	72	Greenland slide presentation
2	137	137	Aposhian slide presentation

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P R O C E E D I N G S

(10:00 a.m.)

SPECIAL MASTER HASTINGS: Good morning to all. Please be seated.

My name is George Hastings. I'm a Special Master of the U.S. Court of Federal Claims. To my left is Special Master Denise Vowell, to my right is Special Master Patricia Campbell-Smith, and together we would like to welcome you all to a special evidentiary hearing of the United States Court of Federal Claims.

I'll apologize for the scratchy throat this morning. Hopefully I'll be a little better, but that will help me keep my opening statement perhaps a little shorter here this morning.

I want to start by saying that today we are here really for two purposes. The first purpose of course of the hearing that we begin today is to hear the claims under the Vaccine Act of two particular children. That's Jordan King and William Mead, two boys who suffer from autism and certain other medical conditions. The first purpose of this hearing then is to determine whether the autism disorders of Jordan King and William Mead and their other related conditions were vaccine caused.

1 However, there is a second very important
2 purpose of this hearing. That is, Jordan and William
3 are two of about 5,000 children who suffer from autism
4 or similar disorders and who have filed compensation
5 claims under the Vaccine Act. These 5,000 claims have
6 been grouped together in a joint proceeding known as
7 the omnibus autism proceeding.

8 The committee of attorneys who represent the
9 Petitioners in the omnibus autism proceeding have
10 designated Jordan's and William's cases as two of the
11 test cases in that proceeding. Therefore, in this
12 hearing today and over the next three weeks we will
13 hear not only about Jordan's and William's particular
14 disorders, but also extensive expert testimony
15 concerning the Petitioners' second general causation
16 theory; that is, the general theory that thimerosal-
17 containing vaccines acting alone can directly cause
18 autism or contribute to autism.

19 As some of you may be aware, last year the
20 Petitioners presented their first general causation
21 theory. In this hearing then the Petitioners present
22 their second theory, which focuses exclusively on the
23 thimerosal-containing vaccines as a possible cause of
24 autism.

25 These two purposes for the hearing explain

1 why up here on the bench you see three Special Masters
2 and not just one. All three of us Special Masters are
3 here in order to hear the general causation testimony
4 to be presented during this hearing, and then each of
5 us will apply that general causation evidence to
6 decide a particular individual test case under the
7 Vaccine Act.

8 I will decide the test case of Jordan King.
9 Special Master Campbell-Smith will decide the case of
10 William Mead. A third individual case was also
11 scheduled to be heard during this trial to be decided
12 by Special Master Vowell, but that family recently
13 chose to withdraw from this particular trial.

14 Therefore, a third testimony case relating
15 to this theory of causation is in the process of being
16 selected, and Special Master Vowell will hear the
17 individual evidence in that case sometime later this
18 year and then decide that third case, again applying
19 the same general causation evidence developed during
20 this trial.

21 I want to begin this hearing thus by
22 acknowledging certain very important people who are in
23 the courtroom today: The families of the injured
24 children. With us today we have William Mead's
25 mother, Ms. Shirley, and several members of the Mead

1 family. We thank you folks for being here with us
2 today. Later this week we will also have members of
3 the King family and other members of the Mead family.

4 All three of us want to extend our sympathy
5 to all those families. Clearly both these families,
6 as with all of the families of autistic children, have
7 been through some difficult times. They are certainly
8 deserving of sympathy, but they are also deserving of
9 great admiration for the way they have coped with
10 their children's disorders.

11 We thank these families for generously
12 agreeing to have their cases designated as test cases
13 in the omnibus autism proceeding. Members of each of
14 the two families will be testifying in this hearing
15 later this week. Again, we thank all the King and
16 Mead family members for their participation in this
17 hearing.

18 We also wish to thank the counsel for both
19 sides who will be presenting your evidence during this
20 hearing. We know that they have worked enormously
21 hard to prepare for this hearing, and we appreciate
22 that hard work. We also thank the expert witnesses
23 who have agreed to testify before us.

24 We thank the Judges of the Court of Federal
25 Claims for the Federal Circuit who have generously

1 allowed us to take over one of their courtrooms for
2 the next three weeks. We thank the U.S. Marshals and
3 all the other wonderful employees of both of the
4 Courts housed in this building who have assisted us so
5 well in preparing for and conducting this hearing.

6 Next we thank all of you here in the
7 courtroom for being here. We welcome all of you
8 again. Finally, we note that a number of people are
9 listening to this hearing at this time by means of
10 telephone conferencing and that a number of other
11 people will listen to the audio portion of this
12 hearing by downloading that audio off the internet.
13 We welcome all of you who may be listening to this
14 hearing by those means as well.

15 For those of you who will be here or be
16 listening to this hearing for more than just today, we
17 would like to give you a brief roadmap for the
18 proceeding. After today we will begin at 9 a.m.
19 Eastern time each day. We will take a lunch break of
20 about one hour probably sometime around 1 p.m. We
21 will adjourn each day probably sometime around 5 or
22 6 p.m., but sometimes earlier or sometimes later
23 depending on the witness schedule for the day.

24 Next, I note that during this hearing the
25 three Special Masters will be taking turns at

1 presiding over the hearing. During the family
2 testimony specific to the Jordan King case I will
3 preside, and during the family testimony concerning
4 the William Mead case Special Master Campbell-Smith
5 will preside. During the general causation hearing,
6 which is going to be most of the testimony, we will
7 rotate the task between the three of us of presiding.

8 Finally, I note that all of us here are
9 guests of the Federal Circuit in this courtroom.
10 Please, and this goes for counsel, witnesses, as well
11 as spectators in the courtroom. Please don't consume
12 any food or drinks of any type in this courtroom.

13 With that, we're ready to start the case.
14 I'll turn first to the Petitioners' counsel, who will
15 present an opening argument on the Petitioners'
16 behalf. Please proceed. Mr. Powers, will it be you?

17 MR. POWERS: Yes, it will, Special Master.

18 SPECIAL MASTER HASTINGS: Please go ahead,
19 sir.

20 MR. POWERS: Thank you, Special Master
21 Hastings and Special Master Campbell-Smith and Vowell.
22 Thanks also to everybody who has joined us live and
23 telephonically and also good morning to counsel for
24 the Department of Justice sitting up here along side
25 us in front of the bar.

1 My name is Tom Powers. I'm the attorney of
2 record for both Jordan King and William Mead. I'm
3 also, along with Mr. Williams, my law partner and
4 co-counsel at table here, representing the Petitioners
5 Steering Committee. That's the group of attorneys
6 that represent the interests of the 4,800 plus
7 families who have claims in the omnibus and the
8 presentation of the general causation evidence in the
9 test cases that have come before us and in the test
10 cases that are before us today.

11 Special Master Hastings might have been
12 sharing my notes on opening because I did want to talk
13 about what the hearing is about, and the first two
14 things on my list were the ones that the Special
15 Master identified.

16 The first, as an attorney, are the ones that
17 are frankly most important to me. Those are the cases
18 of the two clients that came to us seven years ago now
19 to represent them on behalf of their children for the
20 thimerosal mercury-induced injuries that they suffer,
21 for the regressive autism that they believe and we
22 believe and that we think the science supports are
23 related to the appearance of their regressive autism
24 symptoms, so obviously the hearings today and the
25 proceedings today are the beginning of the formal

1 resolution of the claims of two very important people,
2 Jordan King and William Mead.

3 It is also important and something that
4 we're very aware of as we take the stand today that
5 we're speaking on behalf of 4,800 other children who
6 have similar claims in the program. This is general
7 causation evidence that all of those families can
8 avail themselves of as they move forward to resolve
9 their individual claims, important claims to every
10 single one of those families.

11 There is, however, a third purpose of these
12 proceedings, and that is a very important one in terms
13 of public policy and what goes on outside this room
14 and outside the decisions that will be written in
15 these particular cases, and that's a decision about
16 science and a debate about the science because while
17 we have lawyers who are advocating positions, we have
18 experts who are offering opinions on both sides, and
19 those opinions certainly differ, often very
20 strikingly.

21 Ultimately what this is about is the
22 science, and what this case is about is not the
23 science necessarily of vaccines strictly. That is,
24 the families here are not taking the position that
25 vaccines generally or conceptually are a bad thing.

1 This is not an antivaccine case that you're going to
2 hear over the next three weeks. This is a case that
3 is focusing specifically on a mercury-based
4 preservative, thimerosal, that at this point in time
5 fortunately is largely a relic of history.

6 It's a relic of history largely because it
7 was an uncontrolled experiment on a huge population of
8 children, a huge exposure across a large population
9 over a long period of time over a substance that, as
10 you will hear particularly in Mr. Williams' portion of
11 this opening that we'll be dividing, is scientifically
12 supported to be related to the appearance of these
13 symptoms.

14 Over the last year and particularly in the
15 first round of test cases beginning with the Cedillo
16 case last June, it appears to be the position of the
17 Department of Health and Human Services that these
18 cases are implicitly sending a public message that
19 vaccines might be dangerous and therefore that the
20 message would get out to the public that people should
21 avoid vaccine and immunization rates should drop and
22 that we'll see outbreaks of infectious diseases.

23 But again we need to focus not on that
24 rhetoric. It's almost like an imaginal line of
25 rhetoric that focuses from the government's side

1 exclusively on got to be pro vaccine and support
2 immunizations. The guns on the imaginal line are so
3 focused on that method that it's important that the
4 Special Masters and the larger public health community
5 understand that what we're talking about for the next
6 three weeks and in hundreds of these claims is a
7 mercury-based preservative that's no longer out there.

8 Unfortunately, it still is in the flu
9 vaccine, most doses of the flu vaccine, and that
10 application of thimerosal quite frankly, based on the
11 science that Mr. Williams is going to describe, that
12 application of thimerosal ought to be in the dust and
13 of history as it is in the rightfully scheduled
14 pediatric vaccines.

15 During the course of the many years that
16 these cases have been litigation, one of the
17 unfortunate consequences of the Department of Health
18 and Human Services' position that they're going to
19 focus their attention on a rigid pro vaccine/pro
20 immunization message and ignore issues around mercury
21 toxicity, mercury exposure and thimerosal exposure is
22 that we've seen a commingling of interest between the
23 pharmaceutical industry and the vaccine manufacturers,
24 the health maintenance organizations and the
25 Department of Health and Human Services.

1 The consequence of that has been to cut off
2 at the knees the essential scientific inquiry that
3 needs to happen to make informed public health
4 decisions about immunization policy, but, just as
5 important, they've cut off at the knees to develop and
6 push out into the public the science that needs to be
7 out there so that people have confidence in the
8 immunization program and have confidence that their
9 vaccines are not only effective, but safe.

10 There are a number of examples. The Special
11 Masters are familiar with some of these because we've
12 been arguing these issues for years. There is the
13 issue of access to the Vaccine Safety Data Link. It's
14 a large, robust link database that independent
15 researchers can go into and link vaccine exposures to
16 a whole range of health outcomes.

17 Beginning in 2003, the Petitioners have
18 asked in various settings to get access to data within
19 the Vaccine Safety Data Link. We learned early on
20 that the federal government has outsourced or
21 privatized the management of the Vaccine Safety Data
22 Link, what was designed to be a public resource to
23 generate public information about public health
24 policy. They privatized it and are spending money
25 paying the trade organization for the health

1 maintenance organizations to sit over and administer
2 the Vaccine Safety Data Link.

3 The HMOs have refused access to the data
4 link to allow independent researchers to explore some
5 of the possible associations that are at issue in
6 these cases. The government has refused access to
7 external researchers. There's no access at all to
8 outcome data for children after 2000.

9 In 2005, the Institutes of Medicine had a
10 hearing and issued a report urging better public
11 access and better public utilization of this rich,
12 robust, unique database, and a lot of those policies
13 have not been implemented by the Department of Health
14 and Human Services.

15 There are studies that have been proposed
16 and haven't been done. We've heard for years now that
17 there was, for example, a study on thimerosal exposed
18 and nonthimerosal exposed children in Italy to look at
19 potential associations between exposed children and
20 unexposed children and health outcomes. We've never
21 seen the study that the federal government supposedly
22 was doing, and four years ago when we took depositions
23 they were saying that those were going to be out in
24 about two years.

25 We still haven't seen the study that is

1 looking at an association between thimerosal exposure
2 and autism and autism spectrum disorders. It's
3 getting pushed out year after year after year. The
4 science is needed, and the science isn't available.

5 About a year ago the National Institutes of
6 Environmental Health Sciences convened an expert panel
7 and recommended two very specific studies. One was
8 using the VSD to extend forward in time and in a
9 larger population the study that Dr. Verstraeten did
10 and published in 2003 in *Pediatrics* looking at an
11 association between thimerosal exposure and
12 neurodevelopmental outcome.

13 That recommended study by the HHS' own
14 entity, own agencies, hasn't been done. There was a
15 recommendation by that expert committee to do a study
16 of twins and siblings and looking at exposures and
17 outcomes. That study hasn't been done.

18 In 2004, when the IOM was looking at this
19 issue, they asked the pharmaceutical industry simply
20 to provide information that would provide people the
21 pure data on when thimerosal truly was out of the
22 nation's vaccine supply to get an idea of what the
23 exposure was in the pediatric population during that
24 slow phase-out of thimerosal as a preservative that
25 began in the year 2000. The IOM report said that the

1 pharmaceutical industry would not provide that
2 information.

3 This is science that needs to be available.
4 It's science that shouldn't be locked up behind the
5 rhetorical position of defending litigation. It's
6 important that the Department of Health and Human
7 Services be less focused on trying to prevail here and
8 more focused on developing the science to build public
9 confidence in vaccines and to have safe vaccines with
10 safe ingredients.

11 This idea that information isn't accessible
12 continues even within the litigation, however. The
13 Special Masters may know, and this was discussed
14 before the Cedillo hearing publicly, that it took
15 about a year for the Department of Health and Human
16 Services to agree to make these test case hearings
17 generally open to the public.

18 There was a concession made by the
19 Department of Health and Human Services in a case that
20 we had identified as a potential test case for hearing
21 during this round of general causation proceedings,
22 and the Department of Health and Human Services has
23 taken the position that the details of that
24 concession, the contents of the decision that might
25 inform how people who have clients from the program

1 evaluate their case and move their case forward and
2 get resolution, they're taking the position that that
3 is confidential and cannot be disclosed publicly.
4 Again, it's a focus on trying to prevail in the
5 litigation and not a focus on good science, safe
6 vaccines and public confidence.

7 Now, Mr. Williams is going to in a little
8 bit more detail walk everybody through the elements of
9 the Petitioners' theory of general causation, but I'm
10 going to do a very condensed version of that to give
11 the Special Masters and particularly people who are
12 here in person and attending a very quick roadmap to
13 how we will be laying out the case and how the
14 evidence is going to be coming in in this case.

15 The first point that we're going to make is
16 that neuroinflammation is a hallmark of regressive
17 autism. The second point that we're going to make is
18 that neuroinflammation leads to what Dr. Kinsbourne
19 has called the overactivated brain. Now,
20 neuroinflammation and overactivation in the brain is a
21 model. It's a useful model for explaining the
22 appearance of autistic symptoms and particularly the
23 symptom of regressive autism.

24 We'll also be putting on evidence that
25 anything that can trigger neuroinflammation

1 potentially can be a trigger for the symptoms of
2 regressive autism. Specifically we'll be looking at
3 the thimerosal issue and mercury, and we'll put on
4 evidence that inorganic mercury -- this is the Hg₂ or
5 Hg₂⁺. You'll see it written different ways.
6 Inorganic mercury is an agent that can trigger
7 neuroinflammation. Specifically, inorganic mercury
8 from thimerosal accumulates in the human brain. It
9 accumulates and it persists.

10 You'll also hear evidence that environmental
11 exposures, a number of them are now known to cause or
12 contribute to the appearance of autistic symptoms, and
13 you'll hear evidence that a gene/environment
14 interaction is a likely culprit in many, many cases of
15 autism; that is, the 88 to 90 percent of the cases
16 where there's no single identifiable genetic cause
17 there's a gene/environment interaction that's going
18 on.

19 What we will conclude through the evidence
20 on general causation is that thimerosal-containing
21 vaccines belong on the list of potential environmental
22 factors. If you have a list of environmental factors
23 that might contribute, thimerosal-containing vaccines
24 belong on that list for consideration whenever one is
25 evaluating what might have caused regressive autism in

1 a child where all the other known causes have been
2 ruled out through differential diagnosis. Those are
3 the elements of the Petitioners' general theory of
4 causation.

5 I want to start wrapping up my comments by
6 talking a little bit about the testimony you're going
7 to hear in the two individual cases. So if where we
8 are at the end of general causation is with a new
9 candidate really on the list of candidates for the
10 etiology of regressive autism, you're going to hear
11 evidence that in Jordan King's case and William Mead's
12 case these two boys have that differential that has
13 been performed by their treating doctors, by the
14 expert doctor, Dr. Mumper, who is the expert in
15 treating autistic children who has evaluated the
16 medical records.

17 What they will tell you is that each of
18 these boys, and these are important facts. Each of
19 these boys developed normally and typically, meeting
20 all of their developmental milestones well into and
21 after their first year of life.

22 You'll also hear testimony that within the
23 first year of life they received a significant
24 exposure to thimerosal. They received a full round of
25 pediatric vaccines containing thimerosal, containing

1 mercury before their first year of life. You'll also
2 hear that their symptoms of autism emerged only after
3 that full round of thimerosal had been administered.

4 Both of these boys have been diagnosed with
5 regressive autism, and regressive autism is really
6 characterized by three key things. This is the
7 testimony that you'll hear. First, I've alluded to
8 there's a period of normal, typical development for at
9 least a year going into the second year with no
10 obvious signs or symptoms of an autism spectrum
11 disorder. Both of these boys, from the testimony in
12 the medical records, meet that criteria.

13 The second element of regressive autism is
14 that at a point in time they actually lose, and this
15 is where the term regressive comes from. They lose
16 previously acquired skills. They lose the ability to
17 interact socially. They lose the ability sometimes to
18 speak, either losing discrete words or entirely losing
19 the ability to speak, so they regress in terms of the
20 skills they've already developed.

21 But just as importantly, they develop new
22 symptoms that were never there before, often
23 behavioral symptoms, self-stimulatory behavior or
24 stimming, as you might have seen it referred to in
25 some of the medical records: Odd facial tics, odd

1 vocalizations, brand new symptoms that weren't there
2 before. So you're presented with a very clear before
3 and after picture, and those are the pictures you're
4 going to see in both of these cases.

5 Based on that and the standard that you
6 apply here in the vaccine program on causation,
7 Petitioners believe that we will have satisfied our
8 burden of proof by showing a medically reasonable
9 theory of causation that's scientifically supported by
10 the peer reviewed, published scientific literature.
11 It is a logical scientific theory. Every element
12 follows in logical sequence, cause and effect, leading
13 to the appearance of regressive autism.

14 There's a temporal relationship between the
15 administration of the thimerosal in these vaccines
16 between day one and the end of 12 months and the later
17 appearance of symptoms after 12 months. All of those
18 elements will have met on the proof that I've just
19 described, and based on that both of these boys ought
20 to be entitled to compensation in this program.

21 But in addition to putting on that evidence,
22 you will hear additional evidence about why we know
23 that each of these boys was particularly susceptible
24 to the environmental insult that they received through
25 thimerosal injection because certainly not every child

1 who received that same load of shots developed
2 symptoms like Jordan's or like William's or developed
3 symptoms of any problem at all.

4 That goes back to the gene/environment
5 interaction. A lot of the genetic issues are unknown,
6 but we can see some indirect and circumstantial
7 evidence in the medical records of both boys that
8 first off they have a problem getting mercury out of
9 their body. They cannot excrete mercury and protect
10 their brain from the environmental insult of mercury
11 provided by thimerosal as well as other children can,
12 so you'll see evidence of that.

13 You'll also see evidence that both boys,
14 particularly in the couple of years after their
15 diagnosis, their systems were undergoing oxidative
16 stress, and that's going to be important evidence to
17 listen to in light of Dr. Deth's testimony that you're
18 going to hear.

19 We absolutely can see that this is indirect
20 evidence because the direct evidence is not available.
21 Evidence that children have ongoing neuroinflammation
22 in the brain is often only available via autopsy or
23 brain biopsy, and that's obviously not going to happen
24 in these cases. Evidence that inorganic mercury is
25 actually sequestered in the brain, the same thing.

1 It's generally autopsy and biopsy tissue sampling that
2 is not going to be done and hasn't been done in these
3 cases.

4 So the evidence is indirect and it is
5 circumstantial, but it is supportive of the general
6 theory of causation and supports awards of
7 compensation for both of the boys here and, as you
8 apply it to other cases down the road and you'll look
9 for similar evidence, when you see evidence in those
10 cases you also apply the general causation evidence
11 here and reach the same conclusion that those cases
12 ought to be resolved with compensation for those
13 particular children too.

14 Before asking Mr. Williams to talk in a
15 little more detail about causation, I do want to make
16 a brief comment about the tone, frankly, of some of
17 the expert reports that we saw from HHS and some of
18 the attacks on the experts that we have appearing
19 here. I would be remiss if I don't speak up on behalf
20 of the families and the people that are treating them.

21 There are doctors out there, Dr. Mumper
22 included, who are, quite frankly, pushing the
23 envelope. They're pushing the envelope because the
24 traditional medical establishment has been telling
25 them there's no known cause. There's no known cure.

1 There's nothing you can do. Cope with it.

2 These families, as you know from hearing
3 testimony in the other test cases and the testimony
4 you're going to have here, are doing more than cope.
5 They're working hard to recover their kids, and they
6 can only do it with the help of doctors like Mr.
7 Mumper and Dr. Green, who is the treating doctor. He
8 won't be testifying, but you've seen his medical
9 records in Jordan's case and in William's case. These
10 are doctors who are willing to challenge the
11 establishment on behalf of their patients.

12 I recall in the Cedillo hearing Dr.
13 Wiznitzer, when I asked him on cross-examination if he
14 believed children with autism and regressive autism
15 could be cured and could they recover and how he could
16 explain how some of the kids seemed to get better; not
17 all the way, but at least partway. He said well, they
18 just grow out of it.

19 This is not something that kids are growing
20 out of. This is something that they are fighting
21 their way back from. Their regressions are something
22 that present a battle. Their allies in their battle
23 are doctors like Dr. Mumper.

24 Again, I just think it's a shame that the
25 tone of some of the attacks that get right up against

1 the line that borders on offensive and the disdain
2 that some of the folks involved in the litigation seem
3 to have for people who are putting their necks and
4 their careers on the line to help these kids.

5 When somebody says well, these were covered
6 kids, that's just anecdotal, not scientifically robust
7 evidence. All of those anecdotes are our clients, so
8 to those, to the attorneys, to the families, it's not
9 an anecdote. It's a child, and it's a child that's
10 made progress of varying degrees, and that's the
11 evidence you'll hear here.

12 Again, I'm going to turn this over to Mr.
13 Williams. What these hearings are about are about the
14 science, the medicine, the integrity of the vaccine
15 program, a transparent process that builds public
16 confidence in the vaccines and ultimately a safe
17 immunization schedule for all children. Thank you.

18 SPECIAL MASTER HASTINGS: Thank you, Mr.
19 Powers.

20 Mr. Williams, please go ahead.

21 MR. WILLIAMS: Special Masters, counsel,
22 thank you for the opportunity to make this brief
23 opening statement. I'm going to briefly run through
24 the scientific evidence that you're going to hear over
25 the next three weeks and show you just a handful of

1 articles, what I think are probably the three or four
2 most important studies and articles that you will see
3 again and again throughout these three weeks.

4 Let me begin by summarizing again what our
5 theory is in this logical sequence of steps from the
6 vaccines with mercury in them to the inflammation in
7 the brain that leads to regressive autism. Thimerosal
8 delivers inorganic mercury to the brain. I'm going to
9 show you an infant monkey study in a minute that was
10 set up to mimic the infant vaccine schedule in this
11 country, and what it established was that inorganic
12 mercury accumulates in the brain of these children.

13 When that inorganic mercury is in the brain
14 it leads to oxidative stress for two reasons: One,
15 because of the neuroinflammation itself. As these
16 immune cells are activated, they release all kinds of
17 chemicals that cause oxidative stress and make it
18 harder for the brain to function, but in addition we
19 also know some of the mercury, some of this inorganic
20 mercury, accumulates in neurons itself, and when it's
21 in the neurons it directly leads to oxidative stress.

22 When a neuron is stressed out from too much
23 oxygen -- it doesn't have enough antioxidants
24 available -- it doesn't function correctly. It
25 doesn't die, but it doesn't work right. This is not

1 something that we've made up here. I'm going to show
2 you right now a paper that is one of the most
3 comprehensive reviews of how neuroinflammation can
4 lead to autism.

5 This is a paper entitled Autism at the
6 Beginning. It's written by a group of scientists from
7 California who run one of the largest research centers
8 in the world on the neurobiology of autism. Eric
9 Courchesne is the lead author.

10 At the beginning of this paper he describes
11 a case of regressive autism. He says: Autism begins
12 in many ways. On the second page he describes a case
13 of clearly pure regressive autism, a little girl who
14 develops absolutely normally until she's 14 or 15
15 months old and then suddenly loses her language
16 skills, loses her social attention skills and, as Mr.
17 Powers describes, starts to develop lots of new
18 symptoms. Thus, autism begins.

19 He cites literature to show that in one case
20 cited the autism began early, rapid and unmistakable.
21 You could see it before the kid was six months old.
22 That happens in most autistic cases, but then in a
23 small handful of cases you get this kind of sudden
24 regression.

25 Now, this is a diagram out of the article

1 itself that shows the brain structure, the complexity
2 of the brain at the time a child is born and at one
3 month and at six months and at two years. The
4 thimerosal injections occur in between each one of
5 those pictures. There's a thimerosal injection in
6 these children right after they're born. There's some
7 more between one and six months, and there's some more
8 between six months and two years. The inorganic
9 mercury accumulates all around those cells in these
10 children's brains as time goes on.

11 Let's go to the quote, Scott.

12 This is just a description in the paper
13 itself of the diagram that I just showed you. These
14 are actual pathological brain drawings from autopsied
15 children.

16 Okay. Next slide, Scott. I don't think we
17 need to show that one.

18 Now, these children also, we know from
19 autopsies of autistic children, get too many neurons
20 in some parts of their brains. The program that's set
21 up to make their brains grow correctly somehow goes
22 awry and they get too many neurons. What this paper
23 explains is how neuroinflammation, this activation of
24 the brain's innate immune system, can lead to too many
25 neurons.

1 It's triggered by adverse events that ignite
2 the neuroinflammatory reactions reported by Vargas.
3 Now, they're citing this Vargas paper, which you'll
4 also see. I'm not going to show that to you now, but
5 Vargas is a study from Johns Hopkins of autopsied
6 brains from autistic children that found
7 neuroinflammation in every one of them. Since then,
8 as you'll see, there's been other studies published
9 that have confirmed that.

10 Next?

11 This is still from the Courchesne paper.
12 Vargas found evidence of astroglial and microglial
13 activation and neuroinflammation in both the white and
14 gray matter in samples from the cerebellum.

15 Okay. Next? Next paragraph?

16 In all three regions there was enlargement
17 of astroglial cell bodies and their processes.
18 Microglial activation -- these are immune cells in the
19 brain -- was present in the cerebellum, in the
20 cerebral cortex and its underlying white matter, and
21 it had pronounced microglial activation with a loss of
22 some neurons.

23 In some parts of the brain you get too many
24 neurons. In other parts of the brain you get too few.
25 It's because the programming of how that brain grows

1 that I showed you from the diagram over time. Between
2 birth and two years, the brain grows four times as
3 large as it is when the child is born, just enormous
4 organization and connection and cell growth going on,
5 and if you get inflammation while that's happening it
6 disturbs the whole orchestration.

7 Now, this is how he explains that
8 neuroinflammation can cause these structural changes,
9 but he not only says it can explain these structural
10 changes. It can explain the functional changes too.

11 The next paragraph, Scott, I believe has a
12 quote about that.

13 Excess glial production or activation have
14 the potential to produce any or all of the previously
15 discussed microstructural findings, but also you'll
16 see he talks about here it also could underlie
17 theories of autism based on functional imaging
18 studies, so neuroinflammation from birth to two can
19 cause structural changes in the way the brain is
20 getting organized and connected, and it can also cause
21 functional changes.

22 Actually, this Johns Hopkins group is now
23 working on ways to try to attack the functional
24 neuroinflammation as a way to potentially cure autism.

25 Next? Next slide, please.

1 This paper also goes on to point out that
2 these inflammatory reactions are going to be
3 identified. Some trigger is going to set them off. A
4 chemical pathogen like a measles virus, or you'll hear
5 evidence of other viruses. There are studies that
6 show malaria at the age of two or three can induce
7 autism in children.

8 You'll hear evidence of lots of postnatal
9 viral infections that can lead to neuroinflammation
10 and autism, as well as chemicals that can do it. I'm
11 going to show you one in a second.

12 Okay. Let's go on.

13 Now, we know that inorganic mercury can
14 ignite this neuroinflammatory process because of a
15 series of studies done in Seattle at the University of
16 Washington in the mid 1990s on adult monkeys. You're
17 going to see these studies over and over again. I'm
18 not going to go through them in detail now, but I just
19 want you to see the first page of each one.

20 This was a whole series of adult monkeys
21 that were given very low doses of methyl mercury, low
22 doses that were intended not to provoke any kind of
23 acute reaction, and then they sacrificed the monkeys
24 at different times over a period of 18 months.

25 What they found, these studies all together

1 found that methyl mercury will enter the brain. It
2 will then have the methyl group detach and it will
3 form Hg⁺⁺, this inorganic mercury, and the inorganic
4 mercury accumulates in the brain over time and is
5 trapped there. It doesn't leave.

6 They estimated the half life of inorganic
7 mercury in the brain of these adult monkeys to be in
8 years, literally in years because it's so bound up
9 with molecules in there and in these neuro microglial
10 cells that it turns them on, but it can't get it out
11 of the brain so it's trapped there.

12 Let's show the next one, Scott.

13 This is another. They published five
14 separate papers out of this single study on adult
15 monkeys. This is talking about the changes in the
16 glial cells in one part of the brain of these monkeys.

17 Next? Next, Scott?

18 This is the paper where they looked to see
19 whether it was organic mercury or inorganic mercury in
20 the brains of these monkeys, and what they found was
21 that it was inorganic mercury.

22 Here's another paper from that study where
23 they confirmed that it was inside the glial cells, the
24 astroglial cells and the microglial cells, where the
25 demethylization took place. In other words, where the

1 inorganic mercury was formed was inside those cells.

2 Okay. Next one, Scott?

3 And they also then looked to see if the
4 number of cells changed in the brains of these
5 monkeys, and they found that they did. The microglia
6 -- those are the immune cells where this mercury is
7 trapped -- multiplied and proliferated and became
8 activated and was still activated at the very end of
9 the study after 18 months.

10 But moreover, they found a decrease in the
11 number of astrocytes, which is another type of glial
12 cell in the brain. The astrocytes provide vital
13 function and support to neurons, and what they found
14 was that as this inorganic mercury accumulated in the
15 brain it not only activated the microglia, but it
16 reduced the number of these supportive astrocytes.

17 You'll see the details of these studies as
18 we present the evidence and as we cross-examine the
19 defense witnesses next week.

20 Okay. Next?

21 So those adult monkey studies establish that
22 the methyl mercury was demethylated, changed to
23 inorganic mercury which was trapped in the brain and
24 which activated neuroinflammation, proving that
25 inorganic mercury in the brain will activate

1 neuroinflammation.

2 Now, this same group of researchers got a
3 grant to do this infant monkey study I told you about,
4 and what's very, very important for this proceeding is
5 that one of the authors of this study, this infant
6 monkey study, is Tom Clarkson, who is a defense
7 witness.

8 Now, he's not going to come this month.
9 Apparently we're going to hear from him in July, but
10 he's a co-author of this paper, which we think is
11 probably the single, central most important paper in
12 the trial. I highlighted his name there so you can
13 see that he was one of the authors of this paper.

14 Let me summarize quickly what this shows.
15 Yes. Let's go here first. The inorganic form of
16 mercury was readily measured in the brain of the
17 thimerosal-exposed monkeys. They had both infant
18 monkeys they fed methyl mercury to, and they had
19 infant monkeys that they injected thimerosal into.

20 There's a quote that shows where it
21 simulated the vaccine schedule, Scott. I wanted to
22 show that one for sure. I think it was on the prior
23 page.

24 SPECIAL MASTER HASTINGS: Just for the
25 record, this article is the Burbacher 2005 article.

1 MR. WILLIAMS: Yes. Thank you, Your Honor.
2 I should identify them better for the record.

3 Now, there's a quote that shows the
4 simulation if I can find it. It's on the first page,
5 Scott, in the right-hand column. Yes. Right here.

6 The dosages and schedule of the
7 administration of mercury were chosen to be comparable
8 with the current immunization schedule for human
9 newborns, taking into account that the monkeys grow
10 four times as fast. Again, this is a defense expert
11 who wrote this and who helped to design this study.

12 Now let's go to the chart of the blood. One
13 of the things, the defense reports are full of how
14 rapidly ethyl mercury is cleared from the blood
15 compared to methyl mercury in these children. The
16 same thing happened with the monkeys. This is a chart
17 of the blood levels of mercury after each injection.

18 You can see that this is in nanograms per
19 milliliter. That's the measure they have chosen. Our
20 experts will explain later how these concentrations
21 are picked, but the point is blood levels are very
22 high after the injection, but then cleared. Within
23 seven days they return almost to baseline.

24 And then another injection happens. The
25 blood levels go up. They come back down again in

1 seven days, over and over again until at the end you
2 can see that the mercury from the blood is cleared
3 very fast in these monkeys. The same thing happens
4 with human infants.

5 However, the inorganic mercury that got into
6 the brain doesn't leave. This is the chart. The
7 purple shows you what happens to the inorganic mercury
8 after each injection. The first injection you get up
9 to about four nanograms per milliliter, but then even
10 though it clears out of the blood it doesn't leave the
11 brain.

12 The second shot, you get another bump up in
13 inorganic mercury; the third shot another bump; and
14 the fourth shot another bump to where the infant
15 monkeys in these studies at the end of the study had
16 16 nanograms per milliliter on average in their
17 brains, and the half-life was the same as in the adult
18 monkeys. It didn't change. It's there. It's going
19 to be there for years.

20 Now, they haven't yet released the data on
21 the activation of the brain cells in this study. That
22 work is being done and it isn't available yet, but we
23 know from the adult monkey studies what inorganic
24 mercury will do, and this is in the same dose level as
25 the adult monkey study. Let me show you that quote.

1 Scott, it's the one that says: Five years.
2 It's on the right-hand side of this. Yes, that's it
3 right there.

4 The effects of the adult monkeys, and this
5 is Dr. Clarkson again endorsing the validity of those
6 five adult monkey studies that I showed you to begin
7 with, saying that the effects of the adult monkeys
8 were associated with brain inorganic levels only five
9 times higher -- only five times higher -- than in the
10 infant monkeys.

11 You're going to hear I think lots of studies
12 that show the developing brain, the developing infant
13 brain, is probably 10 times more sensitive to the
14 effects of mercury than the adult brain, and yet we
15 only have a difference of five times here between the
16 measured levels of inorganic mercury in these brains.

17 Dr. Clarkson also endorses the general
18 nature of our theory.

19 Scott, if you look at the last thing here?

20 This article notes, referring again to the
21 Vargas autopsy study: It is important to note that an
22 active neuroinflammatory process has been demonstrated
23 in the brains of autistic patients, including a marked
24 activation of microglia.

25 So these authors put all this together in

1 the way that I've been trying to explain to you to say
2 that inorganic mercury is delivered to the brain with
3 these injections of thimerosal. It accumulates in the
4 brain and it activates microglia, and if you activate
5 the immune system in the brain with neuroinflammation
6 you can cause regressive autism.

7 Okay. Next, Scott?

8 I'm not going to take the time now to show
9 you these autopsy studies, but since the Vargas study
10 was published in 2005 there was another study on
11 autopsies of autistic children published this last
12 year, Lopez-Hurtado, which found exactly the same
13 thing. They found neuroinflammation in all the brains
14 of these autistic children.

15 And then recently, literally recently -- in
16 fact, one study was just published this week -- an
17 autopsy study of children with autism that found again
18 neuroinflammation, which seems to be the hallmark of
19 the autistic brain.

20 Next slide?

21 Now let me say something about epidemiology.
22 The defense reports are full of citations to the
23 various epidemiology studies that have been done in
24 Europe and elsewhere on thimerosal and vaccines and
25 whether there's been some change in the rate of

1 autism.

2 We're going to have Dr. Greenland here soon
3 to explain this in great detail, but not one of these
4 studies has ever looked at regressive autism. There's
5 going to be some dispute about what percentage of
6 autistic children in the grand spectrum are truly
7 regressive, but the general consensus I think you're
8 going to hear is it's 15 percent or less.

9 What Dr. Greenland will explain to you is
10 that it's 15 percent or less of the cases, and you're
11 looking at all cases of autism. You can't see a
12 change in regressive autism in these studies. The
13 studies are just simply uninformative on the question
14 of whether thimerosal vaccines are related to
15 regressive autism.

16 There is no published case control study on
17 regressive autism. There's no cohort study on
18 regressive autism. As I've just explained, none of
19 the ecologic studies that look at patterns and trends
20 have ever looked at regressive autism.

21 Now, there are a number of environmental
22 toxins that are going on the list of possible causes
23 of autism, and one of the more recent ones is a drug
24 called Terbutaline. Terbutaline is a drug given to
25 pregnant mothers to try to stop premature labor so the

1 baby isn't born too preterm. It's not used very much
2 any more because now it's been accepted it causes
3 autism.

4 It's given in the typically sixth to eighth
5 month, so very late of the second trimester up to the
6 third trimester of pregnancy. There's a case control
7 study that you'll see a lot of later in the trial by
8 Connors, et al. This is the same group, by the way,
9 at Johns Hopkins that did some of the autopsy studies.

10 Connors, et al. They did a study on twins
11 and siblings, and what they found was that if there
12 was an autistic child and his twin or sibling was
13 given Terbutaline, they were two to four times as
14 likely to get autism as the twins or siblings of
15 autistic children who weren't exposed to Terbutaline.

16 So that has now put Terbutaline on the list
17 of toxic agents that can cause autism. Guess what
18 mechanism they've now figured out Terbutaline uses to
19 cause autism? It's neuroinflammation. The same group
20 again did an animal study on Terbutaline trying to
21 figure out what is it about Terbutaline that can lead
22 to autism, and what they found is it caused this same
23 type of neuroinflammation and it caused behavioral
24 changes in these rodents.

25 You'll see that in detail, but here's an

1 example of another agent that's known to cause autism
2 late in pregnancy, near the time of birth, and causes
3 it through the neuroinflammatory process.

4 Okay. Next slide?

5 Let me run through just really quickly more
6 for the audience than for the Special Masters who our
7 experts are going to be. We're going to have Sander
8 Greenland, our epidemiologist; Vasken Aposhian, whom
9 you've seen before who is a toxicologist; Dr. Richard
10 Deth, who is a research pharmacist; Marcel Kinsbourne,
11 whom you know, a pediatric neurologist; and then Dr.
12 Elizabeth Mumper, a pediatrician who runs a clinic
13 that treats hundreds and hundreds of autistic
14 children.

15 Let me just summarize quickly. Marcel
16 Kinsbourne, as you probably know, is the author of the
17 chapter on childhood neurodevelopmental disorders,
18 including autism, in this book, which is the leading
19 textbook of pediatric neurology in the country. In
20 all seven editions of this book, he's been the author
21 of that chapter.

22 Dr. Greenland is the co-author of this book,
23 which is the leading textbook on epidemiology methods
24 taught in graduate schools around the country. This
25 is the second edition of the book. The third edition

1 just came out and I won't have a copy until tomorrow,
2 but again we have one of the leading textbook authors
3 on the subject who's coming here to address you.

4 Dr. Aposhian is a world-recognized authority
5 on toxicology that you've heard of many times before.
6 Dr. Deth has performed and published many of his own
7 studies on thimerosal and neurons and how thimerosal
8 can lead to oxidative stress. And then finally Dr.
9 Mumper is the medical director for the Autism and
10 Research Institute and manages a large clinic that
11 treats autistic children.

12 Now, there's a debate between the sides here
13 as to whether autism is totally genetic or whether
14 there has been an increase in the rate of autism over
15 the last many years. I think we will be able to
16 convince you that the epidemic is real, that the
17 increase is real.

18 First of all, there's no such thing as a
19 genetic epidemic. If autism was all genetic, you
20 wouldn't see a change in rates. You can only see an
21 increase if something is triggering it, so it's an
22 interaction between the environment and the genetic
23 susceptibilities of these children.

24 There's been no change in the criteria for
25 regression. The defense experts all try to say well,

1 it's just an expansion of the criteria for diagnosis
2 or it's just better ascertainment of the cases. We
3 really don't have an increase in autism. We just have
4 a better awareness of it and are better able to
5 diagnosis it.

6 That doesn't make sense for regressive
7 autism because a true regressive autistic case is so
8 dramatic nobody would miss it. It's not like they
9 could have overlooked hundreds and hundreds of
10 regressive autistic cases over the last 20 years.

11 And yet the percentage of autistic cases
12 that are regressive has not changed. It's really
13 pretty much stayed the same over 20 years, which means
14 the regressive cases have increased, but if the
15 regressive cases have increased, that has to be a real
16 increase. They couldn't possibly have missed
17 regressive cases.

18 So there is genetic susceptibility.
19 Obviously we know there's a genetic component to your
20 susceptibility to the autism spectrum disorder. We
21 know that several environmental factors have already
22 been identified as triggers of autism, and even
23 Respondent's scientists will acknowledge that some of
24 these environmental factors are triggers. Some
25 viruses are triggers. Some drug agents like

1 Terbutaline are triggers. I already actually went
2 through the Terbutaline example so I won't go through
3 it again.

4 Another very important concept is in every
5 study of mercury disposition in animals, in rodents,
6 in primates and in humans there is always a wide
7 individual variation in how much mercury gets out of
8 the blood, how much mercury goes into the brain. If
9 you're injecting several million kids with the same
10 level of mercury, you're going to have a wide
11 distribution of effects. Some kids can clear it very
12 quickly and some kids can't.

13 We believe it's the kids who are at the high
14 end of the curve who are the ones that have the most
15 trouble clearing mercury, and we know from all the
16 studies that there's always some animals or some
17 humans that are in that category. Those are the ones
18 that are at most danger of having the inorganic
19 mercury trapped in the brain in higher quantities and
20 causing this neuroinflammatory process.

21 Okay, Scott.

22 And then there's another reason why some
23 children are especially vulnerable. At birth there's
24 a wide variability in how mature the liver is at
25 clearing mercury. Some kids are born with a much more

1 mature biliary functioning system than others.

2 The blood-brain barrier develops from birth
3 to three, four, six months of age, and it varies
4 tremendously between kids. Some kids have a much
5 better blood-brain barrier when they're born than
6 others.

7 We know that some kids don't excrete mercury
8 as fast as others. We know some don't detoxify it as
9 fast as others, and we know that some kids don't have
10 the full antioxidant metabolism that's required for
11 healthy neuronal function and so they're at risk for
12 any provocation of stress on the neurons from
13 oxidative stress. In other words, they're equipped to
14 handle some oxidative stress, but they can't handle
15 excess oxidative stress as well as most children can.
16 You're going to see evidence of that.

17 So we believe you will be convinced when
18 we're done that thimerosal injections during infancy
19 are a substantial contributing cause of
20 neuroinflammation and the resulting symptoms of
21 regressive autism.

22 And then just one quick note about the legal
23 standard for causation in the program. We know we
24 have to prove a medically plausible theory of
25 causation, and I believe we're going to do that. We

1 know we have to prove a logical sequence of cause and
2 effect, and I think we're going to be able to do that.

3 And we of course have to show a temporal
4 relationship between the exposure and the injury. As
5 Mr. Powers explained, these two kids in this case
6 didn't develop any symptoms until after they got this
7 whole range of doses of inorganic mercury.

8 That's the end of our opening statement.
9 Thank you very much for your attention, and we'll get
10 on with the science.

11 SPECIAL MASTER HASTINGS: Thank you very
12 much, Mr. Williams.

13 For the government, did you have an opening
14 statement?

15 MS. RICCIARDELLA: Yes, we do, sir.

16 SPECIAL MASTER HASTINGS: Please go ahead.

17 MS. RICCIARDELLA: Could we also switch the
18 computers, please?

19 SPECIAL MASTER HASTINGS: Ms. Ricciardella,
20 please go ahead when you're ready.

21 MS. RICCIARDELLA: Thank you. Good morning.
22 My name is Lynn Ricciardella, and I, along with my
23 colleagues at the Department of Justice, represent the
24 United States.

25 Special Masters, I've been working on the

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1 autism omnibus litigation for the Department of
2 Justice for over four years, and during that time I
3 have looked at hundreds of pages of medical records in
4 my autism cases, as have my colleagues here today.

5 In every case those records tell the same
6 message, and that is how dedicated and loving the
7 parents are to their autistic children. It shows what
8 lengths parents will go to and what sacrifices they
9 will willingly make to help their autistic children.

10 That recognition extends not just to the
11 parents. In the majority of cases that I've reviewed,
12 the records show that the extended family is also
13 intimately involved in that child's care, so I'd like
14 to take this opportunity to open today with an
15 acknowledgement from all of us at the Department of
16 Justice, along with our colleagues at the Department
17 of Health and Human Services, that we have tremendous
18 respect for the families who have to deal day in and
19 day out with autism and who do so courageously and
20 admirably.

21 I also want to echo Special Master Hastings'
22 sentiments and especially acknowledge the Mead and the
23 King families for graciously allowing their cases and
24 their children's medical conditions to serve as the
25 test cases in this litigation. Thank you.

1 Now, as you are undoubtedly aware, Special
2 Masters, the issue of whether vaccines cause autism
3 has understandably garnered much public attention, and
4 with regard to the cases pending in this Court
5 specifically there has been much discussion and
6 rhetoric espoused in the public by those who have
7 formed a judgment through misinterpretation of the
8 evidence or by ignorance of it.

9 Respondent, however, has chosen to litigate
10 our case inside the courtroom in the proper context
11 before the three of you who have the extremely
12 important job of deciding these cases. We have
13 decided to litigate our case not with supposition or
14 accusation, but with good, solid, reliable evidence.
15 As we did for Theory 1, we intend to provide you with
16 good, solid, reliable evidence that you can apply not
17 just to these two cases, but to most, if not all, of
18 the pending cases in the omnibus.

19 Now, what is good, reliable evidence? Well,
20 the United States Supreme Court has already said what
21 it is in Daubert. It's evidence based on research
22 with those who have specific training and experience
23 in the subject matter being discussed. It's
24 hypotheses that have been tested. It's opinions that
25 rise above the level of pure speculation. It's

1 evidence of research that's been reduced to writing,
2 exposed to the peer review process, scrutinized,
3 discussed and replicated.

4 It's testimony from experts who have
5 experience in the specific area for which they're
6 testifying, experts who treat autistic children,
7 experts who research autism, who research the
8 behaviors of autism and the neuropathology and the
9 neuroanatomy of autism, experts who research specific
10 types of mercury and experts who actually treat
11 mercury poisoning.

12 Now, Respondent will present testimony from
13 some of the world's most prominent experts in their
14 field. Unlike Petitioners' experts who broadly
15 speculate about an unlimited universe of scientific
16 possibilities, Respondent's experts root their
17 opinions in decades of meticulous, specialized
18 research.

19 You'll hear experts from Respondent who are
20 experts in toxicology who each possess their own
21 individual expertise, but who all ground their
22 opinions on the most well-recognized and well-
23 established tenants of toxicology, namely dose, form
24 of exposure and route of exposure. These renown
25 toxicologists will explain how Petitioners' experts

1 directly and indirectly ignore scientific foundations,
2 replacing scrutinized evidence with novel theories and
3 speculative hypotheses.

4 You will learn that the mechanisms of damage
5 hypothesized by Respondent's experts have never been
6 validated and are not accepted by the rest of the
7 scientific community. You will hear from neurologists
8 who focus their research on the neuropathology and the
9 neuroanatomy of autism.

10 However, no one has conclusively found or
11 discovered the neuropathological origins of autism.
12 Each expert will confront that the findings reported
13 in the literature indicate that the pathogenesis of
14 autism arises in the early stages of brain development
15 in utero.

16 Now, the neuropathology of mercury toxicity
17 has also been studied, and it's not consistent with
18 the findings that have been reported in relation to
19 autism. You will hear that there is no
20 neuropathological evidence whatsoever that thimerosal
21 could injure the brain in a way that would result in
22 autism.

23 You will hear from the world's experts in
24 the diagnosis, treatment and research of autism. You
25 will hear from the experts who actually write the

1 criteria that the rest of the world uses to diagnose
2 autism. You will hear from experts who have a
3 particular expertise in regressive autism. They will
4 tell you it's not rare, and there is no evidence
5 whatsoever that there are any biological differences
6 between regressive autism and nonregressive autism.

7 You will hear from Respondent's experts in
8 epidemiology who will explain that multiple, credible
9 studies have been done in different countries using
10 different methodologies, but they all come to the same
11 conclusion: There is no association between
12 thimerosal-containing vaccines and autism.

13 Special Masters, it's very important to keep
14 in mind what the issue before the Court is in this
15 litigation. This issue is about thimerosal-containing
16 vaccines administered to children. This issue is not
17 about whether mercury is good or bad. This issue is
18 not about whether any form of mercury is good or bad.

19 Let's be clear. The allegation levied in
20 this litigation is whether these children developed
21 now we're hearing regressive autism because of
22 exposure to a specific form of mercury by way of a
23 specific route of administration given at specific
24 times and in specific amounts.

25 Now, as you consider the evidence I'd like

1 you to please keep in mind four essential concepts.
2 The first is what is the substance being discussed?
3 This case is about thimerosal, which is 50 percent
4 ethyl mercury. Now, as Mr. Williams went on at great
5 length, a lot of Petitioners' case is now about
6 inorganic mercury. As you reviewed the Petitioners'
7 expert reports, you saw that a lot of them rely on
8 methyl mercury. This case is about ethyl mercury.

9 Pay particular attention to the way in which
10 Petitioners' experts conveniently move between the
11 different types of mercury. Well, there are different
12 types of mercury, but none has ever been shown to
13 cause autism.

14 The second concept I'd like you to keep in
15 mind is dose. This case is about exposure to small
16 quantities of ethyl mercury administered to children
17 at specific times, usually at birth, at two months, at
18 four months and at six months of age. Again, pay
19 close attention to Petitioners' evidence. A lot of it
20 will concern very high dose, continuous exposure to
21 methyl mercury.

22 Now, nobody here disputes the fact that
23 mercury can be harmful, and nobody here disputes the
24 fact that mercury is a neurotoxin, but Respondent's
25 experts will explain the importance of dose in

1 assessing the risk of chemicals.

2 Every substance can be harmful to humans in
3 sufficient doses, including water, salt or oxygen.
4 The dose of thimerosal administered in a routine
5 childhood vaccine, however, is thousands, if not tens
6 of thousands, times smaller than the amounts of
7 thimerosal known to elicit adverse effects in humans.

8 Now, as we heard a lot during the first
9 theory of causation, the most fundamental tenant of
10 toxicology is that dose makes the poison, and that's
11 why the proper focus of this litigation should not be
12 whether mercury is a neurotoxin. It is. The proper
13 focus of this litigation should be whether ethyl
14 mercury is neurotoxic at the specific levels contained
15 in childhood vaccines.

16 Now, the third concept to keep in mind is
17 who is the exposed subject? This case concerns human
18 beings, specifically children administered thimerosal-
19 containing vaccines postnatally. This case is not
20 about in vitro studies. Petitioners will rely on in
21 vitro studies performed in petri dishes or studies
22 done in animals, but once again this case concerns
23 humans.

24 The fourth and final concept I'd like you to
25 keep in mind is critically important, and that is what

1 is the clinical outcome that's being discussed? This
2 case is about autism. This case is not about the
3 death of snail neurons in a petri dish when thimerosal
4 is placed directly on top of them. This case is not
5 about high doses of methyl mercury that could
6 potentially cause subtle neurological signs and
7 symptoms. This case is about autism.

8 Special Masters, in the six years since the
9 Court created the omnibus autism proceeding
10 Petitioners' hypothesis has not moved beyond the realm
11 of pure speculation. It was a relatively new
12 hypothesis back in 2002 when the Court created the
13 OAP. It's no longer new.

14 If you recall, the Petitioners asked that
15 the hearings in these cases be delayed because they
16 said the science was continuing to evolve. They were
17 right. The science did evolve, and this issue has
18 been studied, investigated and tested not just here in
19 the United States, but by the worldwide scientific
20 community, and every time it has been looked at it has
21 been rejected.

22 Now, Mr. Powers talked this morning about a
23 scientific debate. There is no scientific debate.
24 The debate is over. There's no scientific
25 controversy. The only controversy is the media

1 controversy, propelled by those groups who were
2 founded on the premise that vaccines cause autism or
3 by those groups who promote and advocate experimental
4 therapies for autism such as chelation. The credible
5 scientific community has already spoken on this issue
6 and has rejected it.

7 Now, Mr. Powers talked also about the need
8 for this case to be about science. That is absolutely
9 correct, but to appreciate how radical and
10 unscientific Petitioners' hypothesis is it's important
11 to look at the origin of that hypothesis.

12 Now, where would you think that origin to
13 have originated? Perhaps within medical experts from
14 within the autism community? Logical, but that's not
15 what happened. Perhaps within the toxicological
16 community, experts who specialize in ethyl mercury or
17 who treat mercury poisoning. That's not what happened
18 either.

19 Would you at least have expected the
20 hypothesis to originate within the medical or
21 scientific community at large? You'd be wrong. Would
22 you ever have expected the hypothesis to originate
23 with a marketing consultant? That's exactly what
24 happened.

25 There was nothing in the scientific

1 literature until the year 2000 when a woman named
2 Sallie Bernard, who is not a medical professional --
3 she's a marketing consultant and the mother of an
4 autistic child. She published an article entitled
5 Autism, A Novel Form of Mercury Poisoning. Now, she
6 wrote the article in 2000, but she published it in
7 2001 in a journal called *Medical Hypotheses*.

8 Now, this was not a peer reviewed article
9 that appeared in a journal of known repute. Let's
10 take a look at how the journal describes itself.

11 We've taken this directly off of the journal's
12 website. Under the Aims and Scope section it states:

13 *Medical Hypotheses* takes a deliberately
14 different approach to review. Most contemporary
15 practice tends to discriminate against radical ideas
16 that conflict with current theory and practice.
17 *Medical Hypotheses* will publish radical ideas so long
18 as they are coherent and clearly expressed.

19 Special Masters, you heard a lot of
20 testimony during the Cedillo trial and the three
21 trials in Theory 1 how the peer review process is
22 really the bedrock of scientific credibility. Well,
23 the editors at *Medical Hypotheses* don't agree.

24 Here's what they have to say about the peer
25 review process: Traditional peer review can oblige

1 authors to distort their true views to satisfy
2 referees and so diminish authorial responsibility and
3 accountability. Instead, the editor of this journal
4 is going to be a chooser, not a changer. In other
5 words, the journal is going to assume that the author
6 is correct rather than have the peer review process
7 assess that credibility and reliability.

8 That's not all the journal says about the
9 articles that it will publish. It says: Even
10 probably untrue papers may be judged worth publishing
11 if they contain aspects, ideas, perspectives, data
12 that are potentially stimulating to the development of
13 future science. Even probably untrue articles.

14 There's another section on this website
15 entitled Guide for Authors. It explains that if you
16 want an article published in this journal you have to
17 pay for it. You have to pay a page charge. The
18 papers won't be published until payment is received.
19 So if you want an article published in *Medical*
20 *Hypotheses* you can. It can be radical, it can be
21 unsubstantiated, and it can probably even be untrue.
22 You just have to pay for it yourself.

23 Now, when the Bernard article came out in
24 2001, the groups that had been advocating for a link
25 between vaccines and autism started to dangerously

1 promote the idea that thimerosal in vaccines was
2 creating an autism epidemic in this country, and thus
3 began their running indictment of the CDC, the CDC's
4 vaccination policies and their continuous accusation
5 against our nation's immunization program.

6 Because of the enormous public health
7 concern generated by these accusations, the scientific
8 and medical community became involved. In 2001, the
9 Institute of Medicine asked its Immunization Safety
10 Review Committee to look into the issue.

11 Now, in 2001 the IOM's committee did not
12 just focus its attention on autism. That was one of
13 the outcomes it looked at, but in 2001 they looked at
14 a variety of neurodevelopmental disorders, and here's
15 what the conclusion that the 2001 committee said it
16 stated the evidence was at the time:

17 That it was inadequate to accept or reject a
18 causal relationship between exposure to thimerosal
19 from vaccines and the neurodevelopmental disorders of
20 autism, ADHD and speech or language delay. The 2001
21 committee specifically recommended that additional
22 studies be done, particularly epidemiological studies.

23 Well, the Safety Review Committee of the IOM
24 met again in 2004, on February 9, 2004, and by this
25 time the issue of thimerosal in vaccines had become

1 highly publicized. They invited the public to address
2 the committee to express its viewpoint. Many of the
3 hypotheses relied upon by Petitioners in this
4 litigation were presented to the IOM in 2004 and
5 rejected by it.

6 Now, between the time the committee wrote
7 its 2001 report and convened again in 2004, multiple
8 credible studies had been done. As I mentioned
9 before, they all came to the same conclusion: There
10 was no association between thimerosal-containing
11 vaccines and autism.

12 This time, in 2004 the committee
13 specifically focused on just the neurodevelopmental
14 disorders of autistic spectrum disorders or autism for
15 short. They made a variety of conclusions, and here's
16 what they had to say about causality: The committee
17 concludes that the evidence favors rejection of a
18 causal relationship between thimerosal-containing
19 vaccines and autism. Now, that was the strongest
20 possible conclusion available to the committee.

21 They also made a conclusion with regard to
22 the biological mechanisms that underlie this
23 hypothesis, and here's what they said: In the absence
24 of experimental or human evidence that vaccination,
25 either MMR vaccine or the preservative thimerosal,

1 affects metabolic, developmental, immune or other
2 physiological or molecular mechanisms that are
3 causally related to the development of autism, the
4 committee concludes that the hypotheses generated to
5 date are theoretical only.

6 Now, the committee did recommend that
7 further research be done to look into the possible
8 causes of autism. Here's what they said about what
9 that focus of research should be: It should be
10 directed towards those lines of inquiry most supported
11 by the current state of knowledge. The vaccine
12 hypotheses are not currently supported by the
13 evidence.

14 While the committee strongly supports
15 targeted research that focuses on better understanding
16 the disease of autism, from a public health
17 perspective the committee does not consider a
18 significant investment in studies of the theoretical
19 vaccine/autism connection to be useful at this time.

20 Special Masters, it's been four years since
21 the IOM came to those conclusions, and in those four
22 years the evidence continues to increase to support
23 that conclusion. As I mentioned earlier, the
24 hypothesis of thimerosal and autism has been studied
25 and tested, and not just here in the United States.

1 It's been tested by the worldwide scientific
2 community, and the hypothesis has been resoundingly
3 rejected.

4 The following are just a sample of those
5 scientific organizations that have rejected this
6 hypothesis: The World Health Organization, the
7 Institute of Medicine, the American Academy of
8 Pediatrics, the European Medicines Agency, which
9 comprises 30 member countries, the Centers for Disease
10 Control and Prevention, the Food and Drug
11 Administration, the Canadian Pediatrics Society, the
12 Canadian National Advisory on Immunization. Again,
13 this is just a sample of the many organizations that
14 have rejected this hypothesis.

15 How did Petitioners' experts deal with the
16 worldwide scientific community against them? They
17 said well, they weren't looking at the right evidence.
18 They argue that the evidence relied upon by the
19 scientific community doesn't apply to a very rare,
20 very small, genetically susceptible subgroup of
21 children who develop regressive autism only as a
22 result of thimerosal-containing vaccines. But that
23 hypothesis is only as reliable and credible as the
24 evidence upon which it is based.

25 Now, once again this concept is also not

1 new. Mr. Powers talked about government rhetoric to
2 worry about and to keep emphasizing how these cases
3 pending in the omnibus will affect our nation's
4 immunization program. Well, it's not just government
5 rhetoric. The IOM in 2004 was concerned about it too.
6 Here's what they said about this hypothesis of genetic
7 susceptibility:

8 The benefits of vaccination are proven, and
9 the hypothesis of susceptible population is presently
10 speculative. Using an unsubstantiated hypothesis to
11 question the safety of vaccination and the ethical
12 behavior of those governmental agencies and scientists
13 who advocate for vaccination could lead to widespread
14 vaccination of vaccines and inevitable increases in
15 incidences of serious infectious diseases.

16 Now, having failed to find the validity they
17 need in the scientific community, Petitioners now turn
18 to the legal one. But the first pronouncement that
19 vaccines cause autism should not come from the
20 courtroom. It should come from science.

21 I'd like to end this morning with the oft
22 cited quotation from the venerable Judge Posner of the
23 Seventh Circuit. He said: The courtroom is not the
24 place for scientific guesswork even of the inspired
25 sort. Law lags science. It does not lead it.

1 Special Masters, the scientific community
2 has considered and rejected the allegations before you
3 in this litigation. So too should this Court. Thank
4 you.

5 SPECIAL MASTER HASTINGS: Thank you, Ms.
6 Ricciardella.

7 MR. POWERS: Special Master, I know we
8 didn't use the full hour. If we could have a very
9 quick, five minute rebuttal opening?

10 SPECIAL MASTER HASTINGS: Go ahead.

11 MR. POWERS: Thank you. Very specifically,
12 I just wanted to address a couple of things because I
13 think it's important to keep some of this in
14 perspective.

15 The discussion you heard from Respondent on
16 the 2004 IOM. It's important to remember several
17 things about the 2004 IOM. Mr. Williams described and
18 showed to you and you've reviewed in evidence a series
19 of papers, important scientific papers from reputable
20 researchers in peer reviewed, published, indexed
21 scientific and medical journals that were not even
22 considered by the 2004 IOM.

23 When one looks at the bibliography of the
24 2004 IOM you won't see, for example, what we've
25 identified as a critical study -- that's the 2005

1 Burbacher/Clarkson infant monkey study -- because the
2 study hadn't been done. You won't see cited the
3 Vahter and Charleston papers. Those are the adult
4 monkey studies that Mr. Williams described from the
5 mid 1990s.

6 You won't see any of that work in the IOM,
7 and in fact the quote from the IOM about the
8 physiological mechanisms that have been examined did
9 not include the neuroinflammatory process. The IOM
10 never saw it because they hadn't been done yet. The
11 brain autopsy studies. They haven't seen the studies
12 that came out in 2005, 2007 and 2008.

13 We reviewed the Petitioners' master
14 reference list that was submitted to the Court, and
15 approximately 275 of the articles on that list were
16 published after the October 2004 IOM report was
17 issued. The 2004 IOM report was a snapshot in time,
18 and science is not a snapshot. Science is a movie,
19 and it moves forward and moves forward by hypotheses
20 being offered and tested.

21 The other point I wanted to make is about
22 the difference between speculation and hypothesis
23 because too often Respondent uses those terms
24 interchangeably. When Petitioners are talking about a
25 hypothesis, we're talking about a hypothesis that

1 means an idea that explains the known facts, an idea
2 that can take a disparate set of facts, organize them
3 in a consistent way and offer an explanation of, in
4 this case, a mechanism that is consistent with the
5 known facts and, just as importantly, can help predict
6 some facts that may come down in the future.

7 So it is more than speculation. These are
8 hypotheses that are testable. They are subject to
9 studies that use their conclusions as the null
10 hypothesis. They're replicable, and over time they
11 will be replicated if, particularly in the clinical
12 area, money goes into the research.

13 One can't help but notice with the huge
14 number of expert witnesses that the Respondent has
15 brought into these cases and the tens of thousands,
16 perhaps hundreds of thousands of dollars being spent
17 to bring those witnesses in in the litigation context,
18 is perhaps some of that money could go to support
19 clinical trials and case control, placebo, blinded
20 trials of some of the medical interventions just as an
21 example of public health resources that could be used
22 in a different way outside the litigation to answer
23 scientific questions and to address the health of
24 these kids.

25 That 2004 IOM, since it's a big part

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1 apparently of the Respondent's position, needs to be
2 put in context. I know that in the 2005 infant monkey
3 study that was authored by the lead investigator was
4 Thomas Burbacher at the University of Washington and
5 Dr. Clarkson, who has been identified as Respondent's
6 witness was the co-author on there.

7 It's important to note towards the end of
8 that study that there's a comment in there about the
9 2004 IOM. There's a comment that explains the
10 conclusion, the approach the 2004 IOM took: It's
11 difficult to understand, given our current limited
12 knowledge of the toxicokinetics and developmental
13 neurotoxicity of thimerosal, a compound that has been
14 and will be continued to be injected into millions of
15 newborns and infants.

16 So the credible, reliable, peer reviewed
17 published researchers, including at least one on their
18 side of the case, have identified a weakness in the
19 2004 IOM. As I said in my opening, you can't cut
20 science off at the knees, and we propose that the 2004
21 IOM closed the chapter on this issue before the story
22 really started to get told.

23 The story that you will hear in this
24 hearing, the presentation and the evidence, is a
25 scientifically sound description about ongoing story,

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1 and we don't know what the end is going to be, but we
2 do know that where we are today is that we have a
3 mechanism of injury that meets the standards of
4 causation in this program, and there is medical
5 evidence that these two children satisfy this burden
6 and are entitled to compensation.

7 SPECIAL MASTER HASTINGS: Thank you, Mr.
8 Powers.

9 Well, we've heard from attorneys this
10 morning. Are we ready to start with the expert
11 witnesses?

12 MR. WILLIAMS: I think we are. Dr.
13 Greenland?

14 SPECIAL MASTER HASTINGS: Dr. Greenland,
15 could you please take the witness chair? Please have
16 a seat, sir. I'll ask you to raise your right hand.

17 Whereupon,

18 SANDER GREENLAND

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

21 SPECIAL MASTER HASTINGS: Please go ahead
22 then, Mr. Williams, when you're ready.

23 DIRECT EXAMINATION

24 BY MR. WILLIAMS:

25 Q Good morning, Dr. Greenland.

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1 A Good morning.

2 Q Before we go into your qualifications, you
3 prepared a couple slides that just summarize what your
4 general opinion is that you're going to be discussing
5 today?

6 A I have.

7 Q Okay. Let's just put up there what your
8 main point is, and if you would just explain it,
9 please?

10 A Well, the epidemiologic literature has not
11 ruled out the possibility that thimerosal-containing
12 vaccines -- I'm going to call them TCVs -- are
13 associated with a prespecified type of autism of a
14 regressive form.

15 I want to emphasize that what I'm testifying
16 about is the limitation of the epidemiologic evidence.
17 That's strictly my narrow scope of expertise and the
18 statistics surrounding it.

19 MR. WILLIAMS: Next slide?

20 SPECIAL MASTER HASTINGS: Mr. Williams,
21 before we go on to the next slide --

22 MR. WILLIAMS: Yes?

23 SPECIAL MASTER HASTINGS: You've got a
24 series of slides that he'll be talking about here?

25 MR. WILLIAMS: Yes.

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1 SPECIAL MASTER HASTINGS: Do you have paper
2 copies of that presentation?

3 MR. WILLIAMS: I don't know how many. We
4 only have two right now.

5 SPECIAL MASTER HASTINGS: All right. Let's
6 mark one of them. What we did in the last trial I
7 think was very helpful. We'll mark these things.
8 This will be Petitioners's Trial Exhibit No. 1.

9 MR. WILLIAMS: Okay.

10 SPECIAL MASTER HASTINGS: We'll place them
11 into the record, and then later on if the witnesses
12 and counsel can help to do this as you go from Slide 1
13 to Slide 2 to Slide 3, if you could mention we're now
14 going to Slide 3. Then later on when we go back and
15 read the transcript we can follow along. It will be
16 much easier to follow the testimony if we have that
17 roadmap.

18 Let's go ahead and mark that. We'll give a
19 copy later on to the court reporter.

20 MR. WILLIAMS: Who does the marking?

21 SPECIAL MASTER HASTINGS: Well, we'll mark
22 it later. We know what this one will be, Petitioners'
23 Trial Exhibit 1.

24 MR. WILLIAMS: All right.

25 //

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1 (The document referred to was
2 marked for identification as
3 Petitioners' Exhibit No. 1
4 and was received in
5 evidence.)

6 SPECIAL MASTER HASTINGS: Go ahead, Mr.
7 Williams.

8 BY MR. WILLIAMS:

9 Q Okay. One more slide about the main points
10 of your testimony, and then we'll go into your
11 qualifications, okay?

12 A Okay. Well, in published control studies
13 that I have seen, but not analyzed, clearly regressive
14 autism is very uncommon, as the expert, Dr. Fombonne,
15 and we'll get to his calculations, as he said.

16 Hence, even if the studies had separated the
17 clearly regressive cases, a true association could
18 easily have been missed. They hadn't done that,
19 however.

20 Q Okay. We're going to go through that in
21 more detail just in a moment, but let's turn to your
22 qualifications if you would, and this is now the
23 fourth slide in the set.

24 A Okay.

25 Q I told the Court that you were the co-author

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1 of this book. Is that the truth?

2 A That's correct.

3 Q Okay. And there's a new edition of this
4 that has just come out?

5 A That's correct.

6 Q And is this textbook used around the country
7 and the world?

8 A It is. It is.

9 Q And you are an author on over 300 peer
10 reviewed articles?

11 A That's correct.

12 Q Okay. Slide 5. Are you a Professor of
13 Epidemiology and Statistics at UCLA?

14 A Correct.

15 Q How long have you been there?

16 A I've been at UCLA on the UCLA faculty since
17 1979.

18 Q And are you frequently invited to give talks
19 and presentations around the world on epidemiologic
20 methods?

21 A That's correct. And also statistics.

22 Q And also statistics. All right. Slide 7.
23 You have a Doctorate in Public Health from UCLA?

24 A That's correct.

25 Q So you were there before you started working

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1 there?

2 A That's correct.

3 Q Explain what these executive committees are
4 and so forth, please.

5 A Well, Society for Epidemiologic Research is
6 the largest society of epidemiologists in the world
7 today. I've served on the executive committee of that
8 society.

9 I've also been chair of the Epidemiology
10 Section of the American Statistical Association, which
11 is the largest statistical society in the world today.

12 Q And then I guess this is coming to Slide 7
13 next. You've been a consultant in epidemiology and
14 statistics for many different governmental agencies
15 and private corporations?

16 A That's correct.

17 Q We don't have the whole list here? There's
18 a lot longer list than this?

19 A Much longer.

20 Q And then you've been an investigator
21 yourself on many grants and contracts --

22 A That's correct.

23 Q -- for NIH and other prestigious
24 organizations?

25 A That's correct.

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1 Q And then we're ready for I think Slide 9.
2 Slide 8? Okay. Slide 8.

3 Again, just some more of your
4 qualifications. You've been a referee for some of
5 these journals. Are these major journals in the
6 field?

7 A They are.

8 Q Explain what these two journals are or three
9 journals are in the last section for us.

10 A Well, *American Journal of Epidemiology* is
11 the most widely circulated, largest journal of
12 epidemiology in the world as far as I know, and
13 *Epidemiology* is maybe number two.

14 And then *Statistics and Medicine* is one of
15 the biggest medical statistics journals in the world,
16 probably the biggest, and the *European Journal of*
17 *Epidemiology* is the main journal in Europe on the
18 continent.

19 Q Okay. Now let's turn to what you've
20 prepared to talk about today. We'll go to what is now
21 Slide 9. Is that right? Okay.

22 I'll just let you explain this, and I'll
23 interrupt you from time to time if I think there's
24 some clarification that needs to be done.

25 A Yes. Well, autism, like many other

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1 diseases, is largely unknown causation and includes
2 neurologic diseases of adults such as MS and ALS as
3 clinically recognizable subtypes with distinct
4 development trajectories and possibly different
5 etiologies. What it has in common with these diseases
6 is that by and large there is not an accepted
7 mechanism that's been worked out in detail about how
8 these diseases arise.

9 An association between TCVs and regressive
10 autism, especially clearly regressive autism, would
11 have been seriously diluted in all the available
12 epidemiologic studies, if there were such an
13 association.

14 Q By diluted, what do you mean by diluted?

15 A Well, that I hope to clarify in the upcoming
16 slides.

17 Q Okay.

18 A The association, if present, would be
19 submerged in the other types.

20 Q Okay. Let's go to Slide 10. I see. The
21 slides are marked on the screen. They're not marked
22 on my copy. I'll be able to do this better now.

23 A This says 10 on my screen.

24 Q Yes, it is Slide 10.

25 A Right. Should I continue?

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1 Q Yes.

2 A Well, specificity of an association means
3 that an exposure has little or no association with the
4 majority of types in a disease category, but some
5 association with one or a few of those types.

6 If a highly specific association is present,
7 failure to separate the types can severely dilute the
8 association of the exposure with the disease category
9 to the point that it can become undetectable.

10 Q You just can't see it in the numbers, right?

11 A That's correct.

12 Q Okay. Slide 11?

13 A Regressive autism may include cases without
14 early developmental abnormalities. This is
15 acknowledged by quite a bit of the peer reviewed
16 literature and also testimony given in this case by
17 Dr. Fombonne.

18 Q In his report, right?

19 A In his report.

20 Q Right.

21 A I'm calling them clearly regressive cases
22 simply for lack of a better term. Such cases would be
23 a minority of regressive cases and thus a small
24 minority of all cases of autism, so even if something
25 called regressive cases is common, but certainly not

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1 the majority of cases, then clearly regressive cases
2 would become quite uncommon.

3 Q And you've gone back to Dr. Fombonne's
4 report and pulled some information out of that that
5 helps to illustrate your point, right?

6 A That's correct.

7 Q Okay. Let's look at that.

8 A Next slide.

9 Q The next slide. There we go.

10 SPECIAL MASTER HASTINGS: And now we're on
11 Slide No. 12.

12 MR. WILLIAMS: Slide 12.

13 THE WITNESS: Dr. Fombonne argues that
14 regressive autism is common enough to be detectible in
15 available studies. He estimates there it's around 20
16 percent of cases could get that label.

17 On the other hand, he cites data that 72
18 percent of cases of regressive autism are not clearly
19 regressive, so that means that clearly regressive
20 cases are only 20 percent times 72 percent of all
21 cases. That would be six percent of the total.

22 He calculates that figure and gives it in
23 his report as an upper bound. He actually expresses
24 skepticism that it's that high a percentage.

25 //

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1 BY MR. WILLIAMS:

2 Q So he's suggesting that the percentage of
3 clearly regressive cases may be less than six percent
4 of all ASD diagnoses?

5 A He seems to state it more strongly than
6 that; that he doubts that it's as high as six percent
7 is my impression.

8 I will say here that not being an expert in
9 Dr. Fombonne's area, I'm relying on his testimony here
10 and the literature he cites, which I've gone back and
11 examined it and what it points to.

12 Q Okay. Let's go to Slide 13.

13 A Well, to take an example of what I'm talking
14 about with this dilution issue, suppose that TCV is
15 associated with a twofold increase in the risk of
16 clearly regressive autism. I'm just picking that
17 number because it's often chosen as a boundary point.
18 Because it is that number or I'm claiming that or it's
19 more or less, but just to take a number that's often
20 used. It's a nice, round figure.

21 Suppose that it's not associated with any
22 other type. It's only associated with clearly
23 regressive autism. Suppose also that without TCV
24 exposure the associated type represents only six
25 percent of the disease category and that the total

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1 number of cases in the category would be 100. I'm
2 taking this figure of six percent from Dr. Fombonne's
3 report, and that's the upper bound.

4 Q Okay. Now we're on Slide 14.

5 A Then, without the exposure, the number of
6 cases with the associated type would be 100 times .06,
7 100 times six percent, which is six.

8 Q So out of 100, you would expect six cases
9 roughly of clearly regressive autism?

10 A That's correct. That's without the
11 exposure. We're assuming this is without the exposure
12 they're six percent.

13 With the exposure, however, the number of
14 cases of clearly regressive autism would double to 12
15 if it doubled the risk.

16 Q Right.

17 A And that would be in excess of six cases
18 over the original six.

19 Q Okay. Let's go on to Slide 15.

20 A This excess produced by the vaccine would
21 result in a total of 100 plus six or 106 cases, which
22 is only a six percent increase in the overall risk of
23 the disease.

24 This six percent increase translates to a
25 risk ratio of only 106 over 100 or 1.06. This

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1 corresponds to Dr. Fombonne's upper bound so that if I
2 took a number more in accord with what he seems to
3 express is more likely it would be even less than that
4 1.06, something even closer to one.

5 Such a small risk ratio is already beyond
6 detection by epidemiologic studies of autism or of
7 most topics for that matter. Epidemiology is simply
8 too crude a tool to be able to detect -- increases in
9 risk of this order are even closer to one -- except in
10 extraordinarily rare instances.

11 Q Now we're going to Slide 16.

12 A Some studies consider more broad categories
13 than autism. Some consider the category of autism
14 spectrum disorder or, even more broadly, developmental
15 disorders. These are some of the studies cited by Dr.
16 Fombonne.

17 If they're looking at a broader category
18 than general autism then clearly regressive autism
19 would constitute an even smaller percentage of these
20 categories, so an association of TCVs with one of
21 these categories would be diluted even more than in
22 the above examples, which means the risk ratio from
23 this doubling of clearly regressive autism would be
24 even closer to one than that 1.06 we calculated in the
25 previous slide.

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1 Q And even more difficult to see in any
2 epidemiological studies?

3 A In that case it would be beyond detection by
4 epidemiologic means.

5 Q Okay. Next slide, Slide 17?

6 A If 28 percent of cases of regressive autism
7 are clearly regressive, and this is one minus the 72
8 percent that Dr. Fombonne cited from his study. The
9 28 percent remaining are clearly regressive, and TCV
10 effects are limited to the clearly regressive type. A
11 study of TCVs among all regressives would still be
12 unlikely to detect the association.

13 Time/trend studies of general autism, which
14 have been cited extensively in this situation, would
15 be unable to detect a specific association of TCVs
16 with clearly regressive autism because a diluted
17 association, something as small as I was illustrating,
18 would be submerged by the large background trends
19 reported.

20 Q Okay. Go to Slide 18.

21 A Now, genetic factors in regressive autism do
22 not rule out or even argue against TCVs as a cause.

23 Q Okay. Why not?

24 A Even when genetic factors must be present
25 for the disease to occur, they in no way limit the

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1 importance of other factors. A classic example is
2 PKU, a genetic disorder which requires presence of
3 dietary phenylalanine to produce mental retardation.

4 Q And PKU is genetically based?

5 A It's a genetically based disease. That's
6 well established, and it's also well established that
7 the mental retardation that can arise from it can be
8 prevented by restricting dietary phenylalanine.

9 Q And that's an example of a postnatal type of
10 brain problem that's caused by an environmental agent,
11 correct?

12 A That's correct. It's a prenatally
13 determined condition, but it's the postnatal exposure
14 that determines the retardation.

15 Q All right. Now let's go to Slide 19.

16 A Now, I feel it's important to discuss this
17 concept of statistical nonsignificance because it
18 arises so much in litigation, as well as in scientific
19 debates, and it seems to be widely misused and
20 misunderstood even by experts.

21 This is a topic that I and several of my
22 colleagues have lectured about all over the world, a
23 major problem in the scientific literature. Failure
24 to detect an association is what this means,
25 statistical nonsignificance. It is not a

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1 demonstration of no association. It only shows that
2 no association -- I should have put that in quotes, no
3 association -- is one among many possibilities that
4 are compatible with the data.

5 Now, the compatibility term used there is by
6 conventional and effectively arbitrary standards, but
7 I'm not going to talk about those standards today.
8 I'll just adopt them like everyone else and simply
9 discuss why even following those standards we have to
10 be careful to understand that failure to detect an
11 association is not a demonstration of no association.

12 Whenever one considers statistical
13 significance or nonsignificance one should ask what
14 other possible levels of association are also
15 nonsignificant. These are given by confidence
16 intervals.

17 Q Okay. The next slide starts to illustrate
18 these, correct?

19 A Yes.

20 Q This is Slide 20. All right.

21 A So to discuss their relation, suppose a
22 study reports a risk ratio of 1.00, no association
23 observed at all, but with 95 percent confidence limits
24 of .5 and 2.0, so one-half to two.

25 These limits would indicate that the

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1 observed risk ratio is not significantly different at
2 the conventional .05 level from a risk ratio as small
3 as .5 or as large as two. That means that all the
4 values within this range would not be rejected by the
5 same statistical test that did not reject the 1.0. No
6 association, and so in effect using this standard they
7 would all still be in the running according to this
8 criterion.

9 Q Just because the relative risk nominally
10 comes out at 1.0 or even 1.2, if the confidence
11 intervals are much wider than that there could be
12 other values if you did the study again?

13 A They wouldn't even have to be much wider.
14 What one needs to understand very carefully about
15 epidemiologic studies and statistical studies of that
16 sort is that they leave open a broad range of
17 uncertainty. They're simply not within their power.

18 Those studies do not have the ability in a
19 scientific sense to rule out these other options or
20 possibilities.

21 Q Okay. Slide 21 now.

22 A So another way of putting this example is
23 that chance alone could have easily produced the
24 observed risk ratio of one even if the study were
25 perfect, even if these were not just epidemiologic

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1 studies based on records of all their problems.

2 It's never the case that these studies are
3 perfect, but even if they were perfect chance alone
4 could have easily produced the observed no association
5 if the true risk ratio were .5 or two.

6 Q Okay. Next slide?

7 A Now, another crucial point is that
8 significance tests and confidence intervals ignore
9 nonrandom errors. Hence, confidence intervals should
10 be taken as showing the absolute minimum range of risk
11 ratios compatible with the data.

12 In other words, they're giving, and this has
13 been stated in the literature, the peer reviewed
14 literature by Paul Meier, who was a renown medical
15 statistician from the 1950s and 1960s. The Kaplan-
16 Meier test is named after him and one of his
17 colleagues.

18 He says these should be taken as showing the
19 absolute minimum range of values compatible with the
20 data. They're only giving you what would be your
21 uncertainty left if the study were absolutely perfect.
22 They must be widened to account for nonrandom sources
23 of uncertainty.

24 When you examine them, think of that core
25 and moving out what blurs it out even further, such as

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1 differences in doses in different persons and cohorts
2 as an example of one source of difference among the
3 studies here.

4 Q That means the confidence intervals, if you
5 think of them in the abstract, would be even wider
6 than the nominal statistical ones?

7 A That's correct.

8 Q Now Slide 22. Did you review the
9 epidemiological studies on mercury-containing vaccines
10 in neurodevelopmental disorders that were cited by the
11 defense and then look for any more you could find?

12 A Yes.

13 Q What did you conclude from that review of
14 the epidemiological literature on mercury-containing
15 vaccines and neurodevelopmental disorders?

16 A I didn't find any published or see any
17 published, peer reviewed, controlled epidemiologic
18 study on TCVs and regressive autism per se. All
19 studies that I saw identified -- that is failed to
20 separate -- regressive autism from other types of
21 autism, and certainly none of them looked at clearly
22 regressive autism in a controlled epidemiologic study.

23 Q Okay. Slide 24?

24 A Here are the studies that I saw identified,
25 given some credibility by most of the reviewers,

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1 including Dr. Fombonne.

2 Q That's just the list of them?

3 A That's just the list.

4 Q You're going to go through them in a second,
5 I take it?

6 A Right.

7 Q Okay. Let's go to the next slide, 25.

8 A The study by Hviid, a reported risk ratio
9 for any TCV. This is any exposure versus none, so it
10 didn't matter if the doses were incomplete and so
11 forth, if there was an incomplete vaccination series.

12 It reported a .85 with 95 percent confidence
13 limits of .60 and 1.2 and a risk ratio for the highest
14 dose category -- now going to the highest dose
15 category where they receive three doses of mercury-
16 containing vaccine. That was an estimate of .96, but
17 the 95 percent limits were from .63 to 1.47, so the
18 results from that study would allow for substantial
19 association with clearly regressive autism.

20 Q In other words, this study by itself is not
21 at all incompatible with a true effect of TCVs on
22 purely regressive autism?

23 A That's correct.

24 Q Okay. It doesn't rule it out?

25 A Not at all.

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1 Q Okay. Slide 26.

2 A It's important to note that I think the
3 children in the study have roughly half the total
4 mercury exposure in early childhood from the vaccines
5 as in the American vaccination schedules, so the study
6 should be expected to exhibit a weaker association of
7 TCV with autism than would an American study if there
8 were such an association. Its confidence limits
9 should be expanded accordingly.

10 Q And now Slide 27, the next study?

11 A The Andrews study from 2004 had 95 percent
12 limits of .88 and 1.12.

13 Again, the vaccination schedules that I saw
14 reported in this study correspond to roughly half the
15 American schedule, so again it would be expected to
16 exhibit a weaker association with autism than would an
17 American study, and its confidence limits would have
18 to be expanded accordingly to apply to the American
19 children exposed to the schedules.

20 Q Okay. And then the next slide on this
21 study? These are two more studies?

22 A Two more studies cited. One, Heron, was
23 another UK study. It reported no analyses for autism
24 that I saw, and another by Jick and Kaye, again among
25 UK subjects, where the confidence interval was from .7

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1 to 3.3.

2 Again, these are using studies that are
3 looking at a population that had lower than American
4 doses according to what I read in these reports.

5 Q Now we're going to go to Slide 29, which is
6 about the Verstraeten study done in the U.S.

7 A Okay. Well, the confidence intervals in
8 this study were wide, ranging from .62 to 1.46 and at
9 the highest category .55 to 3.48.

10 The conclusion reached by the first author
11 was an association between thimerosal and neurological
12 outcomes could neither be confirmed nor refuted, and
13 therefore more study is required. He stated that in a
14 letter to *Pediatrics* following the study.

15 Q Let me ask you. If the defense experts and
16 the defense lawyers argue that this series of studies
17 we've looked at provide convincing evidence that
18 there's no association between thimerosal-containing
19 vaccines and clearly regressive autism what would you
20 say about that assertion?

21 A I'd say I'm not convinced. I would say that
22 the epidemiologic evidence as I've described it here
23 for the dilution reason that I've given -- if I take
24 into account all the uncertainties associated with
25 these studies, both the statistical error, the summary

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1 confidence interval that I would get combining these
2 studies and then take into account the dose
3 differences and what's not understood about the dose
4 differences, I could not possibly rule out the kind of
5 small risk ratio overall that we saw before arising
6 from a relatively large risk ratio for clearly
7 regressive autism, using the figures that Dr. Fombonne
8 gives in this report.

9 Q Okay. Now, these studies that we looked at
10 were virtually all -- I guess they all were --
11 ecological studies. None of them were case control
12 studies, right, the ones we've been looking at?

13 A No, no. These are all controlled
14 epidemiologic studies. One was a case control study.
15 I believe the others were based on cohorts so far.
16 These were controlled epidemiologic studies.

17 Q These were the controlled studies?

18 A Yes.

19 Q Now you have a discussion of the ecologic
20 studies coming up?

21 A Yes.

22 Q Okay. Let's go to the next slide, Slide 30.

23 A Well, then there were other studies that
24 have been cited or I saw cited that we would call
25 ecologic studies in epidemiology. It's important to

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1 distinguish these studies from what I call controlled
2 studies in the earlier slides. They're not considered
3 adequate substitutes for controlled studies, and
4 they're especially unable to reliably distinguish
5 small associations from no association.

6 I'm citing a book chapter by Morgenstern,
7 the chair of the Epidemiology Department at University
8 of Michigan, and also another book chapter that I
9 wrote for a CDC volume in 2004 where we cite extensive
10 literature.

11 It's been known for many decades that these
12 studies can produce completely misleading results very
13 easily because they don't disaggregate people and
14 identify individually whether a person who got a
15 particular exposure such as a vaccination got the
16 particular outcome being studied, such as autism.

17 Q There's no connection to individual exposure
18 in these studies?

19 A By their nature, they lack data connecting
20 the outcomes of the individuals with autism to their
21 exposures, such as vaccination.

22 Q Okay. Slide 31?

23 A Here are three major ones that I have seen
24 cited. They did not analyze regressive or clearly
25 regressive autism cases that I saw, and specific

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1 association TCVs with clearly regressive autism, if it
2 existed, would have been completely submerged so I
3 would say these studies really have virtually no
4 evidential value regarding this particular issue on
5 clearly regressive autism.

6 Q Okay. Let's go to the next slide about
7 Fombonne's study in particular.

8 A Looking at Fombonne's study in more detail,
9 it analyzed PDD, pervasive developmental disorder,
10 which is a much broader category that subsumes autism,
11 as well as other disorders, so its results are even
12 more diluted than the other ecologic studies.

13 As the authors note, not all children in the
14 exposed cohorts of the study were exposed to
15 thimerosal, leading to further dilution. This is
16 another problem with the study.

17 Q Okay. The next slide, still on the same
18 study. Slide 33 now.

19 A Well, from the data presented there would be
20 about 60 cases of general autism in the study, so only
21 about a dozen cases of regressive autism and perhaps
22 only four clearly regressive.

23 Now, regardless of whether that's so, I
24 would say regardless of that the article was
25 uninformative about possible association of TCVs with

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1 regressive autism, and a reanalysis of the study data
2 would not be capable of detecting such an association
3 if it existed.

4 Q Just because of the imprecision of the
5 study?

6 A Of all the problems that we named before:
7 Ecologic, it's looking at PDDs, and we have a
8 situation in which there would not be enough clearly
9 regressive autism to elevate the risk enough to be
10 detected beyond the statistical noise level.

11 Q Okay. So taking all of these studies
12 together, what do they mean with respect to the
13 question here as to whether TCVs cause clearly
14 regressive autism?

15 A Well, because the currently published
16 evidence cannot rule out a very small association of
17 TCVs with autism, and by that I mean something very
18 close to one, like 1.06 or even closer to one as we
19 saw before.

20 Therefore, that evidence cannot rule out an
21 association of TCVs with clearly regressive autism,
22 even a risk ratio of two, so the question of whether
23 TCV is associated with clearly regressive autism
24 remains unanswered by the current epidemiologic
25 literature.

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1 Q Let's do a little math here for a second.
2 Suppose the real risk of clearly aggressive autism
3 tied to the full American schedule is in the range of
4 1.06 to 1.1, something like that, a six to 10 percent
5 increase in risk.

6 Even if it's not detectible by these types
7 of studies, if 40 million children receive that
8 vaccination schedule throughout the '90s you're still
9 talking about quite a few number of kids, aren't you,
10 that would be affected?

11 A Yes.

12 Q It would be essentially six percent of 40
13 million at risk, wouldn't it?

14 A Well, no. The six percent refers to the
15 case series. The six percent would be applied over
16 and above the number of autism cases that would be
17 seen, not to the 40 million.

18 Q Okay.

19 A But to however many cases that 40 million
20 would be expected to generate.

21 Q Well, we could do the math, and we're still
22 talking probably hundreds and hundreds of cases that
23 would not be detectible by these studies?

24 A I would expect.

25 Q Okay. Let's go to the next slide, 35.

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1 Now, here I will comment on some aspects of
2 Dr. Fombonne's report. In relying on it and his
3 expertise in his specialty to discuss these issues,
4 I'd like to look closely at his citations and go back
5 to the literature he was citing.

6 I found that some of the citations were
7 unaccompanied by any evaluation of the statistical
8 strength of the study cited. The strength of those
9 studies -- I'll discuss that a bit more -- is related
10 to the confidence intervals that we would get from
11 them if we indeed calculated or could calculate them
12 or the authors had given them to us.

13 I do have one case where there was enough
14 data for me to do that. The studies turn out to
15 largely not have enough statistical power or precision
16 to rule out a hypothesis that there is a link between
17 the TCVs and clearly regressive autism.

18 I also found that some of the arguments
19 given and studies cited have little or no bearing on
20 whether TCVs could cause regressive autism, and I
21 found some citations that do not show what they're
22 cited as showing. Now, this is with all due respect
23 to Dr. Fombonne.

24 I think that these problems, he was not
25 aware of them is my reading of the document and I

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1 think was doing this quite innocently, but it relates
2 to the very problem I was discussing in the beginning
3 of people failing to realize that it's important to
4 see confidence intervals and put things in context of
5 all sources of uncertainty when looking at studies
6 like this, but now I'd like to give some examples of
7 these problems that I noted.

8 Q Okay. Slide 36.

9 A For example, he claims at paragraph 38, and
10 here's a direct quote: Unusual acceleration of head
11 growth was seen with similar frequency in the
12 regressive group as compared to the early onset group.
13 Then he cites a study by Webb and colleagues in 2007.

14 This finding again illustrates both the
15 presence of objective developmental abnormality before
16 the regression and the similarities between the
17 regressive and nonregressive groups. That's his
18 quote. That's what he says.

19 I went and looked at the web study very
20 closely just to get a sense of how it was showing
21 this, and I saw that it provides poor statistical and
22 epidemiological evidence and no logical support for
23 the idea that TCVs do not affect autism risk.

24 Here is the reasons: On the statistical,
25 the Webb article had only 28 cases of autism spectrum

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1 disorder total and only 11 classified as regressive,
2 far too few to statistically detect all potentially
3 important differences.

4 If we consider the clearly regressive autism
5 type, which Dr. Fombonne argued was not maybe a third
6 or a fourth of all the regressive types, there would
7 only be two or three clearly regressive cases in this
8 whole study.

9 Q Okay. Let's go to Slide 38.

10 A Then another problem is that the prevalence
11 of cases classified as regressive was 39 percent in
12 the article. That's about two to three times the
13 prevalence as cited by experts that I read and
14 articles that I read, including Dr. Fombonne.

15 That suggests that many or most of the
16 regressive cases in this study were not purely
17 regressive. When that happens, when you have this
18 incorrect classification of cases, that would obscure
19 any real differences between true regressiveness and
20 other cases.

21 Now, I would note that in the study they
22 base their classification of regressive, as I recall
23 correctly, on parental report. There was no further
24 follow-up as was done in some of the DOJ
25 investigations is my understanding, so then it's not

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1 surprising that they would end up with quite a few
2 more autistics classified as regressive than you would
3 see in a more careful study.

4 Q Okay. Let's go to Slide 39.

5 A Then there's the logical. This may be the
6 most subtle point, but also perhaps the most
7 important. Even if regressive cases exhibited the
8 same head growth and abnormalities as the other types,
9 would it actually count against the possibility that
10 TCV can cause regression? The answer is no.

11 The abnormality may mark a susceptibility to
12 autism, a susceptibility that had been triggered early
13 in most cases and later in regressive cases, so as
14 with the PKU example it's possible to have a
15 retardation trigger earlier or later. Somebody with
16 PKU, with that genetic deficiency, if they start
17 consuming phenylalanine they'll develop brain problems
18 and retardation at any number of ages depending on
19 when that exposure occurs.

20 Q And the next slide, Slide 40?

21 A Now, the reason why I emphasize this logical
22 problem is because it applies very broadly to the
23 cited literature. Considering again that paragraph of
24 Dr. Fombonne's report, he states:

25 An evaluation of 163 autistic children with

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1 regression showed that 72 percent were not developing
2 normally before the regression, and he cites a study
3 by Richler, et al. This is where the 72 percent I
4 used in the earlier calculation came from.

5 He goes on to state: Thus, normal
6 development can be documented in children with
7 regressive autism before the regression occurs, even
8 though the parents are unaware of it.

9 Q Okay. Go to the next slide, 41.

10 A Well, first that second sentence, the
11 concluding sentence, ignores that the cited study
12 could not document abnormalities in the other 28
13 percent of 163 regressive cases. Thus, it only serves
14 to document that clearly regressive cases appear to
15 occur. It actually documents two if we take it at
16 face value that there are a minority of regressive
17 cases who are a minority of all autistic cases.

18 The study, the 28 percent, it does not even
19 argue against TCVs causing regression in other cases
20 since children showing abnormalities could include a
21 population vulnerable to TCV effects. It's simply not
22 bearing on the issue here.

23 Q Let's go to the next slide, 42. You're
24 talking now about another study that Dr. Fombonne
25 cites.

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1 A Another study that Dr. Fombonne cites later
2 by Nelson, in paragraph 61 he cites it, and he's
3 talking about assertive biomarkers of prenatal
4 anomalies.

5 Dr. Fombonne states: In 99 percent of
6 children with autism, levels of at least one of these
7 substances, referring to these biomarkers, which are
8 not overt clinical signs or symptoms. They're
9 something that has to be measured through a test. At
10 least one of these substances exceeded those of all
11 controlled children among the autistics.

12 Although the results were not specific to
13 autism, they point unequivocally toward prenatal
14 anomalies in children with autism or intellectual
15 impairment.

16 Q Okay. Go to the next slide, 43.

17 A Even if this assertion were accepted at face
18 value it would not in any way detract from the
19 possibility or even the plausibility that TCVs can
20 cause clearly regressive autism.

21 Such effects could arise precisely because
22 certain subclinical anomalies are present, leaving the
23 child vulnerable to TCV effect. They could even be
24 clinical anomalies, but I just inserted subclinical
25 there because that's what they were discussing were

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1 biomarkers.

2 Q So they could just be biomarkers of
3 susceptibility?

4 A That's correct. They could be.

5 Q As opposed to biomarkers of developed
6 autism?

7 A That's right.

8 Q Okay. Slide 44.

9 A But then when I looked more closely at the
10 Nelson article it examined only 69 cases of autism
11 spectrum disorder. That's the broad category. So any
12 failure to find biomarker differences among autism
13 subtypes could be a simple consequence of insufficient
14 numbers of subtypes.

15 Again, there were no confidence intervals
16 given and no way to evaluate how much uncertainty
17 would be left by these small numbers, but they must be
18 very small. There can't be many clearly regressive
19 autistics in a series of 69 cases of autism spectrum
20 disorder. There would just be a few.

21 Now, the last example I want to give and the
22 most problematic for me is that other data cited by
23 Dr. Fombonne do not show what he asserts they show.
24 Again, I'm not saying he's distorting the literature.
25 I think he simply made the mistake of not looking at

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1 what I'm about to go over.

2 Q Okay. Slide 45?

3 A He says in paragraph 41, and in 121(e) he
4 also cites this study: Testable predictions could be
5 made if TCVs were hypothesized to be such an
6 environmental trigger.

7 First, the parents of children with
8 regressive autism born in the 1990s were exposed to
9 much smaller doses of thimerosal and vaccines than
10 were their children. Thus, if the above postulate
11 were true, referring to the hypothesis that the TCVs
12 are an environmental trigger, if that postulate were
13 true we would expect to see a lower rate of autism in
14 these older individuals than in relatives of
15 nonregressive autistic children.

16 But that is not the case, so he asserts that
17 there is the same rate of autism in these older
18 individuals as in relatives of nonregressive autistic
19 children, and he cites a study which is extensively
20 cited elsewhere by Lainhart, et al. in 2002.

21 Q Okay. And the next slide, 36? Go ahead.

22 A I went and examined that study carefully
23 since it seems to be pivotal to his argument. It
24 turned out that it compared only 18 parents of cases
25 labeled as regressive to 70 parents of cases labeled

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1 as nonregressive.

2 Now, based on the figures that he was giving
3 I would expect, first of all, that among the cases of
4 these 18 parents labeled as parents of regressive
5 there would only again be perhaps what, four or five
6 that would be parents of clearly regressive cases, so
7 these are very small numbers. Also, they compared
8 rates of broader autism phenotype, not autism, as Dr.
9 Fombonne states.

10 Furthermore, five of the 18 parents of the
11 regressive and 23 of the 70 parents of the
12 nonregressive had autism phenotype according to this
13 study. Thus, the parents of regressive cases did in
14 fact exhibit a slightly lower rate than parents of
15 nonregressive cases.

16 Q Is that the opposite of what he said?

17 A Well, it's not the opposite. The opposite
18 would be if they had more, but he said there was no
19 difference, and in fact it was slightly lower going in
20 the direction of what he was saying it wasn't doing.

21 Q Okay. All right. Next slide?

22 A Well, I don't want to capitalize on that
23 oversight because the Lainhart data are too scanty to
24 draw any reliable conclusion.

25 From there what they published, their

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1 numbers, I was able to calculate a 95 percent
2 confidence limit for the difference using methods that
3 are in many textbooks, including our own. The limits
4 that I got were very broad, minus 30 percent to about
5 plus 20 percent.

6 Regardless, there are other ways of
7 calculating these limits and they could come out
8 differently, but not so much different that it would
9 change this conclusion. The data are quite compatible
10 with the possibility that parents of regressive cases
11 had much lower rates of autism phenotype than parents
12 of other autistics, so the actual data do not show
13 what Dr. Fombonne cited them as showing, which is no
14 difference.

15 Q Okay. Slide 48. Now you're going to give
16 some responses to Dr. Goodman's report, another of the
17 defense epidemiology experts.

18 A Correct. Now, this report was very
19 problematic for me because I think that it was very
20 distorted. Unlike Dr. Fombonne's report, it was
21 saying many things which I would question whether Dr.
22 Goodman could get up and defend in a scientific
23 meeting before an audience of his peers, including
24 myself among them.

25 It presents absence of evidence as if it

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1 were evidence of absence. It exaggerates the
2 information content of the available evidence, and it
3 insinuates that any view departing from his own
4 preferred conclusion are unscientific. This should be
5 his own preferred conclusion.

6 He makes these arguments based on specious
7 analogies with astrology and unsupported claims about
8 mechanisms, claims that have no supporting evidence at
9 all.

10 Q You go into some more detail in the next
11 slides on this points, right?

12 A Yes.

13 Q Slide 49. Let's go to 49. There we go.

14 A Here's an example of the kind of exaggerated
15 claims made in his report. He says: The totality of
16 current epidemiologic evidence strongly supports the
17 conclusion that thimerosal-containing vaccines are not
18 related to the development of autistic disorder.

19 Q Okay. Next slide?

20 A Let's look at that. Nowhere in his report
21 does he define what it means for epidemiologic
22 evidence to strongly support a conclusion of no
23 effect.

24 There's a good reason that he doesn't.
25 There's no agreement among scientists about what kind

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1 of evidence is required for strong support or what
2 strong support means, especially for a null hypothesis
3 and a null association of the sort we're debating here
4 and especially in epidemiology.

5 I hope that epidemiologic evidence can only
6 rarely inarguably, strongly provide strong support --
7 again, there are words dropped here -- to claims of no
8 effect, and the TCV/autism controversy is not one of
9 those rare instances. I've stated that before, and
10 I'll state it again counter to what he's claiming.

11 Q All right. Let's go to the next slide, 51.

12 A Nowhere does Professor Goodman account for
13 the potential problems of the studies he cites. He
14 does a lot of hand waving citing Bradford Hill and
15 saying how these studies couldn't have major problems,
16 but he doesn't even discuss the major problem of these
17 studies in trying to make an inference about the cases
18 that we're discussing.

19 Instead, he presents results of the studies
20 in a table and argues that their statistics should be
21 taken at face value and combined. He presents no
22 estimate of the uncertainty that would be warranted if
23 methodologic issues such as the difference in dose
24 levels between the different countries in which these
25 studies were conducted, if those were allowed for.

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1 Q He doesn't even talk about dose differences?

2 A I didn't see where he made any accounting
3 for it. He made mention in passing.

4 Q Okay. Slide 52?

5 A He presents no further analysis to show that
6 these studies rule out subtype effects. None of the
7 data he presents concerns subtypes, so he doesn't even
8 go through the kind of calculations that I was
9 discussing earlier.

10 Instead, he claims that the combination of
11 studies which show high precision, as does Dr.
12 Fombonne in his paragraph 121(f), both fail to
13 recognize that the dose differences among the studies
14 would lead to wider confidence limits than they
15 expect, wide enough to allow for an overall risk where
16 they show six percent, which I want to remind us that
17 that's the upper bound that Fombonne put on the
18 increase from clearly regressive cases if there was a
19 doubling of risk of those.

20 Q Okay. The next slide is more about Dr.
21 Goodman's report. He further argues that the
22 regressive subtype is scientifically unfounded, a
23 scientifically unfounded category akin to astrologic
24 sign, in flat contradiction to numerous experts and
25 studies, including Dr. Fombonne at paragraph 83 where

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1 he recognizes that subtype and the Richler study which
2 provides evidence that it's real.

3 They recognize the subtype as a legitimate
4 clinical entity by virtue of having cases that have no
5 earlier symptoms that they could detect. I think his
6 arguments here are nothing more than rhetorical
7 nonsense.

8 Q Slide 54 shows some of those.

9 A Astrologic sign has no resemblance to TCV.
10 TCV involves direct injection into the body. In
11 contrast, astrologic sign refers to stars light years
12 away.

13 The fact that TCV is injected, that fact has
14 fueled concerns about its impact whereas it's the
15 enormous distance of the stars and the planets that
16 make astrology seem so outlandish. If astrology was
17 replaced by something talking about an exposure in the
18 house like fumes emitted from carpets it wouldn't be
19 an outlandish topic.

20 He cites this Peto study that's famous, but
21 that study isn't about what's going on here. It
22 concerns artifacts arising from analysis of multiple
23 subgroups, many subgroups in clinical trials. Here
24 are 12 astrologic signs, and we know that by chance
25 when you examine a lot of subgroups you're bound to

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1 find some things that are statistically significant,
2 even if there's nothing going on.

3 But the point at issue for me today and here
4 and in the literature that I have been citing is about
5 a single subgroup within a subgroup that's been talked
6 about at length in the literature, regressive autism,
7 and then that smaller subset which hasn't been talked
8 about in as much length, but appears to exist from the
9 Richler study and even seems to be conceded by Dr.
10 Fombonne.

11 Q Okay. And by the small group, the small
12 subgroup within the small group, you're talking about
13 the truly regressive autism?

14 A Yes.

15 Q Yes. Okay. All right. Let's go to the
16 next slide, Slide 55.

17 A So to go on about how ridiculous it is and
18 to call into question its credibility here, and I mean
19 to intentionally. There's not even a speculative
20 mechanism as to how the stars or planets could
21 influence individual health.

22 Whereas mechanisms have been proposed
23 whereby which thimerosal could affect regressive
24 autism. For example, in Kinsbourne's report on
25 general causation. Now, I am not saying that those

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1 mechanisms are real. I am not saying that they are
2 generally accepted. I am not saying anything of that
3 sort. I'm simply pointing out that people who have
4 worked in this area have presented these mechanisms.

5 They have been criticized. I'm well aware
6 of that. I am not an expert in that area. I'm not
7 here to comment on that. It's simply the fact that
8 there is nothing approaching that regarding astrology,
9 and that analogy he's drawing as far as I'm concerned
10 is something that would belong in a bad political
11 campaign, not in science.

12 Q Okay. Let's go to the next slide, Slide 56.

13 A Then he goes on and invokes fictional --
14 they're completely fictional scientific principles
15 claiming that arguments are scientific only if that
16 patient is distinguishable from the larger group on
17 the basis of a recognized causal or mechanistic
18 factor.

19 This distinction based on disease phenotype,
20 e.g. regressive autism, are only meaningful if that
21 phenotype is shown to be associated with a different
22 causal pathway or has a fundamentally different
23 biology than other phenotypes.

24 Q Okay.

25 A That's on page 9 of Professor Goodman's

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1 report.

2 Q And you say that what he's arguing there is
3 not scientific at all?

4 A Not at all.

5 Q Slide 57? Go on.

6 A All he's asserting here is that in the
7 absence of evidence we should dismiss anything that
8 fails to conform to this prejudice regarding
9 mechanisms.

10 In particular, he's claiming that we should
11 assume the same mechanism is operative among distinct
12 disease types whenever we don't know the mechanisms
13 that cause a disease. If you go back to the previous
14 slide to take his quote directly if you can --

15 Q Let's go back.

16 A I'd like to make this point.

17 Q Let's go back to Slide 56.

18 A He says: Distinctions based on disease
19 phenotype are only meaningful if that phenotype is
20 shown associated with a different causal pathway.

21 He's stating as a general principle. Where
22 was this principle when people started to distinguish
23 leukemia subtypes? Dr. Goodman is an oncologist,
24 among other things, so he should well know that people
25 were distinguishing subtypes of leukemia based on

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1 observable differences before anybody had any good
2 idea on the sources and causes of leukemia.

3 Even today, all the causes of leukemia are
4 not well mapped out. Most of the cases do not have an
5 identified risk factor, even though there are some
6 causes that are known like intense ionizing radiation.
7 People throughout medicine distinguish phenotype and
8 even recognize that the mechanisms could be different,
9 in fact may well be different, based strictly on
10 observed differences, different types.

11 Gradually, as medical science progresses,
12 for example, people started to recognize that there
13 were different subtypes of lung cancer. That was
14 before people finally realized that there was one
15 particular subtype that was dramatically increased by
16 smoking where you're talking about a relative risk of
17 10 or 20. It wasn't even an accepted association
18 until the 1960s or 1950s at the earliest. Doctors
19 were still promoting cigarettes as health aids clear
20 up to 1950.

21 Q Okay. Let's go to the next slide. I guess
22 58 is what we want to go to now.

23 A Well, actually we didn't --

24 Q What slide would you like?

25 A Well, we'll go on to the next one.

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1 Q Okay. Slide 58.

2 A So to see why Dr. Goodman's claim has no
3 scientific substance, it's important to understand
4 that the causes of autism in general, let alone the
5 regressive type, are not understood in any way that
6 has been demonstrated empirically, nor are the
7 mechanisms.

8 As a profound demonstration of the ignorance
9 of autism experts, these experts have failed to
10 conclusively identify the causes of the rise in
11 reported autism incidence and have failed to predict
12 its continuing course.

13 Now, I'm not saying that the rise in autism
14 incidence is real or part of a diagnostic issue. Dr.
15 Fombonne seems to be convinced that it's largely
16 diagnostic. It may well be, but at this point there
17 seems to be disagreement remaining in the literature
18 regardless of what people say about TCVs about what
19 are all the factors responsible for this increasing
20 report of incidence of autism. Nobody has been able
21 to predict how its course is going to go successfully.

22 Q Okay. Let's go to Slide 59.

23 A Dr. Goodman claims that absent any evidence
24 one way or another we should simply assume that early
25 autism and regressive autism are caused by identical

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1 mechanisms. This is the strong assertion in need of
2 proof.

3 He has basically shifted the burden of proof
4 away from a strong assertion that they are the same
5 mechanism and towards an admission that perhaps
6 they're not the same mechanism or perhaps there are
7 some mechanisms they share and others that they don't.

8 Dr. Goodman offered no evidence that the
9 mechanisms behind the two types are identical because
10 there is no such evidence. This argument is just
11 coming from his authority. It's not scientific. I
12 don't take that because I'm Dr. Goodman. I'm Dr.
13 Greenland. You should take my word for it. You
14 should look at the evidence. He doesn't give any. As
15 far as I can see, there isn't any.

16 Q Okay. Let's go on to the next slide.

17 A So as I said, he attempts to shift the
18 burden of proof to those who would allow -- simply
19 allow -- that different disease types could involve
20 mechanistic differences. I think his claims are
21 nonsense in both scientific and every day terms.

22 It is open minded and hence scientific to
23 allow for the full range of possibilities, including
24 differences in effects, in the face of such extensive
25 ignorance about the mechanisms of autism development.

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1 It's unscientific to assert that there is no
2 difference in mechanism when there is no understanding
3 of mechanism or very little.

4 Q All right. I think that summarizes your
5 testimony. We have a couple slides again just to make
6 your main points again. If you would reiterate those,
7 please?

8 A So again the epidemiologic literature has
9 not ruled out the possibility that thimerosal-
10 containing vaccines are associated with a prespecified
11 type of autism of the regressive form, and that's been
12 my point.

13 Not to say that there is such an
14 association, but simply that the evidence that I am a
15 qualified expert to discuss doesn't rule out that
16 possibility.

17 Q Okay.

18 A And specifically upon which controlled
19 studies have not analyzed clearly regressive autism.
20 Clearly regressive autism is very uncommon, so there
21 are very small numbers of cases in the studies to
22 date.

23 Hence, even if the studies have separated
24 the clearly regressive cases or even if we got their
25 data and could separate them out, a true association

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1 could easily be missed -- could have been missed and
2 could easily be missed -- because the numbers aren't
3 there at this point.

4 MR. WILLIAMS: Okay. Thank you very much.
5 That's all the questions I have.

6 SPECIAL MASTER HASTINGS: All right. Let me
7 ask. It is now 12:30. Do you want to go ahead and
8 start with your cross-examination of Dr. Greenland?

9 MR. MATANOSKI: No. We'd rather break for
10 lunch if we may.

11 SPECIAL MASTER HASTINGS: Okay. Had you
12 talked with the Petitioners about the issue of the
13 break for lunch?

14 MR. MATANOSKI: Yes. Yes, we did, and we
15 both acknowledge that we could shorten it a bit. We
16 thought maybe 45 minutes.

17 SPECIAL MASTER HASTINGS: Forty-five
18 minutes?

19 MR. POWERS: Forty-five minutes, which puts
20 it about 1:15.

21 SPECIAL MASTER HASTINGS: 1:15. All right.

22 MR. MATANOSKI: If I may?

23 SPECIAL MASTER HASTINGS: Go ahead.

24 MR. MATANOSKI: Could I ask for a copy of
25 the 52 pages of slides --

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1 SPECIAL MASTER HASTINGS: Yes. I wanted to
2 discuss that.

3 MR. MATANOSKI: -- for the lunch break so
4 that we could take a look at those?

5 SPECIAL MASTER HASTINGS: Right. Just for
6 those folks who are at home, we are going to take a 45
7 minute lunch break and start again at 1:15. We're off
8 the record at this time.

9 (Whereupon, at 12:30 p.m., the hearing in
10 the above-entitled matter was recessed, to reconvene
11 at 1:15 p.m. this same day, Monday, May 12, 2008.)

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1 to be clear for myself and for the Court what you were
2 saying and what you weren't saying in your report.

3 Now, my understanding of what you're saying
4 is that even though the body of epidemiologic
5 literature has found no association between
6 thimerosal-containing vaccines and autism spectrum
7 disorders, it's still theoretically possible that such
8 an association exists with a small subgroup, namely
9 those who develop regressive autism, correct?

10 A I would change one word order there, and
11 that's --

12 Q Go ahead.

13 A -- the epidemiologic data has not found an
14 association, but the rest I would say yes.

15 Q But it's theoretically possible that it
16 still exists in a small subgroup, regressive autism?
17 What I'm actually understanding you to say today is
18 clearly regressive autism. Is that correct?

19 A Correct.

20 Q And you did a variety of calculations in
21 your report to show theoretically how high that risk
22 could be, correct?

23 A Correct.

24 Q Now, you did state in your report on page 16
25 that the brief overview given above, meaning the

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1 epidemiologic studies that had been done to date,
2 supports the idea that the association of you say MCV.
3 I say TCV. When you say TCV you know what I'm talking
4 about?

5 A Yes.

6 Q It's a mouthful to say thimerosal-containing
7 vaccines, so I'll use the acronym. The association of
8 TCV with autism is small or nonexistent. Do you
9 recall writing that in your report?

10 A Yes.

11 Q Do you still agree with that?

12 A Yes.

13 Q Now, there have been a few studies that have
14 purported to find an association between thimerosal-
15 containing vaccines and autism, and you refer to those
16 in your report as ostensibly positive studies. I'm
17 referring to those done by Dr. Mark Geier and his son,
18 David.

19 A Yes.

20 Q Have you reviewed those studies?

21 A I have read them.

22 Q Okay. And you noted though that those
23 studies have been criticized by other reviewers,
24 correct?

25 A Correct.

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1 Q Have you formed your own assessment of those
2 studies?

3 A I concurred with the reviewers. This is why
4 I did not include them in my review.

5 Q You found those studies to be not credible?

6 A I would put it as deficient in methodology
7 such that I would not count them as evidence if others
8 were willing to go along with that.

9 Q Now, Doctor, if there was indeed an
10 increasing incidence in the overall number of autism
11 cases that some have termed an autism epidemic and if
12 it was shown that thimerosal-containing vaccines were
13 the reason for that increasing incidence, would that
14 increase likely be picked up by the epidemiologic
15 studies?

16 A If it was restricted to a subgroup then it
17 wouldn't have.

18 Q No. I'm not talking about subgroups. I'm
19 just talking about there's been a purported autism
20 epidemic. If there's really indeed an increasing
21 incidence in the number of autism cases that some have
22 termed an autism epidemic, would that be detected
23 epidemiologically?

24 A I think I'm not understanding your question.
25 Please restate it.

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1 Q If there was an increasing incidence in
2 autism, if the number of cases of autism were
3 increasing tenfold, for instance, and if that increase
4 were due to thimerosal-containing vaccines, would that
5 be picked up by epidemiologic studies?

6 A Yes, a tenfold increase certainly would be.

7 Q And would you agree that the body of
8 epidemiological literature has not supported the
9 hypothesis of an autism epidemic?

10 A My understanding is that there is an
11 increasing diagnosis of autism. The cause of that,
12 whether it's diagnostic changes or actual changes in
13 the occurrence of the disease, seems to be a matter of
14 convention from my understanding.

15 Q I'm asking hypothetically. If indeed it was
16 shown that there is an autism epidemic, would you
17 agree that the epidemiological literature does not
18 support the hypothesis that an epidemic is caused by
19 thimerosal-containing vaccines?

20 A I would agree.

21 Q I want to be clear about your opinion in
22 this case or in this litigation. Is your opinion
23 predicated on the assumption that children with
24 clearly regressive autism have an elevated risk due to
25 thimerosal, and children with nonregressive autism

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1 have little to no elevated risk due to thimerosal?

2 A Which portion of my opinion? Some parts
3 make the assumption for the calculations that I made
4 that the risk was only increased by thimerosal for
5 those with clearly regressive, but other parts of my
6 argument didn't refer to that assumption.

7 Q In the slide presentation that you presented
8 during your direct testimony, some slides referred to
9 regressive autism as being the subgroup under
10 consideration, and some slides referred to clearly
11 regressive autism.

12 Which one are you saying is purportedly
13 associated or that the epi studies have been unable to
14 detect?

15 A Well, the general argument is that if there
16 is a subgroup that is as uncommon as, for example,
17 clearly regressive autism would appear to be then
18 whatever that subgroup may be the epidemiologic
19 studies could not have picked up an increase in risk
20 in that group if it had been confined to that group,
21 even if it was a large increase.

22 Q So if the risk is confined to that group the
23 clearly regressive autism, are you assuming then that
24 there is no elevated risk to any other group, any
25 other cases of autism?

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1 A In the calculations I made, yes.

2 Q Now, Doctor, you don't claim in your report
3 and I don't understand you to be claiming here today
4 that you have any expertise in autism, do you?

5 A I am not claiming that.

6 Q And you are not claiming in your report or
7 here today that you have any expertise in regressive
8 autism in particular, correct?

9 A I am not claiming that.

10 Q How do you define regressive autism?

11 A Simply by whatever definition is being used
12 in a report. I go along with it, not being an expert
13 in the --

14 Q What report?

15 A It depends on which study we're talking
16 about. For example, one of the reports -- I forget
17 the primary author -- described regressive autistic
18 cases among their case series. Well, several did.

19 For the purpose of analyzing that report, I
20 would then simply accept whatever the authors were
21 using, as well as Dr. Fombonne when he would discuss
22 the matter as well.

23 Q Now, on page 1 of your report you call
24 regressive autism a prespecified type of autism. Why
25 did you use the term prespecified?

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1 A That was with respect to the idea that it
2 might have been defined after the fact solely based on
3 exposure to thimerosal.

4 Q After what fact?

5 A After the introduction rather of the
6 hypothesis that TCVs cause autism.

7 Q Who told you about that hypothesis?

8 A I don't remember when I first read of it. I
9 remember seeing things in the news long ago, but I
10 don't recollect exactly.

11 Q And who told you that? Where did you hear
12 that thimerosal-containing vaccines cause regressive
13 autism only?

14 A I don't recall where I first saw that.

15 Q Now, Doctor, did you present in your report
16 any evidence that regressive autism is a form of
17 autism that is biologically distinct from any other
18 cases of autism?

19 A I did not.

20 Q And can you present any evidence that would
21 lead you to distinguish regressive autism biologically
22 from nonregressive cases of autism?

23 A I would have to rely entirely on other
24 experts.

25 Q And you didn't present in your report any

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1 evidence that the causal risk factors for regressive
2 autism are different than the risk factors for other
3 cases of autism, correct?

4 A That's correct.

5 Q Can you tell us what the risk factors for
6 autism are in general?

7 A I know that there is supposed to be some
8 syndromes, genetic syndromes that are associated with
9 it, but that most of the cases, from what I'm read,
10 are supposed to be sporadic, of unknown origin.

11 Q And can you offer evidence that shows that
12 thimerosal is a risk factor for autism, regressive
13 autism, but not for other cases of autism?

14 A I cannot.

15 Q Are you aware of any published literature
16 stating that regressive autism is caused by
17 thimerosal-containing vaccines?

18 A Could you repeat that, please?

19 Q Certainly. Are you aware of any published
20 literature that states that regressive autism is
21 caused by thimerosal-containing vaccines?

22 A Well, I'm aware of published literature that
23 states that.

24 Q Where? Which literature?

25 A Well, it appears to me that the Geiers, for

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1 example, make this type of claim, so if you say just
2 published literature --

3 Q Besides the Geiers, are you aware of any
4 other literature that makes that claim?

5 A Well, I've certainly read other items,
6 writings -- not necessarily peer reviewed or
7 scientific -- that made these claims.

8 Q But you can't recall today what those are?

9 A No.

10 Q Are you aware of any study that has
11 suggested the hypothesis?

12 A No. Excuse me. No. Let me correct that.
13 I'm certainly aware of the Geier study and so forth.

14 Q The Geiers' epidemiological studies that you
15 agreed had methodological problems?

16 A That's correct.

17 Q Doctor, if I understand your opinion in this
18 litigation, you're not stating an opinion as to the
19 likelihood that such a regressive subgroup exists
20 that's uniquely susceptible to thimerosal-containing
21 vaccines, are you?

22 A That's correct. I'm not.

23 Q And you're not claiming here that it's been
24 scientifically shown that the subgroup exists, are
25 you?

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1 A That's correct.

2 Q So your opinion is not that the subgroup
3 actually exists. You're saying that it's theoretical
4 possible that it exists, correct?

5 A Well, no. There is some evidence and
6 support in, for example, the study cited by Fombonne,
7 by Richler, which apparently looked for background
8 factors in the regressive autistic cases.

9 Q Did they talk about thimerosal?

10 A No.

11 Q I'm talking about the subgroup of regressive
12 autism that's uniquely susceptible or I should say
13 clearly regressive autism because that's what you're
14 focusing on today.

15 A Yes.

16 Q The subgroup of clearly regressive autism
17 that's uniquely susceptible to thimerosal-containing
18 vaccines. You're not saying that it actually exists?

19 A I misunderstood your compound.

20 Q No problem.

21 A What I was stating there was that it appears
22 from the literature there is a clearly regressive
23 subgroup, and on the other hand I am not aware of any
24 literature that supports the idea that there is a
25 clearly regressive subgroup specially susceptible to

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1 thimerosal, but my comment was simply that that hasn't
2 been investigated so there isn't evidence bearing on
3 it.

4 Q Okay. But you're saying that such a
5 subgroup does exist? It's rare enough that it has
6 gone undetected by the epidemiologic studies, correct?

7 A That's the way it looks to me.

8 Q Doctor, theoretical possibilities though are
9 applicable to any study, aren't they?

10 A Certainly.

11 Q I mean, we could refute known associations
12 or lack of associations just based on hypothetical
13 subgrouping of the study subjects, can't we?

14 A Well, perhaps I could give an example since
15 I'm not 100 percent clear on what you're asking, but
16 to take an example that would I think make it obvious
17 with smoking and lung cancer.

18 This is an association which is enormous,
19 and people noticed associations of smoking with lung
20 disease as far back as the 1600s when tobacco began
21 spreading in Europe, but it took all the way into the
22 1960s before the Surgeon General went so far as to
23 recognize it as a health hazard and publish a report
24 on that.

25 Nonetheless, to this date we also know and I

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1 think fewer people realize that most smokers don't get
2 lung cancer, and we don't know why. We don't know
3 what it is about particular individuals in every
4 detail, in every case at least, that leads to them
5 getting lung cancer when they do smoke.

6 So even though it's something that is very
7 well known, there is still to this day and after a
8 half century of intensive research much unknown, which
9 would be an issue, for example, if this was one of the
10 cases in which people were suing tobacco companies
11 because of their disease. In fact, it's arisen.

12 So there always remains even in a case as
13 extreme as that where there's centuries of observation
14 and a half century of intense scientific research and
15 well-recognized causation. Even in a case like that,
16 to this day there are points of contention. That's
17 how science is in reality. It's supposed to infirm
18 for all time 100 percent knowledge with medical
19 science.

20 Q Right. I think you're saying what I was
21 suggesting. To take your example of smoking and lung
22 cancer, I could say yes, studies have shown an
23 association between smoking and lung cancer, but I can
24 say to you well, Doctor, how do you know nobody has
25 ever looked at whether smoking causes lung cancer in

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1 tall men with brown hair.

2 Or I could define the subgroup to say no one
3 has ever looked at the association between smoking and
4 tall men not just with brown hair, but with dark brown
5 hair. You could take it on and on, correct?

6 A Well, what I would expect more to hear, and
7 in fact this is something that people talk about, is
8 what is it about the vast majority of smokers who
9 smoke heavily through their life and don't get lung
10 cancer?

11 The search is there for the genes that would
12 identify those who do and those who don't get lung
13 cancer, so indeed there's a focusing on subtypes, but
14 not brown hair. I haven't heard that used as a
15 respecter of autism.

16 Q Well, because it's a ridiculous example, and
17 it's ridiculous because I haven't offered you any
18 explanation as to why tall men with brown hair are
19 somehow different than the populations that have been
20 studied, correct?

21 A Correct, but there are factors where there
22 are theoretical explanations, and people continue to
23 pursue these issues.

24 Q Now, Doctor, I understand your opinion is
25 that the epidemiologic studies don't disprove the

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1 hypothesis that thimerosal-containing vaccines cause
2 clearly regressive autism, correct?

3 A Correct.

4 Q But you're not saying, are you, in this
5 litigation that the study proved the hypothesis
6 either, are you?

7 A Correct. Definitely not.

8 Q And in your report you don't actually state
9 the likelihood of an association between thimerosal-
10 containing vaccine and clearly regressive autism, do
11 you?

12 A I do not.

13 Q Doctor, is there any evidence that clearly
14 regressive autism is more likely than not caused by
15 thimerosal-containing vaccines?

16 A I'd say all the evidence that I've seen
17 discussed has some bearing on it, so --

18 Q I didn't ask about bearing. I asked is
19 there any evidence that it's more likely than not that
20 thimerosal-containing vaccines cause clearly
21 regressive autism?

22 A You said any evidence. My specialty is
23 epidemiologic evidence, so if you would narrow it to
24 that?

25 Q Well, how about epidemiologic evidence?

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1 A Epidemiologic evidence? Then I would agree
2 with your statement.

3 Q Doctor, as a member of the scientific
4 community do you believe that clearly regressive
5 autism is caused by autism-containing vaccines?

6 A I don't have any belief one way or the
7 other.

8 Q Do you have any belief one way or the other
9 that autism is caused by thimerosal-containing
10 vaccines?

11 A I do.

12 Q Okay. What's your belief?

13 A Well, let me --

14 Q I'm talking about autism in general.

15 A Autism in general. That if there is an
16 effect, I would bet that if there is an effect it must
17 be concentrated if there is. Notice the hypothetical,
18 please. It must be concentrated in a very small group
19 to have gone undetected to this point in time.

20 Q But you can offer no evidence that such a
21 group exists, correct?

22 A That's correct.

23 MS. RICCIARDELLA: Thank you. I have no
24 further questions.

25 SPECIAL MASTER HASTINGS: Any redirect?

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1 MR. WILLIAMS: I have no redirect.

2 SPECIAL MASTER HASTINGS: No redirect?

3 MR. WILLIAMS: No redirect.

4 SPECIAL MASTER HASTINGS: Okay. All right.

5 Dr. Greenland, thank you very much. You're excused at
6 this point.

7 THE WITNESS: Thank you.

8 (Witness excused.)

9 SPECIAL MASTER HASTINGS: Should we proceed
10 with Dr. Aposhian at this point?

11 MR. WILLIAMS: We have some logistics to get
12 him to the airport. Can we have five or 10 minutes
13 right now and then start Dr. Aposhian?

14 SPECIAL MASTER HASTINGS: All right. Let's
15 take a brief break. We'll start back with Dr.
16 Aposhian as soon as you're ready.

17 MR. WILLIAMS: Thank you.

18 SPECIAL MASTER HASTINGS: Thank you.

19 (Whereupon, a short recess was taken.)

20 SPECIAL MASTER HASTINGS: We are ready to go
21 back on the record. We are going to proceed then with
22 Mr. Williams' examination of Dr. Aposhian.

23 Dr. Aposhian, would you raise your right
24 hand?

25 //

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1 Whereupon,

2 VASKEN APOSHIAN

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

5 SPECIAL MASTER HASTINGS: Please go ahead,
6 Mr. Williams.

7 DIRECT EXAMINATION

8 BY MR. WILLIAMS:

9 Q Dr. Aposhian, I know that you have testified
10 before the Special Masters before, but for this record
11 I do want to briefly run through your qualifications
12 again. Would you tell us what is your current status
13 in academia?

14 A I am Professor Emeritus of Molecular and
15 Cellular Biology, my primary appointment, and also
16 Professor Emeritus of Pharmacology in the School of
17 Medicine at the University of Arizona.

18 Q And are you still active in the scientific
19 arena?

20 A Yes. I have grants from foundations and
21 grants from the federal government to do research, and
22 my lab is still going.

23 Q Let's go to Slide 3, please.

24 A I have no slides up here.

25 MR. WILLIAMS: You don't see the pictures?

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1 His monitor is not on.

2 SPECIAL MASTER HASTINGS: Just for the
3 record, let's mark the paper copy of his slide
4 presentation as Petitioners' Trial Exhibit 2.

5 (The document referred to was
6 marked for identification as
7 Petitioners' Exhibit No. 2
8 and was received in
9 evidence.)

10 BY MR. WILLIAMS:

11 Q Can we try to go forward with you reading
12 this, or is that not going to work?

13 A Whatever you wish.

14 MR. WILLIAMS: I hate to waste more time,
15 but he can't see his --

16 SPECIAL MASTER HASTINGS: We've got a
17 technical expert here. Let's go off the record.

18 (Whereupon, a short recess was taken.)

19 SPECIAL MASTER HASTINGS: We're back on the
20 record.

21 Mr. Williams, resume your examination.

22 SPECIAL MASTER HASTINGS: Thank you.

23 BY MR. WILLIAMS:

24 Q Dr. Aposhian, what is your education?

25 A I have a Bachelor of Science degree in

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1 Chemistry from Brown University, a Master of Science
2 and a Ph.D. in Physiological Chemistry from the
3 University of Rochester.

4 Q And then did you spend time at Stanford
5 University after you got your Ph.D.?

6 A Not exactly. I had an academic position at
7 Vanderbilt University, and I resigned that tenure
8 track position to have the opportunity to work with a
9 man who a year later got the Nobel Prize -- it was
10 very valuable to me -- to learn biochemical genetics,
11 enzymology and basic biochemistry from Arthur
12 Kornberg, one of our best biochemists.

13 Q Now turning to Slide 4, have you published a
14 number of articles in the peer reviewed literature?

15 A Yes. I don't keep track. I would say over
16 200, but in my CV I don't put numbers. I've also been
17 the associate editor of a number of journals and have
18 peer reviewed many, many papers for various journals.

19 Q And is your work still cited frequently in
20 textbooks and other scientific literature?

21 A Yes, and we were very pleased to hear from
22 the editor of *Chemical Research and Toxicology*, which
23 is sponsored by the American Chemical Society, that in
24 the year 2006 the most downloaded article for this
25 journal was an article by me and my wife.

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1 Q And has a lot of your published work dealt
2 with heavy metal toxicology?

3 A Yes, almost completely.

4 Q All right. Now, did you prepare an outline
5 of what you're going to talk about today?

6 A Yes. Would you like me to go over it?

7 Q I think it would be helpful very quickly,
8 yes.

9 A All right.

10 SPECIAL MASTER HASTINGS: That's on Slide 5,
11 is it not?

12 MR. WILLIAMS: Yes, Slide 5. There's
13 Introduction. I want to begin with an introduction in
14 which I'll define evidence-based toxicology. No. 2,
15 Basic comments regarding modern toxicology;
16 introductory remarks regarding autism spectrum
17 disorders;

18 A brief review of mercury toxicology; methyl
19 mercury, thimerosal and ethyl mercury; brain
20 concentrations of mercury species; developmental
21 biology and autism; and the first hypothesis: One
22 cause of autism is cells cannot efflux mercury,
23 including thimerosal ethyl mercury.

24 The second hypothesis: Terbutaline is an
25 example of a teratogen that can cause some types of

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1 autism via a neuroinflammation mechanism. Under this
2 we'll discuss Terbutaline. We were going to discuss
3 teratogens. I think we may have taken that out. I'm
4 not sure. No. 9, Thimerosal and ethyl mercury. Pink
5 disease we took out. We didn't have a chance to
6 change that. And then I'll present a summary.

7 BY MR. WILLIAMS:

8 Q Okay. Now, on Slide 6 there are a number of
9 definitions of measures. I don't want to take the
10 time to go through this now, but we prepared this for
11 reference purposes later if we need to come back and
12 figure out how to convert one measure of a
13 concentration to another. Is that right?

14 A Yes. Yes.

15 Q Okay. Let's leave that be for now. We may
16 need to come back to it.

17 All right. Slide 7. You prepared this.
18 Would you go ahead and explain why you wanted to --

19 A Yes. I wanted to make some comments that I
20 think are relevant.

21 First of all, science by definition is a
22 search for the truth. Autistic children are not
23 normal. What is or are the abnormality or
24 abnormalities at the molecular level of autistic
25 children we do not know.

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1 What do first class scientific investigators
2 do when they don't know? They formulate a hypothesis.
3 That is the purpose of my testimony; to formulate a
4 probable hypothesis that thimerosal is involved in
5 some manner, either directly or indirectly, either
6 prenatally or postnatally in the etiology of autism
7 specifically affecting the brain.

8 Q Okay. Now, you used the term earlier
9 evidence-based toxicology. What is evidence-based
10 toxicology? This is on Slide 8.

11 A Most of my testimony and slides are not my
12 expert opinion. I want to make it very clear. What
13 I'm presenting are the data, the evidence or comments
14 from peer reviewed papers or from symposium that have
15 usually been peer reviewed.

16 Throughout this testimony, these peer
17 reviewed comments are in dark blue font. My personal
18 expert opinion when I do occasionally put it forth is
19 in red font. As many slides as possible are labeled
20 or include a literature reference, so again it's not
21 my opinion on those slides.

22 Most of my testimony and slides therefore
23 deal with a relatively new term; that is, evidence-
24 based toxicology. I'm presenting you what other
25 experts have written in peer reviewed articles.

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1 Q Now, you also have some comments you want to
2 make about modern toxicology.

3 A Yes. May I have the next slide, please?
4 The next slide, please?

5 Q This is Slide 10.

6 A Slide 10. Now, let me say at this point
7 that many people don't understand that people in
8 science have disagreements, and even though the
9 disagreements are based on how they interpret
10 something differently there is no disrespect intended
11 and so under no circumstances --

12 For example, I've known Tom Clarkson for
13 years, and I have a tremendous respect for him.
14 Obviously I have different opinions, as he does, on
15 certain factors that will be presented, but I want to
16 make it clear that these are differences in
17 interpretations, not meant to be personal in any way.

18 So let's say does dose determine the poison?
19 We now know in 2008 other factors also determine the
20 poison, and now I'm quoting from the classic textbook
21 in toxicology from a chapter written by Robert Goyer,
22 a toxicologically oriented pathologist, and Tom
23 Clarkson, who is one of the Respondent's, and in this
24 chapter, which is chapter 23, I've taken Table 3-1 out
25 verbatim.

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1 It points out: Factors influencing toxicity
2 of metals; interactions with essential metals;
3 formation of metal protein complexes; age and stage of
4 development; lifestyle factors; chemical forms
5 aspeciation; immune status of the host. These are
6 factors that influence the toxicity of the metal.

7 As the next slide will point out, this is a
8 chapter again in the same textbook, a different year I
9 think, by Melinsky and Klaassen. Klaassen is one of
10 the most eminent toxicologists we have in this
11 country. He's probably on more national committees,
12 more government advisory committees, than anyone else
13 that I know in toxicology.

14 I quote now: As we described earlier, the
15 most critical factor influencing toxicity is not
16 necessarily the dose, but rather the concentration of
17 a xenobiotic at the site of action, a xenobiotic being
18 a foreign chemical by definition. Xenobiotics are
19 delivered to most organs by the systemic circulation.
20 Therefore, the fraction of a chemical that reaches the
21 systemic circulation is of critical importance in
22 determining toxicity.

23 Several factors can greatly alter the
24 systemic availability, including 1) Limited absorption
25 after oral dosing; 2) Intestinal first pass effect; 3)

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1 Hepatic first pass effect; and 4) Mode of formulation,
2 which affects, for example, the dissolution rate, how
3 the stuff comes to part or goes into solution, or
4 incorporation into the micelles for lipid-soluble
5 compounds.

6 All substances are poisons. This is a
7 direct quote. There is none which is not a poison.
8 The right dose differentiates poison. That's by
9 Paracelsus, who lived between 1493 and 1541.

10 Toxicology has progressed since then. It's
11 almost 500 years, all right, so again dose is not the
12 only factor that determines the poison and we'll come
13 back to this over and over again during this
14 presentation.

15 Q Okay. Let's go to the next slide, Slide 12,
16 please.

17 A This is on the web, the IOM, the Institute
18 of Medicine Forum on Autism -- not on vaccines, but on
19 autism -- and the Environment, which was held in April
20 2007. This is a quote from Phillip Landrigan, who is
21 a professor of pediatrics and also an epidemiologist
22 at Mt. Sinai School of Medicine, one of the best we
23 have:

24 Chemicals in the environment can injure the
25 human brain. Children are especially vulnerable to

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1 brain injury caused by chemicals, and this
2 vulnerability is generally greatest during the nine
3 months of pregnancy and the earliest years of life.
4 The brain injury caused in children by chemicals is
5 sometimes symptomatic, but more often produces a range
6 of abnormalities that impair function and that can be
7 detected only through special testing.

8 The next slide, please? Children are not
9 little adults. We try teaching our students that over
10 and over again. Children are not little adults. As
11 shown below, it takes a premature neonate on the
12 average almost four times longer to get rid of a
13 chemical.

14 What is plotted here on the left is
15 children's half-time relative to adults, half-time
16 being how long it takes to get rid of half of the
17 concentration. On the bottom we're plotting the
18 various stages. As you can see, especially when you
19 look at the first bar graph, that's almost four times
20 greater than what would be called normal at the number
21 one level.

22 Next slide, please?

23 Q Let me just ask you on this one, though.

24 A Yes?

25 Q The third bar over is the bar for children

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1 who are one week to two months of age.

2 A Yes.

3 Q Is that still statistically significant
4 above an adult's ability?

5 A Yes, it is. It is. If you go back to the
6 original paper you'll see it is. That's the third
7 one. Yes.

8 Q Okay. All right. Now, you have some
9 remarks prepared about autism spectrum disorder, going
10 to Slide 15.

11 A Yes. Now, if you remember from your college
12 chemistry or college physics, a spectrum consists of
13 well-defined bands.

14 Next slide, please? And this is the visible
15 spectrum that you see with very definite colors from
16 one end to the other.

17 The next slide, please? Now, as far as
18 autism spectrum disorders are concerned, there are no
19 bands, and most clinicians will admit this; that we
20 have Asperger's, the high functioning ASD kids, at one
21 end and severe autism, the very barely functioning
22 children, at the other end, but in between there is
23 not very much.

24 This has caused Dr. Spence, who is at the
25 National Institutes of Health, to say we need a

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1 standardized definition of autism and related
2 disorders. This is one of the major problems in
3 trying to define these different kinds of autism
4 spectrum disorder.

5 Next slide, please?

6 Q This is Slide 17.

7 A Autism is a complex disorder. Autism is a
8 multi-system disorder whose outcome is likely to be
9 more profoundly impacted by the environment than any
10 other disorders and diseases. This is put forth by a
11 professor at the University of California-Davis again
12 at this superb IOM autism workshop that was held last
13 year.

14 Three percent of all developmental defects
15 are attributed to exposure to toxic chemicals.
16 Twenty-five percent of all developmental defects may
17 be due to a combination of genetic and environmental
18 factors.

19 Next slide, please?

20 Q Slide 18.

21 A Now, I introduced this slide because I think
22 it says a number of things. This again was presented
23 at the Institute of Medicine workshop. Again, it's on
24 the web as a recording of that workshop.

25 Autism is estimated to cost \$3.2 million per

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1 child over a lifetime. Using the conservative
2 estimate in the United States of 500 children means
3 the epidemic will cost society close to \$2 trillion.
4 \$2 trillion. Many families are on the brink of
5 bankruptcy as they struggle to get insurance and the
6 medical attention their children need.

7 Recently clinical investigations have
8 identified numerous co-morbid disease states in
9 children with autism. These include other disorders
10 that go along very often with autism:

11 Immune system abnormalities; inflammatory
12 bowel disease; oxidative stress; disordered urine and
13 serum chemistries; including elevated porphyrins;
14 methylation disturbances; increased body burden of
15 metals, including mercury and lead; chronic viral,
16 fungal and bacterial infections; and also, as I put in
17 and added to this, microglial activation in the brain,
18 which we'll also speak about in a few minutes.

19 Q Okay Can you tell us what you mean by
20 oxidative stress?

21 A Because of a number of physiological
22 challenges or exposures, the body begins to make free
23 radicals. These free radicals are very reactive
24 chemical substances, and they can damage the structure
25 of DNA, they can damage the structure of proteins, and

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1 they can damage other structures, so it's a very
2 critical kind of injury that one likes to prevent, and
3 one can prevent that by giving antioxidative stress
4 protection.

5 Q Are there recommended diets and recommended
6 therapies for people who suffer from oxidative stress?

7 A It depends on what you mean by recommended.
8 If you mean are there alternative medicine sources?
9 Are there health food store sources? Yes.

10 There are only one or two that established
11 medicine would recommend, but we have natural
12 mechanisms in our body that try to overcome these free
13 radicals, these oxidative stress phenomena.

14 Q All right. Let's go to the next slide, No.
15 19.

16 A I think you want 20. Is it 20?

17 Q Slide 20. I have a different numbering
18 system.

19 A This is taken from the *Journal of Science*.
20 I find diagrams and figures much more instructive than
21 numbers and tables, all right, and so let me just
22 point out to you some of the genetic terms of
23 inversion, insertion, deletion and copy number
24 variation.

25 If you look at the lower right-hand corner

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1 of this slide you'll see the reference. We have a
2 gene A, B, C. That could even be three different
3 parts of a gene, or this whole thing could be a
4 chromosome. It doesn't matter. We're talking about
5 genetic information now.

6 Now, what is normal is the reference A, B,
7 C. When an inversion occurs it means C, for example,
8 will be put before A rather than after B. This does
9 happen. Chromosomes are known to have this happen to
10 them, and disease are known to be caused by this.

11 An insertion is when some extra genetic
12 information or extra DNA information is inserted, as
13 you see with the letter D for dog in the second to the
14 right. Below that is deletion, which is quite
15 obvious. In this case we've taken B out.

16 Then of course copy number variation is
17 again another known cause of a number of disorders,
18 and here you see we've put in -- the person who put
19 this diagram together or figure together for *Science*
20 added four copies of C rather than one copy of C.

21 Q All right. Let's go to Slide 21.

22 A Again at the IOM forum, Lipkin, a very good
23 scientist from Columbia University: To emphasize that
24 our working model for autism is one with three
25 dimensions where a genetic susceptibility,

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1 environmental triggers and temporal contacts act in
2 concert to cause disease. It's not just genetics.

3 Q And again the blue is not your opinion?

4 A Yes.

5 Q That's the opinion of the scientist
6 presenting at this IOM conference?

7 A Exactly. Exactly.

8 Q Okay. Let's turn to mercury toxicology
9 then.

10 A A brief review of mercury toxicology. Next?

11 Q Slide 23.

12 A This shows the influence of the mother and
13 other sources for mercury exposure of infants. In the
14 mother we have methyl mercury from fish. We also have
15 methyl mercury from chicken. Now, some of the
16 Respondents did not realize that or forgot what they
17 had learned earlier.

18 The next slide, which please don't show yet.

19 The next slide will give just one reference to the
20 showing that there is methyl mercury in chickens.

21 There is methyl mercury in chickens because this
22 country imports chopped up or pulverized fish bones
23 and pulverized fish products to feed the fowl.

24 I did a study. The Government of Chile
25 asked me to go down and look at some people. One time

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1 we did a very large study of arsenic exposure. I saw
2 this huge mound by the port, and it was probably the
3 height of a 10-story building. I asked my host what
4 is that? He said oh, that's chicken feed that we are
5 going to send to America.

6 I said but what is it made of? He said oh,
7 that's our waste products, stuff we don't want, the
8 fish bones and other things that are ground up. This
9 is where the methyl mercury in chickens in this
10 country come from. There are many papers dealing with
11 this. They're not read very often.

12 We have mercury from amalgam, from the
13 mother's amalgams. We have thimerosal ethyl mercury
14 from vaccines that the mother may have had. These
15 forms of mercury all can pass the placenta and get
16 into the fetus.

17 In addition, a child from the mother will
18 get thimerosal, especially if the child is being
19 breast fed. The child will get thimerosal ethyl
20 mercury from its own vaccines. They will get methyl
21 mercury from breast milk, methyl mercury from fish,
22 methyl mercury from chicken, methyl mercury from
23 amalgams of the mother and of course the vaccines that
24 the child has been given if the child was given
25 vaccines containing thimerosal.

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1 Q Is it fair to say, do you think, that
2 virtually all children born in the United States have
3 some exposure to mercury whether they get it in
4 vaccines or not?

5 A I think that's correct. I think that's
6 absolutely correct.

7 Q And that load can vary from region to region
8 and diet to diet?

9 A That's correct. When I referee journal
10 articles some new investigators will say this mercury-
11 free human or this mercury-free animal, and what we'll
12 always say is what is the evidence they're mercury-
13 free? No one can really give that evidence. There's
14 always some of this in us.

15 Q Okay. Then on the next slide you give your
16 reference.

17 A This is just one of many references.

18 Q Okay. Slide 25.

19 A Okay. Again, I must apologize for reading
20 this or reading many of these slides because if I were
21 giving my expert opinion I could extemporaneously say
22 this.

23 There's nothing more boring to a student in
24 a university than to hear a professor reading a
25 lecture, but I think it's essential that I read it so

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1 that you know the exact words that the peer reviewed
2 expert -- not me -- is saying. If we were in the
3 university setting I could throw in some dirty jokes,
4 but this is not allowable here, of course, just to
5 brighten things up.

6 Q Well, in this one you're quoting one of the
7 Respondent's experts, right?

8 A Pardon?

9 Q In this one you're quoting one of
10 Respondent's experts?

11 A Yes. Yes. Anyway, here we go. This is
12 Clarkson, again a good friend of mine. I've
13 entertained him in my home with his wife. Tremendous
14 respect for the man. We both get along very well,
15 even though he's Respondent's.

16 Classification of Mercury Species or Forms.
17 The mercury species are sometimes classified
18 chemically as inorganic and organic. The inorganic
19 would include by this chemical classification
20 elemental mercury, which is Hg^0 , in the form of a
21 liquid or the vapor; mercuric mercury, Hg^{+2} ; and
22 mercurous mercury, Hg^{+1} .

23 Elemental mercury, Hg^0 , exists in liquid
24 form at room temperature. Vapor from the liquid,
25 which we call mercury vapor, is more hazardous than

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1 the liquid form. The liquid form has very little, if
2 any, toxicity if it gets into the stomach, for
3 example, but the vapor is different.

4 The toxicological classification of mercury
5 compounds used by many toxicologists is based on their
6 toxicological properties, and here we break them down
7 into elemental, inorganic and organic. In this
8 classification, although elemental mercury is
9 inorganic, it is put into a separate category because
10 of the many different toxicological properties.

11 Q If you swallow liquid mercury it basically
12 passes through without being absorbed, true?

13 A Essentially. There are many cases in the
14 literature, interesting cases. They used to put
15 mercury, liquid mercury, into tubes when they wanted
16 to block the exit from the stomach. They would put
17 the mercury in there to give it some weight. It would
18 go down, and it would block anything from going out of
19 the stomach.

20 There are a number of cases when the balloon
21 broke and they had mercury there and it stayed there
22 for quite some time or stayed in the intestines.
23 There were absolutely no toxicological effects. Many,
24 many papers in the literature deal with this.

25 Q Whereas as you say, if you inhale elemental

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1 mercury vapor then you can have toxicological effects?

2 A Yes. If you inhale elemental mercury the
3 vapor is very quickly taken up in the lungs. It
4 passes quickly into the blood, is transported very
5 rapidly to the blood-brain barrier.

6 Since it's lipid soluble it needs no special
7 mechanism. It just diffuses across the blood-brain
8 barrier and gets into the brain where it's converted
9 to mercuric mercury very quickly.

10 Q Okay. I guess we've covered everything on
11 that slide.

12 A I think so.

13 Q Let's go on to Slide 26.

14 A Exposure at toxic levels to inorganic
15 mercury usually occurs in an occupational setting and
16 is not a danger to the general public. This is still
17 the statement of the experts. Now comes my statement
18 in red. This statement deals with external exposure,
19 not endogenous inorganic mercury production in the
20 body.

21 It's different if the mercury production is
22 in the brain. If the mercury from methyl mercury is
23 demethylated it gives mercuric mercury, and then it
24 becomes a real problem. The organic species of
25 mercury would include methyl mercury, thimerosal,

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1 ethyl mercury and some phenylmercury compounds, all of
2 which we know quite a bit about.

3 Exposure. The major source of mercury vapor
4 in the atmosphere is a natural degassing of the
5 earth's crust. The atmospheric mercury is distributed
6 globally and eventually is converted to a water
7 soluble form and returned to the earth's surface by
8 rain.

9 Methyl mercury in fish is found in a water-
10 soluble, protein-bound form. Inorganic mercury is
11 also found in food. The sources are known, and it
12 does not amount to very much.

13 Next slide, please?

14 Q Slide 27.

15 A Mercury vapor emitted from dental amalgam is
16 the main source of mercury vapor affecting the general
17 public. In fact, mercury vapor emitted from dental
18 amalgam is the main source of mercury exposure to the
19 general public. Mercury levels in the general
20 atmosphere and in drinking water are so low they're
21 not important.

22 Deposition and toxicokinetics, elemental
23 mercury, swallowed liquid mercury, is only slowly
24 absorbed from the GI tract -- we said that -- and is
25 generally of no toxicological significance.

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1 Mercury vapor is readily absorbed from the
2 lungs. The mercury becomes dissolved in the blood and
3 diffuses to all the tissues in the body. It is highly
4 diffusible and lipid-soluble.

5 Q Let me ask you a question about coal-fired
6 power plants. Do they release mercury into the air?

7 A They do. As far as the mercury in the
8 general environment is concerned, something like 70
9 percent of it comes from coal-powered utility plants.

10 Q Excuse me. It's not distributed equally all
11 around the area of the plant, is it?

12 A No. It's highly concentrated. The closer
13 you are to the plant the greater the amount of mercury
14 that you're going to inhale, but I think Landrigan
15 showed in his El Paso study by the time you get a mile
16 away from the plant the concentrations were quite low.

17 Q And what form of mercury is that that comes
18 out of the coal plant?

19 A Elemental mercury. Elemental mercury.

20 Q In vapor?

21 A In the vapor form, yes.

22 Q Yes.

23 A Primarily. Deposition and toxicokinetic.
24 We've gone through most of that.

25 Q Yes. Let's go to Slide 28, I think.

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1 A Again continuing with Goyer and Clarkson's
2 chapter, mercurous mercury exposure is rare, but it
3 happens in, for example, pink disease. These
4 compounds have a low solubility in water and are
5 poorly absorbed from the GI tract. In certain cases
6 the compound or the mercurous mercury can depose to
7 Hg⁰ and one atom of Hg⁺². Very little is known
8 regarding disposition of mercurous mercury in the
9 body.

10 Now, mercuric mercury is a real culprit.
11 Absorption from the GI tract of mercuric compounds in
12 food for humans is about 15 percent, whereas for
13 methyl mercury it's 90 to 95 percent, if not higher.
14 There's also a difference in the distribution between
15 red cells and plasma.

16 For inorganic mercury, the ratio of cell to
17 plasma is two to less than one, but for methyl mercury
18 it's 10, so there's 10 times more found in the red
19 cells or in cells in general than in plasma.
20 Therefore, 10 times more mercury in red blood cells
21 than plasma.

22 After exposure to mercuric mercury or
23 mercury vapor, the greatest concentration of mercury
24 is in the kidneys. Methyl mercury has a greater
25 attraction to the central nervous system, especially

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1 the posterior cortex.

2 Q The posterior cortex meaning the back of the
3 outside of the brain?

4 A Yes.

5 Q Okay. Let's go to the next slide, No. 30.
6 Excuse me. No. 29.

7 A Yes. I think just the last sentence here is
8 probably worth taking the time to read. Dental
9 amalgam. Fillings in girls and women of reproductive
10 age should be used with caution to avoid increased
11 prenatal mercury exposure.

12 Q And again this isn't your opinion. This is
13 a published opinion?

14 A Everything in blue is the opinion of a
15 published expert that I've taken sometimes word for
16 word from a published article, a peer reviewed
17 article.

18 Q Okay. Now, earlier in opening I showed the
19 Special Masters that series of five papers that came
20 out of Seattle on the adult monkeys. Have you
21 prepared some slides about those studies?

22 A Yes. It may begin with the next one. I'm
23 not sure.

24 Q I think it is.

25 A Yes. Okay. This is one of those papers by

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1 Vahter and Burbacher is also. There's a list of
2 distinguished authors of this set of papers.

3 Monkeys were given methyl mercury for six,
4 12 or 18 months orally or mercuric chloride continuous
5 for three months. I want to be certain that we
6 understand that in these studies a subtoxic dose was
7 given because we're going to talk about eventually the
8 difference in mechanism between a subtoxic dose and a
9 toxic dose or a small dose via a large dose of methyl
10 mercury and the different mechanisms that are probably
11 involved.

12 It took about four months to reach blood
13 steady state. The blood total mercury elimination,
14 $T_{1/2}$, was 26 days. The blood inorganic mercury, which
15 was primarily mercuric mercury, was about seven
16 percent of blood total mercury.

17 Brain inorganic mercury, again primarily
18 mercuric mercury, was nine percent of total brain
19 mercury at six to 12 months and by six months after
20 exposure had stopped. Six months after exposure had
21 stopped. Seventy-four percent of the total brain
22 mercury in these monkeys was inorganic mercury.

23 Q Let me stop you. Let's explain what is
24 total mercury versus its component parts in these
25 kinds of studies.

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1 A Yes. When these people used to do an
2 analysis by a now relatively old-fashioned technique
3 at the time, absorption, they would measure the total
4 mercury, and that's inorganic mercury plus organic
5 mercury. Then they would measure I think -- it
6 slipped my mind. Let's say they would measure
7 inorganic mercury, and the difference between
8 inorganic and total would be organic mercury.

9 These are old studies. Today we do it
10 entirely different. These studies in the old days
11 would take weeks to get the answers, whereas we have
12 the basic equipment in my laboratory. We could do in
13 less than one day what they did in a month.

14 Q Yes. What I'm trying to make sure we get
15 across is that if the Special Masters see a term total
16 mercury, that would include both organic and
17 inorganic, right?

18 A Yes. Yes. Absolutely.

19 Q And if it's inorganic or organic it would be
20 specified as one or the other?

21 A Yes. Yes.

22 Q Okay.

23 A Yes.

24 Q Now, you were explaining that in the group
25 of monkeys that were fed methyl mercury for 12 months

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1 and then they stopped feeding them and then waited six
2 more months before they sacrificed them and looked at
3 their brains, their inorganic mercury continued to go
4 up in percentage, right?

5 A Exactly.

6 Q Why was that?

7 A Because the methyl mercury was slowly
8 demethylated to mercuric mercury, and mercuric mercury
9 cannot pass the blood-brain barrier either way to any
10 great extent.

11 That mercuric mercury, almost every first
12 year biochemistry student knows if you want to inhibit
13 an enzyme and you don't know what to use, if you use
14 mercuric mercury it's probably going to work because
15 mercuric mercury is a classical enzyme inhibitor,
16 especially if the enzyme has a thiol, an -SH group, in
17 the active center.

18 If the mercuric ion ties up that -SH group,
19 usually as we'll point out later in a very important
20 paper, the activity, enzyme activity, will be
21 completely inhibited.

22 Q Now, in this study did these investigators
23 try to estimate the half-life in the brain of that
24 mercuric mercury?

25 A Yes. Let's see. Where is it here? Yes.

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1 The brain inorganic mercury elimination, $T_{1/2}$, was a
2 matter of years. I mean, methyl mercury got out in a
3 matter of weeks or months, but there are some people
4 that think it's not a matter -- it's many, many, many
5 years.

6 I'll tell you at one point where a number of
7 studies have been published where a farm animal ate a
8 methyl mercury fungicide, one in New Mexico. It was
9 in a Coke bottle. He tipped it over and lapped it up.
10 Two days later the farmer killed that animal and fed
11 the meat to his children. One child died quite soon.
12 Another one lived until she was 21 years of age.

13 At 21 years of age, at the autopsy they took
14 the brain out and did a mercury analysis. The
15 inorganic mercury at that time, in fact the total
16 mercury, was 100 times above normal, and most of it
17 was inorganic mercury, so inorganic mercury really
18 stays in the brain a long, long time.

19 Q Is that evidence that what happens in humans
20 is similar to what happened in these adult monkeys?

21 A Absolutely. Absolutely. Absolutely.

22 Q The methyl mercury can transfer into the
23 brain past the blood-brain barrier?

24 A We know. We know this from the Clarkson
25 studies in Iraq. We know it from the Minamata studies

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1 in Japan. We know it from many studies in animals
2 that methyl mercury will form a bond with amino acid
3 cysteine, and that molecule, that cysteine methyl
4 mercury molecule, looks like another amino acid called
5 methionine.

6 This cysteine methyl mercury compound will
7 be taken up by the methionine transport carrier
8 protein, and it will get methyl mercury into the brain
9 that way.

10 Q Once the methyl mercury is in the brain it
11 can come back out again too, can't it?

12 A Pardon?

13 Q The methyl mercury can come back out again?

14 A It's a much slower mechanism, and we really
15 don't know what that mechanism is. Some of us think
16 that it's because of being bound to glutathione, but
17 the mechanism, as you can see, or the half-time is --
18 let's see.

19 The brain inorganic mercury half-time is a
20 matter of years, as we say. No. We want the methyl
21 mercury half-time. It's around here someplace.

22 Q I know it's in the paper.

23 A Yes. It's someplace in here. I'm sorry. I
24 thought we had it here.

25 Q We may have that on another slide.

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1 A It's a matter of 30 or 40 days, maybe 50
2 days.

3 Q Okay. So the methyl mercury half-life in
4 the brain is 30 or 40 or 50 days, which would mean
5 after a year or so it's essentially all gone.

6 A A lot of it is gone, yes.

7 Q Whereas the inorganic mercury that's
8 produced in the brain by the breakdown of methyl
9 mercury, that stays there for years?

10 A That stays there for years.

11 Q Let's go to Slide 31. This is still the
12 same paper from Dr. Vahter, right?

13 A Yes. It more or less points out --

14 Q Well, this is what I was just asking you
15 about.

16 A Yes.

17 Q What does it say? After it estimates the
18 half-times in blood of 50 to 80 days, what does it say
19 then?

20 A In human subjects exposed to methyl mercury,
21 mean half-time in blood of 50 to 80 days with
22 considerable variation between individuals have been
23 reported. They give the references to this.

24 The high blood mercury level in heavy
25 individuals indicate methyl mercury is distributed to

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1 fat to a limited degree, so if you don't have very
2 much fat it gives rise to a higher dose of methyl
3 mercury per lean body weight.

4 In other words, if the methyl mercury
5 doesn't go into fat because there's less fat around,
6 there's going to be more methyl mercury in the blood
7 and more methyl mercury going in the tissues.

8 Q Some of these monkeys in the study were
9 especially heavy, right?

10 A Yes.

11 Q And in those heavy monkeys they were still
12 basing the dose on the total body weight, right?

13 A Yes.

14 Q So they got more methyl mercury than the
15 lighter monkeys, but their blood level got much
16 higher, right?

17 A Yes.

18 Q And why is that again?

19 A Because in those animals with less fat then
20 the blood level is going to be higher because there's
21 not enough fat for the methyl mercury to go into from
22 the blood.

23 Q And then you have another paper here cited
24 by a Swedish author.

25 A Yes. It just points out again that dietary

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1 lipids affect whole body retention and relative organ
2 distribution of methyl mercury and inorganic mercury.

3 It means that diet is important.

4 Q Another variable in how much mercury --

5 A Another variable. Yes, sir.

6 Q All right. Slide 32. What was the point of
7 this paper?

8 A All right. This is a very recent paper,
9 year 2008, a very important paper.

10 When you talk to most people, even those
11 with experience in mercury research, and you ask them
12 what does mercuric mercury do to the brain -- we know
13 it's there; what does it do -- most people will say
14 well, it ties up sulphhydryl groups.

15 What does that mean? Well, there are
16 sulphhydryl groups in proteins. Can you be more
17 specific? Well, they'll say what do you mean? Being
18 an enzymologist I'll say what enzyme specifically is
19 methyl mercury or is inorganic mercury, mercuric
20 mercury, inhibiting in the brain?

21 There have been very few good studies along
22 these lines for a variety of reasons until this study
23 came out. Now, in this study they took a thioredoxin
24 system. Now, they were able to use enzymes that were
25 made by DNA recombinant technology so there's no

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1 contamination with other enzymes.

2 One of the axioms of enzymology is don't
3 waste clean thinking on dirty enzymes. Don't waste
4 clean thinking on impure enzyme fractions.
5 Recombinant DNA enzymes are very, very pure. You
6 don't have to worry about contamination there.

7 And so essentially what they showed here was
8 that, first of all, let me say the thioredoxin system
9 is critical for cellular stress response, protein
10 repair and protection against oxidative stress.
11 Mercuric mercury or mercuric chloride, which contains
12 mercury chloride, and methyl mercury inhibited
13 recombinant rat thioredoxin reductase with IC_{50} .
14 That's the concentration that would cause inhibition
15 of 50 percent of the activity, so that's a
16 quantitative term, the IC_{50} .

17 It had IC_{50} values of 7.2 and 19.7 nanomoles
18 respectively. That means that mercuric mercury was
19 more inhibitory than methyl mercury. Overall mercury
20 inhibition was selective towards a thioredoxin system.
21 The latter system consists of thioredoxin reductase,
22 which has selenol cysteine in its active center and
23 thioredoxin, which are widely distributed in the main
24 organs and tissues and are also synthesized in nerve
25 cell bodies and transported to synaptic terminals.

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1 Fully reduced human thioredoxin bound
2 mercury and lost all five free thiols and lost
3 activity after incubation with mercuric chloride or
4 methyl mercury, but only mercuric chloride generated
5 dimers. These dimers were very stable and very
6 inhibitory.

7 Q Now, is the mercuric chloride going to break
8 down in this system into Hg^{++} ?

9 A Momentarily you must say, but I think I have
10 a slide. It may be the next one. It's the next one.
11 We'll get back in just a minute.

12 Q Yes. You're right. The next slide does
13 discuss this. Let's go to 33.

14 A We can wait. Let me just say that you asked
15 mercuric chloride breakdown. Yes, it does break down,
16 but we don't have free mercury ions or free arsenic
17 ions or free metal ions floating around in the blood,
18 the plasma or in cells.

19 They are attached very quickly to sulphhydryl
20 containing compounds like glutathione, like cysteine,
21 another -SH containing amino acid, and also proteins
22 that have -SH, have cysteine, either in the active
23 center or in the outer structural part, so it breaks
24 down, mercuric chloride, to mercuric ion. That
25 mercuric ion is very quickly bound to something, so

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1 there's no free mercuric ion floating around for two
2 or three days.

3 Q Is this the same type of mercuric mercury
4 that we talked about in the adult monkey studies
5 that's left in the brain?

6 A Yes, it is. Yes, it is. Now getting back
7 to this. In particular, the remarkable potency of the
8 mercury compounds to bind to selenol-thiol in the
9 active site of thioredoxin reductase should be a major
10 molecular mechanism of mercury toxicity.

11 I was the author of a chapter on the
12 toxicology of methyl mercury in I think it was the
13 year 2000 National Research Council monograph that was
14 written, and I wish we had that sentence because at
15 that time we could just say mercury tied up an -SH
16 group.

17 Here it says: In particular, the remarkable
18 potency of the mercury compounds to bind to selenol-
19 thiol in the active site of thioredoxin reductase
20 should be a major molecular mechanism of mercury
21 toxicity. I agree 100 percent with these authors.

22 Q And this was new information just this year?

23 A Year 2008. I think it was last month. It
24 was just published. The page number just came out
25 within the last week. It was prepublished and put on

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1 the web first.

2 They also performed human tissue culture
3 studies and lysate studies, and now I want to say in
4 my own words the results of this research are very
5 pertinent and important. The thioredoxin system is of
6 course in the brain and most tissues. It appears to
7 be uniquely sensitive to mercuric mercury and methyl
8 mercury. It is unfortunate the ethyl mercury was not
9 investigated in this system.

10 Q All right. Now we want to talk a little bit
11 about the different forms of organic mercury here.

12 A The next slide, please?

13 Q Slide 35.

14 A This is the chemical formula for thimerosal.
15 If you look at the left side of the molecule it says
16 CH₃. You'll see mercury. The bond between the
17 mercury and so forth is cleaned very quickly in the
18 body. It's metabolized very quickly to yield ethyl
19 mercury. It's this ethyl mercury that does most of
20 the traveling in the blood and gets across the blood-
21 brain barrier.

22 The next slide, please? I don't know
23 whether it's necessary to read all of this. It points
24 out the difference in solubility. Ethyl mercury has a
25 solubility of 1.4 times 10 to the minus four grams per

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1 100 milliliters of water, and that can be compared to
2 not one gram per milliliter of water, but 100 grams of
3 thimerosal per 100 grams of water. A tremendous
4 difference in the solubility.

5 Next slide?

6 Q When thimerosal or merthiolate was
7 formulated, why were they interested in having a
8 soluble form of mercury? Is that part of its
9 preservative stance?

10 A Let me stop for a second. Merthiolate,
11 which is also thimerosal, breaks down to ethyl
12 mercury. No one really knew at the time. It was
13 claimed that thimerosal and/or merthiolate was
14 bacteriostatic. It would stop the growth of bacteria.

15 But in the latest slide I'll point out what
16 the FDA now says about it; that that isn't necessarily
17 so. Can we have the next slide perhaps?

18 Q Yes. Slide 37.

19 A So thimerosal is rapidly metabolized to
20 ethyl mercury. The statement is taken from one of Tom
21 Clarkson's articles.

22 Q Okay. And then the next slide, 38?

23 A Here we go. Ethyl mercury or methyl mercury
24 do not just float around free in body fluids and
25 cells. They have a high affinity for binding to and

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1 are transported via thiol-containing compounds such as
2 glutathione, cysteine and cysteine-containing
3 proteins.

4 Q What does thiol mean?

5 A It's an -SH group. It's a radical. It has
6 a valence. It can form a chemical bond with carbon
7 compounds, carbon atoms.

8 Q And the S in the -SH is sulfur?

9 A S is for sulfur. H is for hydrogen. The
10 hydrogen is very reactive. It will come off very
11 quickly, especially in the presence of oxygen or
12 something like mercuric mercury or methyl mercury,
13 which will react with it very quickly.

14 Q Okay. All right. The next slide, Slide 39?

15 A Now, the safety and efficacy of thimerosal
16 have been questioned by the FDA as shown in the
17 following slides.

18 Q Okay. Slide 40?

19 A Slide 40 states, and this is now from the
20 *Federal Register*: Rule will be based on page 11 of
21 the *Federal Register* 436 published January 5, 1982,
22 which states: The panel concludes -- this is an FDA
23 panel. The panel concludes that thimerosal is not
24 safe for over-the-counter topical use because of its
25 potential for cell damage if applied to broken skin as

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1 allergy potential.

2 More importantly, in my opinion, but it
3 states here, it is not effective as a topical
4 antimicrobial because its bacteriostatic action can be
5 reversed. I'm going to make this comment, but it's
6 really one that Congressman Burton made once on a
7 committee that I was involved in. He said: If they
8 did not think it was safe enough to apply topically to
9 adults, what evidence did they have for its safety for
10 injection into children?

11 The next slide, please? This is again in
12 the *Federal Register*. A ruling came out by the FDA.
13 It came out October 11, 2005. It's effective April 1,
14 2007, about a year ago, and I quote:

15 A number of active ingredients have been
16 present in over-the-counter drug products of various
17 uses as described below. However, based on evidence
18 currently available there are inadequate data to
19 establish general recognition of the safety and
20 effectiveness of these ingredients for the specified
21 use.

22 Now, there are about 200 compounds that they
23 list in this *Federal Register*, and one of them,
24 thimerosal, was quoted as one of these ingredients.

25 Q Okay. Now let's go to some studies about

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1 what happens to thimerosal in infants.

2 A The major studies in infants -- not all of
3 them -- have been done by Pichichero from the
4 University of Rochester. I think, but I don't
5 remember whether Clarkson is one of the co-authors of
6 these papers.

7 It deals with mercury concentration and
8 metabolism in infants receiving vaccines, and
9 essentially they gave to infants age six months and
10 younger vaccines that contained thimerosal. They list
11 the vaccines. The first group received vaccines
12 containing thimerosal, but then 21 control infants
13 received thimerosal-free vaccines that were available.

14 They state: We obtained samples of blood,
15 urine and stools three to 28 days after vaccination.
16 Estimated blood half-life of ethyl mercury was seven
17 days, although they changed that number in a
18 subsequent number.

19 Their interpretation? Administration of
20 vaccines containing thimerosal does not seem to raise
21 blood concentration of mercury above safe levels in
22 infants. Ethyl mercury seems to be eliminated from
23 blood rapidly via the stools after parental
24 administration of thimerosal in vaccines.

25 My comment: This sample size is highly

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1 unlikely to capture the full range of human variation
2 in handling mercury exposure.

3 The next slide, please? This is the 2002
4 paper, the same paper. This shows you some of the
5 variation. Now we're plotting blood mercury in
6 nanomoles per liter versus days since the last
7 vaccine. The dark or the triangles -- I think they're
8 called diamonds -- are for infants of age two months,
9 and six months are shown by the squares.

10 As you can see, in one case, the very high
11 one, you have 20 nanomoles of mercury per liter of
12 blood, and in other cases you're down to almost 2.5 so
13 you almost have a tenfold -- almost a tenfold --
14 variation in how children respond to injections of
15 vaccines containing thimerosal.

16 Q Now, this was on 40 infants. If you had
17 done this study on 4,000 infants would you expect the
18 range to be even wider?

19 A Probably. Probably. From everything that
20 we know that we've seen, I think it would be much
21 wider. We'd have much more.

22 Next slide? This is in the most recent or
23 more recent Pichichero paper done in Argentina with
24 newborn infants in this slide. This is now a time
25 course, days since the last vaccination, and again you

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1 see the huge variation, anywhere a little above zero
2 to eightfold or eight nanograms per mil. There's
3 variation. You've got to expect that in children or
4 almost any human as far as the way they handle
5 mercury.

6 Q Even at 30 days after vaccination, there was
7 still a range of values for them.

8 A Yes. Yes.

9 Q Does that show that not all children will
10 process the mercury as fast as others?

11 A I'm sorry?

12 Q What does that show about the children if
13 the range varies at 30 days?

14 A Well, they're processing it differently
15 because they probably have some difference in their
16 metabolism, which may be genetically determined.

17 Q Okay. Let's go to the next slide.

18 A This again shows the same sort of thing in
19 two month old infants, and again you'll see the
20 variation is anywhere from a little bit above zero to
21 five nanograms per milliliter here. Again there's
22 variation.

23 Out at the end at 30 days since the last
24 vaccination you're almost as bad as you were at the
25 very beginning with a very high outlier, again showing

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1 that individuals handle mercury differently. There's
2 no set response.

3 Q Okay. And then the next slide, please?

4 A Again it shows the six month old infants.
5 So you're getting variation all the time no matter how
6 old the kids are. You're getting variation. Here
7 it's between zero and five at the beginning.

8 Q Okay. Slide 48. This is still the
9 Pichichero 2008 paper, correct?

10 A Yes. What did we want to say about this?
11 Oh, yes. In the earlier paper, the 2002 paper, these
12 same authors claimed that the blood half-time for the
13 mercury was seven days. Now for some reason or other
14 they've cut it down by half to 3.7 days.

15 Again, this shows the variation not only --
16 I mean, these studies I think were done in the same
17 laboratory or parts of them were anyway, and it shows
18 the variation that can occur when you're measuring
19 mercury and/or a group of people responding
20 differently to mercury.

21 It's amazing that it took 30 days for blood
22 mercury to return to prevaccination levels, so when
23 you say that mercury leaves the body very quickly
24 after vaccination to me in the life of an infant 30
25 days is a long time.

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1 It was addressed, as Pichichero himself
2 states in this paper, that some methyl mercury was
3 detected in all the blood samples of the young
4 children.

5 Q So they had some background methyl mercury
6 exposure too?

7 A Yes.

8 Q If they had a difference in processing ethyl
9 mercury, would you expect a difference in processing
10 methyl mercury? Would that be independent?

11 A Based on what we know, both of them would be
12 demethylated. That's about the major similarity that
13 I would venture at this present time. Ethyl mercury
14 would be demethylated to mercuric mercury, and the
15 methyl mercury would be demethylated to mercuric
16 mercury.

17 Q Once the ethyl group or the methyl group is
18 taken off of an organic mercury compound what's left
19 is the same thing, right?

20 A Yes. Absolutely. Absolutely.

21 Q Hg⁺⁺?

22 A Hg⁺⁺, which is going to react with something
23 very quickly.

24 Q Okay. Slide 50? Wait a minute. We didn't
25 finish Slide 49. I'm sorry.

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1 A We should make a note that as far as now
2 it's my opinion. These were supposedly normal
3 children that Pichichero dealt with. They were not
4 autistic children -- they were too young -- or they
5 were not autistic prone children who may process
6 mercury in vaccines differently.

7 No mass balance data was given. By mass
8 data I mean if you give 10 milligrams of something to
9 a human being you want to know where that 10
10 milligrams went to. You either want to find 10
11 milligrams in the urine and the feces, or if you don't
12 find the 10 milligrams, you find only five milligrams
13 in the urine and feces, then you're going to say
14 there's five milligrams that stayed in the body
15 someplace.

16 The next question would be where did those
17 five milligrams go? In this case they don't know.
18 How much thimerosal ethyl mercury was given is known,
19 but what percent of the dose was eliminated was not
20 stated and experimentally could not be determined
21 because of the protocols they used.

22 How much ethyl mercury stayed in the brain
23 or in other tissues? They don't know. They didn't
24 try to do that. The authors state they were unable to
25 determine the fate of the mercury after it leaves the

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1 blood. They're now talking the mercury that came from
2 thimerosal. No mercuric mercury was determined.

3 The paper is flawed, and I think the next
4 slide -- yes. Now, this is an independent
5 evaluation. The *Pediatrics Journal*, which does not
6 take letters indiscriminately. The letters to the
7 editor that you send in to the *Pediatrics Journal* are
8 peer reviewed and then published if the editor thinks
9 they're worth publishing, so the citation really is
10 *Pediatrics* post publication peer reviews, March 30,
11 2008.

12 Dr. Indech discusses invalidating
13 assumptions of the Pichichero paper, and I quote:
14 While the methodology admits the underlying assumption
15 that lowered levels of these chemicals result from
16 body elimination of them, perhaps the more rapid
17 decline in measurement levels of ethyl mercury is due
18 to stronger, undetectable binding to tissues in the
19 central nervous system.

20 The pharmacokinetics of such a process would
21 be identical to that observed, yet such a process may
22 give rise to autistic symptoms whereas total excretion
23 from the body would not. In short, simply because the
24 levels decline you can't make the assumption that the
25 toxin has been eliminated from the body. The paper is

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1 fundamentally flawed. End of quote.

2 Q In fact, if the same thing happened in these
3 infants that happened in the infant monkeys what would
4 you expect? Would you expect some of this mercury to
5 end up in the infants' brains?

6 A Absolutely. No question about it. I think
7 Burbacher did show that the thimerosal injected via
8 vaccines -- whatever he did with the thimerosal.
9 Actually it was direct injection of thimerosal, I
10 think. That much of the mercury did end up in the
11 brain.

12 Q By the way, are you aware of any way under
13 current technology that you could measure the amount
14 of mercuric mercury in a child's brain?

15 A A living child?

16 Q A living child.

17 A Absolutely there's no way we can do it. I
18 thought we had a way, and I called some people up who
19 are very good with this sort of thing and they said
20 no, no way.

21 Because there are ways of measuring lead in
22 our bones by putting our forearms in a sort of machine
23 and it will tell you how much lead I have or a child
24 has in his bones. I thought we could use that same
25 thing for mercury in the brain, but they said

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1 absolutely not. We cannot measure the amount of
2 mercury in a human living brain.

3 Q Because in this trial we're not going to
4 have any evidence directly of inorganic mercury in the
5 brains of these two boys, but is that because nobody
6 could do it?

7 A You can't do it because they're alive. We
8 have autopsied data where that has been done, as we'll
9 point out later, papers that we'll quote of children,
10 autistic children who died and at autopsy the brains
11 were removed and the mercury, both inorganic and
12 organic mercury, was determined.

13 Q But you can't do it in a living child's
14 brain?

15 A Absolutely not. We're not Nazis.

16 Q Okay. Slide 51.

17 A Well, in preparation for what's coming:
18 Thimerosal pharmacokinetics obtained -- Pichichero, et
19 al -- using nonautistic children are not the same as
20 those expected from autistic children. The latter
21 appear to have different efflux kinetics as we point
22 out in later slides.

23 Q All right. And now we're going to go to a
24 discussion of brain concentration of mercury species,
25 correct?

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1 A Yes.

2 Q Okay. This is a paper from the National
3 Institutes of Health in Bethesda published in the year
4 2004, a paper that really has withstood the criticism
5 of time, Mercury Concentrations in Brain and Kidney
6 Following Ethyl Mercury, Methyl Mercury and Thimerosal
7 Administration to Neonatal Mice.

8 The main objective of this study was to
9 define and compare mercury concentrations in the
10 organs of neonatal animals exposed to methyl mercury
11 or thimerosal. The toxicity of these two mercury
12 species in a neonatal animal model is believed to be
13 similar to humans with respect to organic mercury
14 pharmacokinetics.

15 Q Now, just for purposes of the audience,
16 neonatal means newborn?

17 A Yes. Yes.

18 Q Okay.

19 A For a period of one or two months I think it
20 is.

21 Q Okay.

22 A For the mice it would be different. For a
23 short period of time.

24 Q Okay.

25 A Neonatal mice seem to be the best rodent

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1 model to study thimerosal disposition in order to
2 closely mimic human exposure. Mice exhibit methyl
3 mercury brain-blood ratios of about one, closer to the
4 three to 10 ratio seen in primates, than the ratio in
5 rats estimated by Magos in 1986.

6 Again let me point out Magos is a very good
7 investigator of mercury toxicity. I don't know him
8 personally, but he has a superb reputation for doing
9 very good work, but 1986 is different than the year
10 2004 as these studies were done. Science progresses.

11 The fact that we no longer think that rats
12 are better to use, that rats are not better to use, is
13 not meant to be an insult to Magos. It's just that
14 times change. We get more information. Magos is a
15 superb investigator. He's one of the Respondent's.

16 Q Let's stop. I want to have you explain what
17 is this blood-brain ratio they're talking about here
18 or brain to blood I guess it is. Yes. They call it
19 the brain to blood ratio. What does that mean?

20 A It's the concentration of whatever species
21 of mercury, usually total mercury, you're concerned
22 about, the concentration in the brain versus the
23 concentration in the blood. That ratio is used by
24 some people. I myself never use it. Used by some
25 people as an indication of how the body handles these

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1 mercury compounds.

2 For example, the reason we don't think the
3 rat is a good model anymore is the rat hemoglobin has
4 more sulphhydryl groups that mercury will bind to and
5 stay in the blood than the human hemoglobin and so it
6 makes the science more complicated. We have a
7 confounding factor if we do studies with rat blood.

8 Q Would you agree that studies on primates
9 would be a better indication of what probably happens
10 in humans than studies on rats?

11 A No question about it. I think most people
12 would agree with that.

13 Q They use rats because they're much less
14 expensive, right?

15 A Yes. And at one time they were the animal
16 of choice for experimental studies, but times change.
17 We learn more as we go on.

18 Q Okay. I interrupted you as you were going
19 through Slide 53.

20 A Yes. In mice it was three to four days for
21 a steady state. More than 80 percent of the mercury
22 in hair in this study was found to be in the form of
23 organic mercury. Blood mercury in these mice was
24 found to be primarily in the organic form. They did
25 other tissue analysis.

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1 Next slide? This shows some of the data.
2 Again, some of the data was lacking, but this is a
3 table that I made up using their data. It shows you
4 that .6 percent of the delivered dose of methyl
5 mercury ended up in the brain of these mice.

6 When they gave thimerosal 0.2 percent and
7 when they gave ethyl mercury 0.39 percent, but much
8 more percentage-wise of the ethyl mercury ended up in
9 the kidney than did in the case of methyl mercury or
10 thimerosal.

11 Next slide, please?

12 Q Okay. Slide 55.

13 A Let's see. For each compound -- thimerosal,
14 ethyl mercury, methyl mercury -- the percent of
15 mercury that reached the brain was significantly more
16 in young mice as compared to mature mice, so in young
17 mice the blood-brain barrier probably is not matured
18 as much as in the older mice.

19 In all cases, the level of mercury that
20 reached the adult brain following an IM injection was
21 less than 0.1 percent of the total administered dose.
22 When compared to levels at 24 hours, mercury
23 concentration at seven days post dosing were
24 significantly decreased in the blood, while
25 concentrations within the brain and kidney remained

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1 relatively constant.

2 In this paper they state with references,
3 and this is going to be a matter of disagreement as we
4 go through this paper or as we go through all these
5 talks. In this paper they state with reference that
6 while methyl mercury gets into the brain by diffusion
7 plus active transport of the methyl mercury cysteine
8 complex, ethyl mercury does not form such a cysteine
9 complex and does not get in that way, but diffuses
10 more readily across the blood-brain barrier.

11 Now, Clarkson will quite rightly say, as he
12 said in his written form, that we don't know how ethyl
13 mercury gets across the blood-brain barrier. It may
14 use the cysteine complex, but as he himself says we
15 don't know. The experiments have not been done.

16 Q We don't know how it gets across, but we
17 know that it does get across?

18 A Yes. Absolutely.

19 Okay. Next slide, please? Now we go on to
20 another study, Zareba, and I think he is from
21 Clarkson's group also. In the blood of neonatal male
22 mice total mercury concentrations after thimerosal
23 were slightly lower than those after methyl mercury,
24 reaching statistical significance only at day one.
25 The rate of decline of blood levels was roughly

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1 similar in both.

2 In hair, the total mercury content was
3 approximately two times higher in methyl mercury than
4 the thimerosal treated group. In the brain, which
5 we're really interested in. In the brain, organic
6 mercury levels were significantly lower, approximately
7 three to fourfold -- we're talking about organic
8 mercury now -- in the thimerosal group than in the
9 methyl mercury exposed group.

10 In other words, the organic mercury in the
11 thimerosal group was decreasing much faster in the
12 brain than in the methyl mercury group. This could be
13 due to either its conversion to mercuric mercury or to
14 it being pushed out of the brain.

15 It goes on to say: Inorganic mercury levels
16 of the brain were similar in both groups except for
17 the first day after exposure. However, in the
18 thimerosal exposed animals, inorganic mercury
19 accounted for a higher fraction, 12 to 22 percent --
20 notice the variation; 12 to 22 percent of total
21 mercury -- whereas in the methyl mercury group it did
22 not exceed 10 percent of the total mercury.

23 Q Now, they gave these mice all the same dose,
24 right?

25 A Yes. Yes.

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1 Q And yet there was almost a twofold variation
2 after one week in how much inorganic mercury was in
3 the brain of the thimerosal exposed mice?

4 A Yes.

5 Q Why was that? Why is that? Why is there
6 such a wide variation?

7 A I guess that's based on the individual
8 genetics of the animal or the human if you're talking
9 about humans. It could be due to difference in
10 susceptibility. It could be due to a different rate
11 of metabolism. It could be due to many factors.

12 Next slide, please?

13 Q Okay. Slide 57.

14 A Again, this is a continuation. For total
15 mercury in the blood for approximately five percent of
16 the dose was similar for ethyl mercury and methyl
17 mercury, but the subsequent fate of mercury in the
18 body differed.

19 Brain organic mercury was higher for methyl
20 mercury, three to fourfold, as compared to ethyl
21 mercury. Brain levels of inorganic mercury was about
22 the same in both cases, unlike the infant monkey
23 study. There's bound to be variation, variability
24 between species also.

25 For kidney, inorganic mercury was three to

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1 four times higher for thimerosal than for methyl
2 mercury, which confirms other studies, including
3 humans. Much higher accumulation of inorganic and
4 organic mercury in the liver in the thimerosal mice
5 than in the methyl mercury ones.

6 It took about three or four days for a
7 steady state to occur, and more than 80 percent of the
8 mercury in the hair was in the organic form. Blood
9 mercury is primarily in the organic form.

10 Q Now, you referred to Dr. Magos before.
11 There's a paper he published in 1985 that keeps
12 getting cited over and over again. We're going to
13 discuss that now.

14 A Yes.

15 Q If you would turn to Slide 58?

16 A Keep in mind this is a paper published in
17 1985. Keep in mind that thimerosal was not on the tip
18 of everyone's tongue at that time, all right?
19 Vaccinations were not being questioned with thimerosal
20 in them.

21 He compared methyl and ethyl mercury by
22 giving them by mouth, so the ethyl mercury is not
23 given by IM, all right, as vaccinations are given. In
24 addition, rats were used. In a later paper they state
25 that mouse is a better model for studying mercury

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1 toxicity than is the rat. We've discussed this before
2 that times change as we get more knowledge.

3 The authors state that one of the first
4 toxic effects of methyl mercury is weight loss. In
5 this paper they stated that ethyl mercury caused a
6 greater weight loss than did methyl mercury. This is
7 one example of greater toxicity for ethyl mercury from
8 Magos' own paper.

9 Ethyl mercury is also more renal toxic than
10 methyl mercury. Mercuric mercury can contribute, and
11 he states in this paper and gives evidence. Mercuric
12 mercury can contribute to injury of ganglion cells
13 also.

14 Q Okay.

15 A Next slide, please? They go on to state
16 there were little differences in the neurotoxicity of
17 methyl mercury and ethyl mercury when effects on the
18 dorsal root ganglia or coordination disorders were
19 compared.

20 Parenthetically, one of the problems in the
21 past has been people concentrated on pharmacokinetics
22 or toxicokinetics of thimerosal, ethyl mercury and
23 methyl mercury and did many, many studies with this
24 and so in the literature the statement creeps in that
25 there are vast differences between methyl mercury and

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1 ethyl mercury.

2 That's not necessarily so. The
3 pharmacokinetics can be different, but the toxic
4 effects in many ways are similar. I'll show this in
5 the subsequent slide that will list all these one by
6 one. The mercuric mercury formed extraneously from
7 alkyl mercury can contribute to the injury of ganglion
8 cells.

9 The authors also use mercury concentrations,
10 cerebral damage, histochemical visualization as
11 indication of a toxic or lack of toxic effect of ethyl
12 and methyl mercury. These effects or measurements
13 that they used in 1985 are not as sensitive as enzyme
14 activity inhibition as far as the thioredoxin paper
15 that I quoted for the year 2008 earlier in this talk.

16 In 1985 when this paper was published,
17 neuroinflammation was not examined since the term
18 neuroinflammation -- very shocking. The term
19 neuroinflammation did not appear in the medical
20 literature until the year 1994-1995. I still can't
21 get over it. When I was first told this I didn't
22 believe it.

23 If you go back to PubMed and do any kind of
24 literature survey, before 1994 you cannot turn up the
25 word neuroinflammation, but now it's a word used all

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1 the time, especially by the Zimmerman group, a very,
2 very good research group at Johns Hopkins University.

3 Next slide, please? You went the wrong way.
4 Yes. Here we are.

5 Now, a paper that's quoted very often,
6 Mercury by Ip, et al. Mercury Exposure in Children
7 With Autistic Spectrum Disorder: Case Control Study.
8 I quote: Thus, the results of our cohort study with
9 similar environmental mercury exposure indicate that
10 there is no causal relationship between mercury as an
11 environmental neurotoxin and autism.

12 This paper is quoted over and over again,
13 and there are subsequent papers that rely on this
14 paper. This article has a major error in it, and I
15 will now point out the error again which appeared in a
16 peer reviewed journal.

17 Paper by DeSoto and Hitlan, Blood Levels of
18 Mercury are Related to the Diagnosis of Autism: A
19 Reanalysis of an Important Data Step. I wish to
20 emphasize again, Special Masters, this is not my
21 opinion I'm giving you. I'm reading directly from the
22 paper, a peer reviewed paper in *Journal of Child*
23 *Neurology*.

24 We have reanalyzed the data set originally
25 reported by Ip, et al. in 2004 and found that the

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1 original P value was in error and that a significant
2 relation does exist between the blood levels of
3 mercury and diagnosis of an autism spectrum disorder.

4 Moreover, the hair sample analysis results
5 offer some support for the idea that persons with
6 autism may be less efficient and more variable at
7 eliminating mercury from the blood. The underlining
8 emphasis I added, but this is a direct quotation.

9 Now, the editor of this journal said in a
10 note that he submitted, and I again quote: But as the
11 editor-in-chief of the *Journal of Child Neurology*, it
12 is troubling to note that the article, Ip, et al., has
13 errors not only in the reporting of the statistical
14 findings, but also in something as simple as a listing
15 of the age range of the subjects.

16 My comment: Please note, the article being
17 criticized is cited on the previous side, the Ip side.

18 Q Now, let me ask you.

19 A Yes?

20 Q This 2004 Ip study that was comparing the
21 blood levels of mercury in autistic kids and
22 nonautistic kids. What they reported initially was
23 there was no difference in the blood levels of
24 mercury. That's been cited as evidence that mercury
25 is not linked to autism by many, many people, right?

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1 A Yes, sir.

2 Q Including at least one of the Respondent's
3 experts in this case?

4 A Yes, sir.

5 Q But in 2007 these people in a peer reviewed
6 paper reanalyzed that data and found that in fact
7 statistically significant was autistic kids had more
8 mercury in the blood, right, so it turns out the study
9 actually shows the opposite of what it was originally
10 published for?

11 A Yes. Yes.

12 Q Okay. Let's go to Slide 62.

13 A So what happens to the organic mercury that
14 enters the brain?

15 Next slide, please? Now, this one slide are
16 my comments just to bring things in perspective. The
17 literature supports this. Ethyl mercury, methyl
18 mercury and elemental mercury are converted to
19 mercuric mercury, Hg^{++} , in the brain. The mercuric
20 mercury reacts with thiols of enzymes and structural
21 proteins. Thiols and sulphhydryls are synonymous
22 terms.

23 Thus, mercuric mercury is a well known
24 enzyme inhibitor and has been used as a research tool
25 for that purpose for many years. Does it inhibit a

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1 crucial enzyme in the brain; for example, a brain
2 mitochondrial enzyme?

3 Mercuric mercury also reacts with selenium
4 compounds to form mercury selenide. The latter
5 compound is very insoluble. It has been claimed to be
6 nontoxic because of its insolubility, but this witness
7 -- I was at a small, closed symposia of 20 people that
8 were brought in to analyze the mercury selenide
9 significance, and when people told me that mercury
10 selenide is free of toxicity I asked them what is the
11 evidence for this and they said well, it's insoluble.

12 I said that's no evidence. Have you done
13 any radioactive studies to show that it doesn't go
14 anywhere but completely out of the body? They said
15 no. Do you have any enzyme studies at low
16 concentrations that would show some biological
17 activity? No. Then why do you say that mercury
18 selenide is free of toxicity; that the mercury is now
19 bound and therefore cannot do anything? The answer is
20 it's insoluble.

21 For most of the people there, even those
22 people that had worked and heard this before, they
23 were willing to agree that there is not enough
24 evidence. There is no evidence in the literature that
25 shows whether mercury selenide is or is not toxic.

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1 So anyone who in the early literature said
2 well, we see these black spots when we do some
3 analytic studies, and those black spots are mercury
4 and selenium tied up. In those days they used to say
5 before we knew about the mercury selenide what do you
6 mean by black spots being mercury and selenide? What
7 form of mercury? What form of selenide? They said
8 oh, we don't know, but we think it happened. The
9 science behind mercury selenide is virtually
10 nonexistent as far as any toxicity or what its
11 function is in the body.

12 In regards with which protein or selenium
13 compound mercuric mercury binds, it is accepted that
14 mercuric mercury remains in the brain for a very, very
15 long time. Those are words used almost exactly by
16 Vahter. Also, the inorganic mercury in the brain of
17 the adult monkeys provoked glial activation and
18 astrocyte death.

19 Q Now you're talking about the adult monkey
20 study from Seattle --

21 A Yes.

22 Q -- that resulted in those five papers that I
23 showed in the opening statement, right?

24 A Yes. Next slide, please?

25 Q Okay. This is a paper involving examination

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1 of the brains of who?

2 A These are people in Greenland who eat a lot
3 of fish, and they did a superb study on mercury
4 accumulation in brains from populations exposed to
5 high and low dietary levels of methyl mercury.

6 Concentration, chemical form and
7 distribution of mercury in brain samples from
8 autopsies. They have a tremendous number. I've
9 forgotten what the end was, but it's in the hundreds
10 if I remember correctly. Their conclusion is this
11 suggests a slow transformation of methyl mercury to
12 inorganic mercury in the brain. The autometallography
13 demonstrable mercury was primarily located in the
14 glial cells.

15 All right. My comments is that this is a
16 study of humans; that they're looking at human brains
17 at autopsy time of people in Greenland, some who ate a
18 lot of fish and therefore high exposure to methyl
19 mercury and some who ate just a small amount of fish
20 with low exposure. We'll come back to the
21 significance of this later on.

22 Q But these people, when they died after a
23 lifetime of eating fish they had a lot of inorganic
24 mercury in their brain?

25 A Yes.

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1 Q And it was in the glial cells?

2 A Yes. Most of it was in the glial cells,
3 yes.

4 Q Okay. Slide 65.

5 A I think we've sort of gone over this before.
6 This is the '94 study. We can go on to the next one,
7 I think.

8 Q Okay. Yes. We've already talked about this
9 paper on a couple slides.

10 A Yes.

11 Q Now, this next paper on 66, this is yet
12 another one of those five studies --

13 A Yes.

14 Q -- that came out of the same adult monkey
15 study, right?

16 A Yes. The major point of this paper is that
17 monkeys' inorganic mercury may be the proximate form
18 of mercury causing changes in astrocytes (support cell
19 growth and are sources of neuronotrophic factors) and
20 microglia, which create neurotoxic agents in the
21 population of cells. Both astrocytes and microglial
22 accumulate inorganic mercury. It just goes on and on.

23 The loss of astrocytes and increase in
24 activated microglia in the thalamus may have impact on
25 the function and survival of neurons in thalamus after

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1 they've been exposed to methyl mercury.

2 Q So this monkey study found that the
3 inorganic mercury in the brain which was activating
4 these glial cells could well be creating harmful
5 effects. Is that right?

6 A Yes. Well, they found that it was
7 concentrated in the glial cells, and we know that
8 mercuric mercury certainly is not the best thing to
9 have in the cell. It can cause a lot of damage.

10 Q Okay.

11 A This is another one.

12 Q Now, the next slide, 67. This is yet
13 another one of those five papers that came out of that
14 same adult monkey study.

15 A I hate to read the whole thing. Would the
16 Special Master like me to read all of it?

17 Q Well, let me ask you this. Look at the
18 second bullet point.

19 In the monkeys that had been exposed for 12
20 months and then they were left alive for six months
21 with no additional methyl mercury exposure, what
22 happened to their glial cells?

23 A Seventy-percent in the six months, 152
24 percent in the 12 months and 120 percent in the 18
25 month methyl mercury exposed group, and the number of

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1 reactive glia in the clearance group remained
2 elevated.

3 The inorganic mercury exposed group showed a
4 165 percent increase in the number of reactive glia.

5 Q One group of these monkeys they fed
6 inorganic mercury to and the rest of them got methyl
7 mercury, and both groups ended up with inorganic
8 mercury in their brain --

9 A Yes.

10 Q -- activating glial cells?

11 A Yes.

12 Q Okay. Let's go to the next slide.

13 SPECIAL MASTER HASTINGS: Let me make a
14 comment.

15 THE WITNESS: Yes, sir.

16 SPECIAL MASTER HASTINGS: Actually, people
17 in the audience were chuckling at my facial reaction
18 to your question, Dr. Aposhian, whether I wanted you
19 to read all of this particular cite. The answer in
20 general is no, I don't have any particular desire to
21 hear you read things.

22 What our hope here was we wanted expert
23 reports in written form. We would sit there and read
24 it in our offices, and then the oral testimony is
25 where you would get into emphasizing what's important

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1 there or go over nuances or answer questions that we
2 had about the written, but I think in general just
3 reading everything you've got here doesn't do us any
4 good.

5 THE WITNESS: All right.

6 SPECIAL MASTER HASTINGS: We can read.

7 THE WITNESS: Okay.

8 SPECIAL MASTER HASTINGS: Go ahead, Mr.
9 Williams.

10 BY MR. WILLIAMS:

11 Q Okay. Well, let's look at this Gallagher
12 paper for a minute, and let me try to ask you what's
13 important about it.

14 This again is a 1982 paper, and it's looking
15 at the structural effects of mercuric chloride and
16 methyl mercury. Now, mercuric chloride. Again, is
17 that a way to deliver inorganic mercury to these
18 animals?

19 A It is a way of delivering inorganic mercury
20 to animals.

21 Q Mercuric mercury. Right.

22 A Pardon? And directly into the brain. These
23 are injections directly into the brain, okay?

24 The major point is that in spite of the
25 distinctive clinical syndromes in these two classes of

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1 mercury compounds, mercuric chloride and methyl
2 mercury have, they are capable of inducing neuronal
3 necrosis in the brain.

4 Q Because some of the Respondent reports
5 suggest or claim that inorganic mercury is harmless in
6 the brain, that it's sequestered there and it's okay
7 for it to be there, right?

8 A That's what some people think.

9 Q Is this paper consistent with that view?

10 A It's not consistent because when they
11 injected the mercuric mercury directly into the brain
12 they got a neuronal necrosis and so it's a direct
13 effect of the mercuric mercury.

14 I want to apologize to the Special Masters.
15 I thought evidential toxicology would be a different
16 way of doing it. I suppose I should have given the
17 usual spontaneous rendition.

18 SPECIAL MASTER HASTINGS: Well, you need to
19 do whatever way you feel is more explanatory.

20 THE WITNESS: Okay.

21 SPECIAL MASTER HASTINGS: I'm just telling
22 you that it helps us for you to tell us what in here
23 is important.

24 THE WITNESS: Okay. Fine. Okay.

25 //

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1 BY MR. WILLIAMS:

2 Q Okay. Let's go to Slide 70, please. Now,
3 this is a very recent paper reviewing the role of
4 thiols, dithiols, nutritional factors and interacting
5 ligands in the toxicology of mercury. We've heard you
6 describe thiols as being the sulfur hydrogen groups.

7 A Yes.

8 Q They're on many enzymes, right?

9 A Yes.

10 Q Dithiols are just two of them?

11 A That's two of them, yes.

12 Q Okay. And what are ligands? What are
13 interacting ligands?

14 A That's something that they would react with,
15 what the metal would bind with.

16 What's important in this slide is that for
17 short-term -- they're discussing short-term high dose
18 -- that there have been studies with high doses and
19 low doses of methyl mercury, and they point out for
20 short-term high dose methyl mercury toxicity as used
21 by Magos in 1985 the approximate toxic agent is most
22 likely methyl mercury itself due to the high dose
23 delivered resulting in a direct toxic effect before
24 demethylization of the methyl mercury occurs.

25 However, for chronic low dose like those

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1 five studies that we've discussed from Seattle -- the
2 Charleston, the Vahter studies -- in those low dose
3 exposures by Charleston and Vahter the proximate toxic
4 agent is most like inorganic mercury due to both on
5 the one hand its long-term accumulation in the brain
6 and extremely long half-life therein.

7 I think this is a very important paper in
8 pointing out the differences between high dose and low
9 dose methyl mercury.

10 Q And this paper also concludes that the
11 result of that adult monkey study showed that
12 inorganic mercury was a toxic agent in the brains of
13 those monkeys, right?

14 A Yes.

15 Q Can you say yes out loud?

16 A Pardon?

17 Q You just nodded your head.

18 A I'm sorry. Yes.

19 Q The court reporter didn't hear that.

20 A Yes. Yes. Yes. I'm sorry. My apologies.

21 Q Okay. Now, did you make an overall slide
22 that compared methyl mercury and ethyl mercury?

23 A I think -- I hope -- it's the next one.

24 Q I think it's No. 71.

25 A Okay. Yes. All right. I sat down to a lot

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1 of information. I wanted to try to compare these
2 because again and again I was so wrongly impressed
3 with everyone saying these two compounds, methyl
4 mercury and ethyl mercury, are so different.

5 But what everyone was describing early in
6 the game were the pharmacokinetics are different.
7 They really had no evidence that the toxicity was that
8 different.

9 Q And by pharmacokinetics you mean what?

10 A What happens, how rapidly the blood level
11 goes up or down, how it's distributed, where it goes
12 in the body. Pharmacokinetics and toxicokinetics deal
13 with numbers, the quantities expressing what happens
14 to a compound in the body essentially in quantitative
15 terms as to where it goes, not necessarily what its
16 toxic effects are. Pharmacokinetics usually deal with
17 numbers rather than symptoms. Usually. There are
18 exceptions.

19 So here we have a column for methyl mercury
20 and ethyl mercury. Both of them are organic
21 mercurials. Both of them induce neuronal necrosis,
22 and the references to these are in the slides. If I
23 added the references in every case it would be a very
24 cumbersome slide.

25 Metabolized to mercuric. They're both

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1 metabolized to mercuric mercury. Cause weight loss,
2 Magos, et al. in 1985. Cause less weight loss, methyl
3 mercury. Ethyl mercury causes greater weight loss,
4 which is one of the first signs of organic material
5 toxicity.

6 Less renal toxicity for methyl mercury.
7 Greater renal toxicity for ethyl mercury. There was
8 little difference in the neurotoxicity of methyl
9 mercury and ethyl mercury on the dorsal root ganglia
10 or coordination disorders according to Magos, and the
11 same thing was true in the methyl mercury column.

12 Toxicokinetics. Different than ethyl
13 mercury in normal children or infant monkeys. Methyl
14 is different than ethyl. In the ethyl mercury column
15 toxicokinetics are different than methyl mercury in
16 normal children or infant monkeys.

17 The brain inorganic mercury level is lower
18 and persistent. The main thing is it's lower from
19 methyl mercury. Methyl mercury doesn't stay in the
20 brain long enough to get as much inorganic mercuric
21 mercury. The brain inorganic mercury level is higher
22 and persistent for ethyl mercury. It probably is
23 because ethyl mercury is converted much more rapidly
24 to inorganic mercury in the brain than is methyl
25 mercury.

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1 Brain organic mercury level is higher, but
2 temporary. Brain organic levels for ethyl mercury is
3 lower, but temporary. Frequency of human cells with
4 chromosome aberrations. Not significant for methyl
5 mercury. They are significant for ethyl mercury.

6 Oral exposure versus IM exposure. Methyl
7 mercury can cause cerebral palsy and mental
8 retardation. It can cause autism. Ethyl mercury can
9 cause autism. Methyl mercury crosses the blood-brain
10 barrier using the methionine carrier protein, and the
11 ethyl mercury crosses the blood-brain barrier by
12 diffusion and/or other means.

13 Q Okay. Let's go on now to a brief discussion
14 of how all this relates to biology and autism.

15 A All right.

16 MR. WILLIAMS: Go on to Slide 73, Scott.

17 THE WITNESS: Okay. This is a slide from
18 Dr. Swedo from the NIMH. I like this slide. I like
19 colorful things anyway.

20 Idiopathic means we don't know, so although
21 we have a small number of cases of autism that we know
22 have a genetic defect and we have a small number that
23 are teratogens, let me just say for the Court a
24 teratogen in the dictionary will say a teratogen
25 chemical causes monster formation or abnormal

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1 childbirth.

2 Teratogens have an effect in utero. By
3 definition, they only affect an embryo once the egg
4 has been implanted, whereas a mutagen reacts with the
5 DNA and can occur before implantation. So teratogens
6 have their action in utero.

7 The next slide? The pathogenesis of autism,
8 again from Dr. Swedo. We have a genetic defect which
9 will cause a neuronal dysfunction and damage and will
10 give autism. Now, each one of these colored ellipses
11 I guess just have a few words in them, but there's a
12 tremendous amount of work to be done in elaborating
13 each one.

14 The next slide, please? This is a plausible
15 pathway for ethyl mercury toxicity. It's built on one
16 that we showed in the Cedillo trial, but we've changed
17 it to some extent here.

18 BY MR. WILLIAMS:

19 Q I think the changed one is 76.

20 A Yes, I think you're right.

21 Q I think this is the one from Cedillo.

22 A Yes. Let's go to 76 then. This one was
23 supposed to be -- here we are.

24 So here we have thimerosal, ethyl mercury.
25 This ethyl mercury will be converted to mercuric

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1 mercury in the brain. That can cause
2 neuroinflammation. It can have an effect on
3 developmental windows of various organs in the body in
4 the child. You have neuroinflammation going on to
5 encephalopathy and regressive autism.

6 We bring in hypersusceptibility here as we
7 pointed out or will point out in I think a subsequent
8 slide, the Woods study that shows at least 15 percent
9 of the population handles porphyrins or mercury has an
10 effect in changing the porphyrin excretion and
11 porphyrin metabolism.

12 Next slide? Okay. What's important here?
13 We know there's a brain growth phenotype in ASD, and
14 inflammatory response has also been described in other
15 parts of the brain. We have the decreased cellular
16 Purkinje neurons and cerebral cortex changes that have
17 been reported by many investigators.

18 Next slide?

19 Q Now, the next slide is one of the autopsy
20 studies --

21 A Yes.

22 Q -- on autistic children, correct?

23 A Yes. This came out again this year, 2008,
24 and it points out again that there's an increased
25 density of glial cells for autistic children. There

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1 is a decreased neuronal density, and then there are
2 various signs of oxidative stress which can be shown
3 by doing various tests. There were also differences
4 in some glial cells.

5 As the Special Master said, you can go on to
6 read this later. Next slide, please?

7 Q Well, let me stop you.

8 A Yes?

9 Q Go back to the bottom point here, Area 22.
10 This paper was selecting areas of the brain that they
11 suspected would be involved in some of the aspects of
12 autism, right?

13 A Yes.

14 Q And in Area 22 what did they find?

15 A They found the greatest increase in glial
16 cells, the greatest neuronal decrease and the greatest
17 increase of nonspecific cells containing lipofuscin,
18 which is an indication of oxidative stress.

19 Q What is lipofuscin?

20 A It's a complex I want to say fat protein. I
21 don't remember exactly what it is, but I remember I
22 have it in my notes.

23 Q Okay. We can ask Dr. Kinsbourne. And then
24 briefly we refer to the Vargas paper, which I'm sure
25 was discussed in Cedillo. That's another autopsy

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1 study of autistic children.

2 A Yes. Their findings indicate that innate
3 neuroimmune reactions play a pathogenic role in an
4 undefined proportion of autistic patients.

5 Q Innate neuroimmune reactions. They're
6 referring there to the glial cells, aren't they?

7 A Yes. Yes, they are.

8 Q In the brain?

9 A In the brain.

10 Q Okay. Now let's go to the next slide.

11 A This might be of interest to the Special
12 Masters. It was certainly of interest to me. It
13 doesn't have anything to do with autism, but it shows
14 you what can happen with mercury and how it can
15 surprise clinicians if clinicians keep their mind open
16 and look for causes or differences in various
17 pathological conditions.

18 They are studying idiopathic dilated
19 cardiomyopathy, and they've studied the amount of
20 mercury and other metals. In controls, the mercury
21 was eight nanograms per gram. In people with this
22 disorder there was 178,400 micrograms, so that's
23 almost 20,000 times more in these IDCM.

24 So this indicates that mercury can
25 concentrate in specific tissues or organs of the body,

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1 even if mercury blood levels are found to be in the
2 normal range. This is a very interesting paper
3 because a lot of people missed it.

4 There's a tremendous amount of mercury. I
5 mean, that's roughly 178 micrograms of mercury in this
6 heart tissue that they found, and this will be of
7 importance later on when we talk about mercury efflux
8 disorders, but here is certainly a case where these
9 people or this person -- I've forgotten what it was --
10 could not get mercury out of their heart cells. No
11 question about it. One hundred and seventy-eight
12 micrograms compared to a control of .008 micrograms.

13 Next slide, please?

14 Q Okay. Now, you refer to a mercury efflux
15 disorder. What do you mean by a mercury efflux
16 disorder?

17 A One cause of autism is the cells cannot
18 efflux mercury. That is, there is no mechanism for
19 getting mercury out of the cell. The normal mechanism
20 by which mercury gets out of the cell usually is that
21 it ties up the glutathione, and the glutathione
22 mercury complex moves out of the cell.

23 Q All right.

24 A In the mercury efflux disorder, it implies
25 that there's mercury in the cell and it can't get out

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1 of the cell so the mercury concentrations in the cells
2 increase.

3 I'd like to give the evidence for this. The
4 next slide, please?

5 Q Now, you discussed Wilson's disease at some
6 length in the Cedillo trial, didn't you, as an
7 example?

8 A I don't remember, to be actually honest with
9 you. I thought we did not, but I know we discussed
10 it.

11 Q Well, quickly, Wilson's disease is an
12 example of another metal efflux disorder, correct?

13 A Yes. I'll make it very short. In Wilson's
14 disease, copper cannot leave certain cells, and the
15 copper accumulates in the cells and it becomes very
16 toxic to the cell.

17 Until John Walsh, a neurologist at Cambridge
18 in England, thought about using chelating agent people
19 with Wilson's disease would die very, very early in
20 life, but because of John Walsh and other people
21 subsequently who used the penicillamine and other
22 chelating agents to get the copper out of their
23 tissue, this at the time and still is one of the few
24 genetic diseases that is treatable. These people now
25 live to at least 40 or 45 years of age.

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1 I wanted to tell you that there is another
2 good example of an efflux disease, well documented in
3 the literature, called Wilson's disease or
4 hepatolenticular degeneration.

5 I think you can skip the next. Keep going.
6 Okay.

7 MR. WILLIAMS: We've been going almost two
8 hours here without a break.

9 SPECIAL MASTER HASTINGS: Do you want to
10 take a break?

11 MR. WILLIAMS: Yes. I probably have about
12 20 more minutes, I think, 20 or 25 minutes to go.

13 SPECIAL MASTER HASTINGS: Okay. Let's take
14 a 15 minute break. We'll be back at 4:00.

15 (Whereupon, a short recess was taken.)

16 SPECIAL MASTER HASTINGS: All right. We're
17 back on the record for the additional direct
18 examination of Dr. Aposhian. Dr. Aposhian, you're
19 still under oath.

20 Mr. Williams, please go ahead when you're
21 ready.

22 BY MR. WILLIAMS:

23 Q While we're waiting for the slide man to get
24 here, let me ask you. In this next section of your
25 testimony we're going to cover some examples of ways

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1 in which autistic children process mercury different
2 than normal children, right?

3 A Yes.

4 Q Okay. And is that what you call your
5 evidence for a mercury efflux disorder?

6 A Yes.

7 Q Okay. The first example is hair?

8 A Yes.

9 MR. WILLIAMS: The next slide, Scott?

10 THE WITNESS: Oh, here we are. This is a
11 study done by Holmes, Blaxill and Haley. Haley is
12 head of chemistry at University of Kentucky or was at
13 the time the study was done.

14 Amy Holmes, a private practitioner who
15 treated autistic children, and she knew the questions
16 about mercury that were unanswered as far as autistic
17 children, and she knew about mercury in hair, and she
18 remembered that most parents keep the samples of first
19 haircuts of the child, so she convinced them and
20 control people to bring in the baby haircuts.

21 The next slide will show the results. The
22 autistic group, and this is now Mercury Levels in
23 First Baby Haircuts. The autistic group was 0.47.
24 The control group was 3.63. Now, this study has been
25 criticized because the control group, 3.63, is too

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1 high as compared to the normal population.

2 One thing one must remember is to get
3 controls for autistics is a very difficult job for all
4 people interested in autism research. You can always
5 get autistic kids, whether it's hair or some other
6 way, but to try to get age matched and sex matched
7 samples is extremely difficult. But even if we look,
8 if we forget the 3.63 and say that what the normal
9 population is is usually about 1.0, you still have
10 twice as much mercury in the hair of controlled
11 children.

12 In addition to this -- now, this was done to
13 atomic absorption -- the next slide I think will show
14 the results of the MIT group where they used neutron
15 activation analysis, a different kind of technique for
16 measuring hair mercury. This also is an abstract of a
17 paper given at the American Nuclear Society.

18 Now, most societies peer review abstracts.
19 Whether this was done here I don't know.

20 BY MR. WILLIAMS:

21 Q Well, let me just ask you though. We've got
22 two studies on the hair of autistic children compared
23 to controls. What did they find? Were they
24 consistent with each other?

25 A Yes, they were consistent, both groups,

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1 although the second one was a smaller sample. They
2 both found that autistic children had less mercury in
3 their hair than their control or so-called normal
4 children.

5 Q And from a toxicology points of view, what's
6 the significance of that difference?

7 A The significance is that there is less
8 mercury in these cases in the blood and therefore
9 probably more mercury in the cells; that the mercury
10 cannot get out of the cells.

11 The work of James also shows that autistic
12 children have glutathione concentrations in their
13 blood, and this also means that there would be less
14 glutathione in the cell to bring out the mercury.

15 Q Is this evidence that autistic children tend
16 to retain mercury compared to controls?

17 A This is one kind of evidence that can be
18 interpreted as meaning that autistic children have
19 more mercury in their cells than nonautistic children.

20 Q Okay. Now, the next example you were going
21 to talk about was the Ip and DeSoto study again.
22 We've already talked about that.

23 A Yes. I just want to bring your attention to
24 the last sentence. Let me just read it: Moreover,
25 the hair sample analysis results offer some support

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1 for the idea that persons with autism may be less
2 efficient and more variable at eliminating mercury
3 from the blood.

4 Q Okay. We had talked about Ip with respect
5 to blood levels before. We're now talking about the
6 Ip study on hair levels, right?

7 A Yes.

8 Q And it was also consistent with the Holmes
9 and the MIT study. Okay.

10 And then there's another example of
11 chelation therapy if we go to Slide 89.

12 A Yes.

13 Q Now, explain quickly what chelation is.

14 A Sure.

15 Q You've had some experience with chelation?

16 A Yes. Metals, as I've told you earlier, are
17 bound to proteins and other substances in the body.
18 They're not floating around free. So in order to get
19 rid of metals you want to put something in the body
20 that's going to have a greater affinity for that metal
21 than the ligand or the protein that's holding onto the
22 metal in the body.

23 And so by giving a chelating agent, if it's
24 the right chelating agent it will have a greater
25 affinity for that metal or the metal will have a

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1 greater affinity for it than for the ligand or the
2 protein to which it is attached in the body.

3 The term chelate comes from the Greek word
4 chelos or claw, and essentially a chelating agent
5 forms a five membered ring, a claw if you will, with
6 the metal and makes that metal more water soluble.
7 Since it becomes more water soluble it is excreted
8 much more quickly and in larger amounts than if no
9 chelating agent was given.

10 Q Okay. And this study by Bradstreet and
11 others was a study of chelation in autistic children?

12 A Yes. What they did was give DMSA. We're
13 involved in the FDA approval of this. DMSA was used
14 originally. The FDA approval is for children with
15 lead levels of 45 micrograms or greater per deciliter
16 of blood, and DMSA is given to get the lead out of the
17 body. It also can be used for off-label studies as we
18 say because its safety has been proven. DMSA will
19 also mobilize mercury and bring mercury out of the
20 body in the same way.

21 What Bradstreet did was to give DMSA, this
22 water soluble chelating agent, to autistic children
23 and control children and, depending on which figure
24 you look at or which table you look at, you find a
25 very definite increase, anywhere from a three to

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1 eightfold increase in mercury excretion when the
2 autistic children were given DMSA chelating agent
3 versus the control children. This is an indication
4 that there was more mercury coming out.

5 Now, let me again say this study has also
6 been criticized. All these studies have been
7 criticized. There are very few studies in science
8 that we cannot criticize. One of the exercises in
9 most graduate schools is to give a student a paper and
10 say we want you to report what's good and what's bad
11 about this. These are peer reviewed studies.

12 You can always find something wrong with a
13 study. This one has been criticized because they said
14 the number of controls was too small. They also said
15 there was bias in picking the controls, but the fact
16 remains the paper appeared in a peer reviewed journal.
17 The fact remains it's been reported many times, both
18 personally at meetings and in the literature, that
19 DMSA does increase the mercury excretion as compared
20 to controls.

21 Q And is the result here consistent with the
22 hair studies we talked about?

23 A Yes, it is. It's consistent with a greater
24 body burden, a greater amount of mercury in the cells.

25 Q All right. Then let's skip to Slide 92,

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1 please. What is this study?

2 A Okay. This is an unpublished study from our
3 laboratory. We just haven't had time to publish it.

4 We have for most of the cases 16 autistic
5 children with 22 controls about the same ages. For
6 mercury in particular we had 14. There are some
7 urines that just got lost in the shuffle, or there
8 were some contaminated urines that were not used. For
9 autistic children there are 14 for mercury studies.
10 There are 14 children and 22 controls.

11 The equipment that we use, the latest
12 equipment there is available, simultaneously
13 determines within 10 minutes all of these metals on
14 one urine sample, so we don't have all the
15 manipulation errors that many people have that are
16 doing atomic absorption where they do one metal at a
17 time.

18 What we notice here is that the only
19 significant difference between autistic children and
20 control children is the mercury excretion. Here we
21 have P less than 0.03. There's another slide which I
22 forgot to bring with me that shows even a greater
23 difference with mercury, but there certainly is less
24 mercury coming out of children, autistic children, who
25 are not given chelating agents than normal children.

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1 Q So again is this consistent now with the
2 hair study and the Ip blood study?

3 A It's what we would expect, yes. We were
4 very excited to find this result. This has been
5 presented at a number --

6 Q We have seen five or six studies --

7 A Pardon?

8 Q -- which show that autistic children seem to
9 retain more mercury than nonautistic children.

10 A Yes. Yes.

11 Q Again, we talked about DeSoto, but there is
12 one quote from DeSoto I think you wanted to show on
13 Slide 93. Do you see the underlined part?

14 A Yes. In the DeSoto paper, just let me read
15 the last part of it. Under Figure 1, they point out
16 the variability found in circulating levels of mercury
17 in hair, so kids are different. There's a wide
18 spread.

19 Also, what is underlined. This is
20 consistent with the idea that autism may be partly
21 related to a lesser ability to rid the body of
22 neurotoxins such as mercury, so again this fits.

23 If I can have the next slide, which I think
24 is the baby teeth? Yes. No. This is another one.

25 Q Yes.

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1 A This we've talked about already, I think.

2 Q We've talked about that one.

3 A Yes.

4 Q Let's go on to the next one.

5 A Yes. I think we skipped the baby teeth,
6 which must have been two or three back there. Adams.
7 Essentially this paper shows --

8 SPECIAL MASTER HASTINGS: Now what are you
9 talking about, Doctor? Which slide?

10 THE WITNESS: Pardon?

11 SPECIAL MASTER HASTINGS: Which slide are we
12 on, or what are you talking about?

13 THE WITNESS: We're now on Slide --

14 MR. WILLIAMS: This is Slide 95, Special
15 Master.

16 THE WITNESS: Yes.

17 BY MR. WILLIAMS:

18 Q This slide is a study of the difference
19 between boys and girls in the way they retain mercury?

20 A Yes. What they're measuring here is the
21 amount of mercury excreted in the urine over a period
22 of time with children.

23 The black spots, these children have
24 amalgams in their mouth. The white spots or open
25 circles, these children have composites used for

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1 dental fillings rather than mercury.

2 Q The amalgams have mercury?

3 A The amalgams are mercury fillings.

4 Q And we know that mercury vapor comes off
5 amalgams.

6 A It's well accepted even by the American
7 Dental Association that mercury is emitted from these
8 amalgams.

9 Q And does this study first show that both
10 types of kids, boys and girls, if they had amalgams
11 did they have more mercury coming out or less mercury?

12 A What it shows is if they had amalgams in
13 both cases more mercury was being excreted than if
14 they had composites, number one.

15 Q Okay.

16 A Number two, more importantly, if you look at
17 the red arrows it shows that by the seventh year the
18 boys are excreting less mercury than the girls are,
19 which is an indication that the boys are retaining
20 more mercury than the girls are.

21 That's what the interpretation of the
22 authors is. Boys retain mercury more than girls by
23 not excreting as much of the mercury.

24 Q Okay. Now, I think you're right that the
25 slide about the tooth study somehow got dropped out of

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1 here, but why don't you just briefly describe the
2 tooth study to the Special Masters?

3 A The study by Adams. We know from the work
4 of Needleman, who used baby teeth as an indicator of
5 biomarker for lead, so Adams thought he would look at
6 baby teeth to use as an indication of mercury.

7 The amount of mercury or metal in the teeth
8 is a reflection of how much is in the body at one time
9 or another. Adams found that the mercury in the teeth
10 of autistic children was at least twice as much as the
11 mercury in the teeth of nonautistic children, again
12 indicating that these children, these autistic
13 children, have more mercury in their tissues and in
14 this case in their teeth, which are certainly
15 considered to be a tissue or an organ.

16 SPECIAL MASTER HASTINGS: Just for the
17 record, I think there's a Slide No. 90 that refers to
18 Adams, as Special Master Campbell-Smith just pointed
19 out to me.

20 MR. WILLIAMS: I knew it was in his report.

21 THE WITNESS: Can we go back, Scott, to 90?

22 SPECIAL MASTER HASTINGS: I think you just
23 described it.

24 MR. WILLIAMS: Slide 90 does discuss the
25 teeth though. You're right. Thank you for pointing

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1 that out.

2 THE WITNESS: Because that study again has
3 been criticized, the tooth study. As they say when
4 you go to meetings, it hasn't been confirmed. That
5 doesn't mean someone tried to confirm it. It means
6 that no one tried to do the exact experiment.

7 In one of these studies we cite, the editor
8 of that journal, the *Journal of Child Neurology*, made
9 a big point of saying that people don't get glory by
10 trying to repeat other people's studies, and the NIH,
11 National Institutes Health, of our government does not
12 give money to investigators to repeat other people's
13 studies.

14 And so the idea that the Adams work should
15 be minimized because it has not been repeated is just
16 pure propaganda. It doesn't belong in scientific
17 argument.

18 BY MR. WILLIAMS:

19 Q Okay. Now one more. Let's go to Slide 97,
20 please. I'll ask this question. Have there been some
21 studies that have now identified at least one genetic
22 marker of susceptibility to this mercury efflux
23 problem?

24 A Yes. Woods from Seattle and his associates
25 have shown genetic polymorphism of the coproporphyrin

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1 gene -- actually the oxidase gene -- and has shown
2 that 15 percent of the population, of the dental
3 population in this case, have a different reaction to
4 mercury than do the rest of the dental population.

5 This finding represents the first report of
6 a polymorphism. In other words, something has been
7 changed in the gene that modifies the effect of
8 mercury on a biological process, and they are now
9 proposing that this be used for a biomarker of mercury
10 exposure. It's a very readily testable phenomenon.

11 Q And is it your opinion that in the children
12 that we've seen that have more mercury in their blood,
13 less mercury in their hair, more mercury in their
14 teeth, do they probably have genetic differences from
15 the others too?

16 A I think there's no question. Most people
17 would say they must have genetic differences to have
18 those kinds of results.

19 Q Okay. Let's go to your second hypothesis
20 quickly about Terbutaline. That's on Slide 98, if you
21 would.

22 A Terbutaline is an example of a teratogen
23 that can cause some types of autism via a
24 neuroinflammation mechanism.

25 Q Okay.

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1 A The next slide points out that Terbutaline
2 has been a drug that has been used in the clinic to
3 arrest preterm labor in women. We're not talking
4 about animals now. We're talking about pregnant
5 women.

6 It has been shown that the critical period
7 corresponds to the second and third trimester in the
8 human fetus. The human fetus is exposed to
9 Terbutaline, and if there is a predisposition to
10 having the damage there's a greater chance that the
11 child will have autism. It causes decomposition of
12 central nervous function like that reported in autism.

13 Q Okay. I showed in the opening statement an
14 animal model of this Terbutaline toxicity, and Slide
15 101 I think has that paper on it.

16 A Yes.

17 Q If you would go to that?

18 A Yes. Results from animals can be used to
19 trigger studies of human populations for exposure and
20 outcomes, and there is a paper by Zeratte I think from
21 the Hopkins group, if I remember correctly.

22 Results are overstimulation of the
23 adenoreceptor during an early critical period.
24 Results are microglial activation associated with
25 innate neuroinflammatory pathways and behavioral

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1 abnormalities similar to what is seen in autism.

2 Q When it says similar to what is seen in
3 autism it's referring to those autopsy children of
4 autistic children?

5 A Yes. Yes.

6 Q The Vargas paper and the Lopez title paper
7 and so forth?

8 A Yes. Yes, sir.

9 Q And then is this microglial activation the
10 same thing that happened to the adult monkeys in the
11 adult monkey study --

12 A Yes.

13 Q -- with the inorganic mercury in their
14 brain?

15 A Yes. Inorganic mercury did cause that.

16 Q Okay. Let's go quickly to your summary
17 slide on 106, please, and summarize your opinions here
18 if you would.

19 A I don't think it's necessary to repeat the
20 first one --

21 Q Okay.

22 A -- because we don't know about species of
23 mercury, but I think it's necessary to speak about the
24 Carvalho, et al. study, in particular the remarkable
25 potency of the mercury compounds to bind the selenol-

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1 thiols in the active site, and thioredoxin reductase
2 should be a major molecular mechanism of mercury
3 toxicity.

4 The first hypothesis: One cause of autism
5 is that cells cannot efflux mercury, including
6 thimerosal, and the DeSoto paper goes on to confirm
7 that. That is a rebuttal of the Ip paper.

8 The second hypothesis: Terbutaline is an
9 example of a teratogen that causes some type of autism
10 via a neuroinflammation mechanism. Again, the Zeratte
11 and other papers show that the behavior of
12 abnormalities after Terbutaline are similar to autism.

13 In my opinion, based on 55 years' experience
14 of being an independent biomedical research
15 investigator funded by the federal government and
16 private foundations, the first and second hypotheses
17 are scientifically reasonable and probable.

18 Q Now let me ask you this question. Do you
19 have an opinion as to whether or not injections of
20 thimerosal in vaccines in human infants would deposit
21 measurable amounts of inorganic mercury in the brains
22 of those kids?

23 A What would happen would be the thimerosal
24 would be broken down to ethyl mercury. The ethyl
25 mercury would cross the blood-brain barrier, and in

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1 the brain that ethyl mercury would be de-ethylated to
2 give inorganic mercury or mercuric mercury which would
3 stay in the brain.

4 Q Just as it did in the infant monkeys? Is
5 that right?

6 A The infant monkey study, certainly a whole
7 batch of them, including the most recent -- I think
8 2005 -- Burbacher paper.

9 Q And do you hold that opinion to a reasonable
10 medical scientific probability?

11 A Yes, I do.

12 MR. WILLIAMS: Thank you very much. That's
13 all I have.

14 SPECIAL MASTER HASTINGS: All right. Do any
15 of you have questions for Dr. Aposhian at this point?

16 SPECIAL MASTER VOWELL: Not at this point,
17 no.

18 SPECIAL MASTER CAMPBELL-SMITH: Not at this
19 point.

20 SPECIAL MASTER HASTINGS: All right. Let me
21 ask one question, Dr. Aposhian, before we go on and
22 see what the Respondent wants to do at this point.

23 Now, you filed an expert report with us back
24 on August 30 of last year. I don't know if you recall
25 preparing that.

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1 THE WITNESS: I remember preparing it and
2 having a very short period of time to prepare it
3 because someone dropped out because of cancer.

4 SPECIAL MASTER HASTINGS: All right. A
5 number of the articles that you talked about today
6 were included in here?

7 THE WITNESS: Some of them were. Some of
8 them of course have been published since then.

9 SPECIAL MASTER HASTINGS: Right. Of course,
10 articles that have been published since you wrote this
11 report couldn't very well be in this report. I
12 understand that.

13 In general, did you put in all the articles
14 that you at the time thought were important to the
15 issue?

16 THE WITNESS: At that time I wrote that
17 article I put in the papers that I thought at that
18 time were important.

19 SPECIAL MASTER HASTINGS: All right.

20 THE WITNESS: I really haven't kept track,
21 but it's sort of like preparing a lecture or at a
22 symposia. You never finalize it until the minute
23 before you walk in and give it, and so there are
24 always changes to be made, especially over the last
25 almost year. I'm sure there are papers.

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1 If the question is are there papers here
2 that are quoted that were not quoted in the initial
3 report, the answer is yes.

4 SPECIAL MASTER HASTINGS: Tell me why. I
5 mean, obviously aside from the obvious ones that were
6 published since then.

7 THE WITNESS: Yes. Let's see. I don't know
8 how to put this without making it personal.

9 I've had two members of my family seriously
10 ill. When I was asked to participate in writing that
11 report they were not ill. Shortly thereafter they
12 became ill, and I had I think a month from the time
13 that I think it was Dr. Lusier who dropped out because
14 he had cancer, so I had a very limited time to prepare
15 that report, whereas I had much more time to prepare
16 this talk. Does that answer your question, sir?

17 SPECIAL MASTER VOWELL: Based on Special
18 Master Hastings' questions, I have a couple follow-up
19 questions, Dr. Aposhian.

20 Were you ever asked to prepare a
21 supplemental report; that is, a rebuttal report?

22 THE WITNESS: I don't think so. I didn't
23 see the Respondent's reports until maybe a month ago.
24 I don't remember the exact timing, but I certainly was
25 not asked to prepare a rebuttal, and there's nothing

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1 in here that I can think of except -- well, actually
2 the rebuttal about this poison determined the dose, if
3 anything that was rebuttal to what was brought up in
4 the Cedillo trial.

5 I must actually state that -- how should I
6 put it -- I certainly would like more time to read the
7 Respondent's reports. To my knowledge, I did not
8 prepare any kind of rebuttal to the present
9 Respondent's reports, to the best of my knowledge.

10 SPECIAL MASTER VOWELL: So you were not
11 aware that there was a March deadline or early April
12 deadline to file rebuttal reports?

13 THE WITNESS: I don't know. I honestly
14 don't know. You can't imagine what it's like to have
15 two people in your family seriously ill.

16 SPECIAL MASTER VOWELL: Oh, yes, I can, Dr.
17 Aposhian.

18 THE WITNESS: Okay. We don't believe in
19 health care providers. We think the family should
20 take care of their own, and so I just don't remember
21 the timing. I'm sorry. But I know no one asked me to
22 prepare a rebuttal.

23 SPECIAL MASTER VOWELL: Well, let me phrase
24 it this way then.

25 Your slides are dated 5-12-08 at least on

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1 Petitioners' Trial Exhibit 2. Is that when these
2 slides were prepared?

3 THE WITNESS: Excuse me?

4 SPECIAL MASTER VOWELL: These slides,
5 Petitioners' --

6 THE WITNESS: Yes. These slides, they were
7 prepared yesterday. Honestly.

8 When did I begin? This is May. I think I
9 was told in April or the end of February when the date
10 of this trial was set and so it would be my normal
11 inclination in any talk that I was preparing to give
12 anywhere that I would try to bring it up to date and
13 try to improve to the best of my ability to give the
14 best talk that was most relevant.

15 SPECIAL MASTER VOWELL: I have nothing
16 further.

17 THE WITNESS: Have I done something wrong?
18 I'm not sure.

19 SPECIAL MASTER HASTINGS: No. I think
20 you've answered our questions.

21 THE WITNESS: Okay.

22 SPECIAL MASTER HASTINGS: Mr. Matanoski, how
23 do you propose to proceed at this point?

24 Obviously Dr. Aposhian did cover some of the
25 topics that were covered in his expert report and some

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1 topics that weren't covered in his expert report. Do
2 you want to cross him on the topics that he did cover?
3 How do you propose that we proceed at this point?

4 MR. MATANOSKI: We have about two and a half
5 hours of cross-examination based on his expert report.
6 It seems that some of the testimony we didn't get
7 today was matters that were in his expert report. I'm
8 not sure how much of that --

9 SPECIAL MASTER HASTINGS: Do speak up.

10 MR. MATANOSKI: I'm sorry. I'm having the
11 same problem with my voice that you are, sir.

12 I believe we probably would still be at
13 about two and a half hours to cover some of the topics
14 that he covered today which were covered in his expert
15 report.

16 Then there are some new questions that have
17 suggested themselves obviously based on things that
18 he's covered today, although as I mentioned in our
19 bench discussion they may be the subject of further
20 proceedings or motions I should say after this trial
21 or during this trial.

22 So we could go ahead and forge ahead with
23 what we have, which would be about two and a half
24 hours. We're prepared to do so, sir.

25 SPECIAL MASTER HASTINGS: Why don't we make

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1 some use of our time? Why don't we begin your cross-
2 examination?

3 MR. MATANOSKI: Very well, sir. Could we
4 then have a brief break for Ms. Renzi, who will be
5 doing it, to get her notes together? I mean brief,
6 sir.

7 SPECIAL MASTER HASTINGS: All right. How
8 much time do you need?

9 MR. MATANOSKI: Ten minutes, sir.

10 SPECIAL MASTER HASTINGS: All right.

11 MR. MATANOSKI: Thank you.

12 (Whereupon, a short recess was taken.)

13 SPECIAL MASTER HASTINGS: Good afternoon
14 again. Please be seated.

15 To those listening at home, we're again back
16 for the last segment of our proceedings this
17 afternoon. Dr. Aposhian is still on the witness
18 stand.

19 Let me mention a couple things before we
20 start with Ms. Renzi's questions here. First, that we
21 thought it would be a good idea, given we have two
22 witnesses scheduled for tomorrow, that we would get
23 some of Dr. Aposhian's cross in today.

24 If you have a logical breaking point at some
25 point before 6:00 I think we don't want to go past

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1 6:00 today. If you have a logical breaking point at
2 some point prior to that, Ms. Renzi, let us know.
3 Maybe we'll stop at that point.

4 The other point being just to say for the
5 record that as Mr. Matanoski mentioned earlier, we did
6 have a conference at the bench earlier today. As he
7 alluded to, at that point there was raised a motion
8 that was filed in the King case and perhaps in the
9 Mead case too, but it's relevant to both.

10 It was filed on Friday afternoon
11 electronically having to do with a reference to a
12 number of medical articles, over 200 medical articles,
13 that were filed last week that were new to the case
14 filed by the Petitioners, cited by them, that were not
15 previously discussed in expert reports of either side
16 and raising that issue, the issue of what to do about
17 that and asking that the Petitioners be prevented from
18 making reference to these articles in their own expert
19 direct examination.

20 The representation had been last week at a
21 status conference that the purpose of filing these
22 articles was to make them available for cross-
23 examination of the Respondent's experts.

24 Mr. Matanoski did mention that some of those
25 articles had been raised today in the examination of

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1 Dr. Aposhian and perhaps in Dr. Greenland as well, in
2 the direct examination of him, and that the government
3 was considering filing an additional motion seeking
4 additional relief here.

5 Again, we note that we will hear that motion
6 whenever you want to present it, or you can file it in
7 writing. We'll wait to hear exactly what you have in
8 mind, but obviously a couple of our questions to Dr.
9 Aposhian were addressed to that issue. We'll wait for
10 what the government proposes to do about that issue
11 explicitly at this point.

12 What that, Ms. Renzi, whatever questions you
13 had for Dr. Aposhian this afternoon, go ahead and go
14 for it at this point.

15 MS. RENZI: Thank you, Special Master.

16 CROSS-EXAMINATION

17 BY MS. RENZI:

18 Q Good afternoon.

19 A Good afternoon.

20 Q Dr. Aposhian, you said you were currently a
21 professor at the University of Arizona?

22 A I'm professor emeritus. I retired on
23 January 31 to take care of my wife and other people in
24 my family, but I still have an active laboratory with
25 funding for research for two more years.

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1 Q Do you know if you're listed on the
2 University of Arizona website as a faculty member or a
3 professor emeritus?

4 A Excuse me?

5 Q Do you know if you're listed on the
6 University of Arizona website as either a member of
7 faculty or as a --

8 A I don't have the faintest idea. I don't
9 read that sort of stuff, but I do have letters that I
10 can send you from the president of the university and
11 from the medical school people saying that I have
12 emeritus status. I would never dare say anything that
13 was not so.

14 Q Okay. Are you listed as a professor at the
15 Pharmacology School of Medicine? Do you know that?
16 Do you have emeritus status there as well?

17 A For the last 32 years I've been listed in
18 the catalog of the medical school as Professor of
19 Pharmacology.

20 Q Do you know Glen Sipes, the chair of the
21 Pharmacology Department at the University of Arizona?

22 A Excuse me?

23 Q Glen Sipes. Do you know Glen Sipes?

24 A Yes. I know Glen Sipes very well.

25 Q Is he a well-respected toxicologist?

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1 A Of course he's a well-respected
2 toxicologist.

3 Q And do you know a man, John Sullivan, at the
4 University of Arizona?

5 A I don't know him personally. I know of his
6 reputation. He's a very good clinical toxicologist.

7 Some people use the term medical
8 toxicologist, but I think the board, and again you can
9 correct me. I think the board uses the term clinical
10 toxicologist.

11 MR. MATANOSKI: The board uses the term
12 medical toxicologist.

13 THE WITNESS: It changed then. Okay.
14 Because two of the members at the University of
15 Colorado spent time in my laboratory, and one of them
16 took time off to study for her board exams in clinical
17 toxicology.

18 BY MS. RENZI:

19 Q Now, you're not a medical doctor. Is that
20 correct?

21 A That's absolutely correct.

22 Q And you're not a medical toxicologist. Is
23 that correct?

24 A It depends on how you define the term
25 medical toxicologist. I was brought in by the Chinese

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1 Government. I was brought in by the Chilean
2 Government. I was brought in by the Inner Mongolian
3 Government as a pro bono consultant to deal with a
4 population of people who were drinking water with
5 elevated levels of arsenic.

6 Q But you don't have --

7 A Excuse me. Let me continue.

8 Q Okay.

9 A And so I took a team with me, and I was the
10 person responsible for everything. I was the person
11 that wrote up the reports. I dealt with humans.

12 Now, am I a medical toxicologist? I don't
13 like the term. I'm a toxicologist.

14 Q But you don't have a medical degree to be
15 called a medical toxicologist?

16 A I have no medical degrees, as I've told you
17 before.

18 Q That means you're also not a neurologist. I
19 that correct?

20 A Pardon me?

21 Q You're not a neurologist?

22 A Obviously I can't be a neurologist when I
23 don't have an M.D.

24 Q Do you consider yourself qualified to
25 comment on the neurological aspects of autism?

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1 A It all depends on what parts of the
2 neurological aspects you're talking about, but I would
3 certainly take second place. I would prefer that a
4 medical neurologist answer such questions.

5 Q Are you an immunologist?

6 A I'm not an immunologist.

7 Q Do you consider yourself qualified to opine
8 on the immunology as it relates to autism?

9 A Again, it depends at what level you're
10 speaking of. If you want me to go into the very fine
11 levels of immunology as far as applying to humans, I
12 would certainly not want to speak that way.

13 I am a basic science bench investigator. I
14 work at the lab bench, and I go study populations of
15 people at the invitation of governments throughout the
16 world.

17 Q Have you ever published a peer reviewed
18 article on mercury in the immune system?

19 A No, I have not.

20 Q Have you ever published a peer reviewed
21 article on autism?

22 A We are now in the process of writing a
23 review article that we've been asked to write by an
24 international journal as a toxicologist's view of
25 autism. I expect the article will be finished

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1 sometime this summer.

2 That was an invitation for the article. We
3 did not ask to do it. They invited us to do it. An
4 invitation.

5 Q Have you ever published a peer reviewed
6 article on thimerosal toxicity?

7 A I don't remember whether some of our
8 abstracts -- I would say no.

9 Q Have you ever published a peer reviewed
10 article on ethyl mercury toxicity?

11 A On what?

12 Q Ethyl mercury toxicity.

13 A Not published, but we've given many talks at
14 symposium. The Institute of Medicine invited me. I
15 actually did not want to go.

16 They invited me in I think in was 2004 I
17 think it was to speak at one of their vaccine
18 committee meetings on "A Toxicologist's View of Autism
19 and Thimerosal".

20 Q Do you consider yourself an expert in
21 autism?

22 A I consider myself an expert on the
23 relationship of mercury to autism.

24 Q And when did you acquire that expertise?

25 A When?

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1 Q Yes.

2 A Let me tell you the story. In I forget
3 whether it was 2002 or 2003 I had a call from the
4 administrative assistant to Congressman Burton of the
5 House Government Oversight & Regulation Committee. I
6 think it's called that.

7 At that time the administrative assistant --
8 she actually -- asked me whether I would come and talk
9 to the committee on mercury toxicity. I said
10 certainly, but why are you interested in mercury
11 toxicity? This was probably five years ago I would
12 say. They said we're really interested in autism, and
13 there's mercury involved. I said okay.

14 I went home and decided I really didn't know
15 what autism was. I have two daughters who have PhDs
16 in clinical psychology. I called them and I said what
17 is autism? They in fact were delighted to know
18 something that their father did not know and so I
19 first learned about autism at that time.

20 Since then there have been many
21 organizations like the Institutes of Medicine and
22 other organizations that wanted someone who had more
23 or less a fresh view of autism that was not part of
24 any establishment as far as autism is concerned and so
25 in the last five years I've become very interested in

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1 autism.

2 Q Are you aware of the Diagnostic and
3 Statistical Manual of Mental Disorders, otherwise
4 known as the DSM-IV?

5 A I'm aware of it.

6 Q What are the criterion for an autism
7 diagnosis?

8 A I would certainly open up the book and read
9 them.

10 Q You don't know them?

11 A There are regulations that I don't know.
12 That's some of them. I can talk about other
13 regulations I don't know either. If it's something
14 that you can find on the web or in a book there's no
15 sense of memorizing, especially since you don't use it
16 every day.

17 What we were concerned about was all our
18 autistic subjects in our urine studies were classified
19 by a physician by the usual standards that you've just
20 mentioned and the other standards for autism.

21 Q You've published several articles on
22 chelation. Is that correct?

23 A I would say many people think my major
24 contributions since 1979 have dealt with chelation.

25 Q Would you agree that you're not qualified to

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1 diagnose or treat a person with ethyl mercury
2 toxicity?

3 A I have never claimed I have been.

4 Q Would you agree that you're not qualified to
5 diagnose or treat a person with any form of mercury
6 toxicity?

7 A It all depends now on how you want to define
8 diagnosis. Very often a physician will call me and
9 say Vas, we have this case here and the urine
10 mercuries are this much. The blood mercuries are such
11 and such. We've done a biopsy, as the case just
12 happened now, of someone's gut and we want to know
13 whether you think it's worth doing a mercury analysis
14 or you think this person may have mercury toxicity.

15 What I usually say, as they well know, is
16 John, Joe, whatever your name is, I'm not a physician,
17 as you know, but based on what you've told me it seems
18 to me that that person is mercury toxic.

19 But would I stand up in a Court of law and
20 say hey, I'm an expert in diagnosing humans? No, I
21 would not because if you're going to deal with humans
22 on a diagnostic and treatment basis -- not a research
23 basis, but a diagnostic and treatment basis -- then
24 you should be an M.D.

25 Q I want to move on to dose. You quoted today

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1 from Casarett & Doull, the book on toxicology,
2 correct?

3 A Yes.

4 Q Would you agree with the statement that's in
5 that book that no other metal better illustrates the
6 diversity of effects caused by different chemical
7 species than does mercury?

8 A Are you asking me whether I agree with this?

9 Q Yes.

10 A I have no disagreement with it.

11 Q Would you agree that different species of
12 mercury have different toxicological properties?

13 A I'm sorry? I didn't hear you.

14 Q Do different species of mercury have
15 different toxicological properties?

16 A That was I think quite apparent from the
17 talk I gave or my testimony earlier.

18 Q Could you please define dose for me? What
19 is dose?

20 A Dose means different things to different
21 people. If you're a scientist and are concerned about
22 dose then you'll want a quantitative value that tells
23 you how much you are giving to a certain animal or
24 human being.

25 You want a quantitative value, and that

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1 quantitative value could be milligrams or grams. It
2 could be milligrams per kilogram. It depends on who
3 is prescribing, and I don't prescribe to humans, of
4 course.

5 Q Would you agree that any substance could be
6 toxic to humans based upon a dose?

7 A The point I have tried to make in the
8 testimony is that dose is not the only criterion for
9 toxicity; that many other criterion come into play
10 when you discuss toxicity, and that was shown in at
11 least two or three of my slides from the textbook that
12 you have just quoted.

13 Q What is the principle of dose response?

14 A Dose response usually means -- not all the
15 time -- that as you increase the dose you increase the
16 response, or as you decrease the dose you decrease the
17 response usually in a fairly straight line, but, as we
18 know, especially in the case of arsenic toxicity that
19 when you get down at lower levels it goes off the
20 straight line.

21 Q Is it still your opinion that the principle
22 that dose makes the poison is no longer accepted by
23 the general toxicological community?

24 A That's not what I said. It is one of the
25 factors that determines toxicity, but it is not for

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1 anyone to get up and say dose determines the poison.
2 It's a very limited way of looking at toxicology, a
3 very limited way of looking at a poison.

4 There are many factors in that very chapter
5 that you quoted with Goyer which I presented earlier
6 and you have copies of various other things that
7 affect the toxicity. It's not only dose that affects
8 toxicity.

9 Q So that principle is no longer accepted by
10 the general toxicological community? Is that what
11 you're saying?

12 A I don't consider it a principle. It's
13 something that man in 1400 or 1500 said, and anyone
14 who thinks that toxicology has not progressed enough
15 to change and have a different view about someone's
16 statement in the year 1490 or whatever it is I think
17 has a very limited outlook on medicine and science.

18 Most of the people that I know, Sipes
19 included, would say dose is one of the factors that
20 determines toxicity or determines poison. It's not
21 the only factor.

22 Q Would you agree that in toxicology a
23 threshold dose is expected before a particular outcome
24 is observed?

25 A Before?

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1 Q That you would have a threshold dose before
2 a particular outcome is observed?

3 A I don't know what kind of generalization
4 you're trying to make. I certainly know that response
5 is related to dose, but dose is not the only thing
6 that determines response. Is that clear?

7 Q We'll move on. How much ethyl mercury is
8 there in a thimerosal-containing vaccine? How much
9 ethyl mercury is there in a thimerosal-containing
10 vaccine?

11 A It depends on which vaccine it is. I think
12 in one case -- I can't remember which vaccine -- it's
13 12.5 micrograms if I remember correctly. In the other
14 case of a vaccine it's 25 micrograms.

15 Q And I know you had this on your slide
16 presentation earlier. How many micrograms are there
17 in a milligram?

18 A There are a million micrograms in a -- I'm
19 sorry. There are 1,000 micrograms in a milligram.
20 Isn't that what it said?

21 Q Yes.

22 A Okay. Thank you.

23 Q And how many micrograms are there in a gram?

24 A There should be a million micrograms in a
25 gram.

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1 Q Dr. Aposhian, is it scientifically valid to
2 compare the doses of ethyl mercury that are in a
3 thimerosal-containing vaccine, and I'll use TCV from
4 now on if that's okay.

5 In a TCV, is it right to compare those
6 doses --

7 A I don't like the term TCV. I don't like
8 abbreviations. Would you mind saying the whole thing?
9 We have computers now that can print things up very
10 carefully, and I think it's much clearer if we don't
11 use abbreviations, if you don't mind.

12 Q If you would like me to say it, that would
13 be fine.

14 A Thank you. I appreciate that very much.

15 Q I'll repeat the question then. Is it
16 scientifically valid to compare doses of ethyl mercury
17 that are contained in a thimerosal-containing vaccine
18 to the exposures of methyl mercury that occurred in
19 Iraq in Minamata?

20 A It all depends on what you mean by compare.
21 If you're saying do you want to see if each of them is
22 toxic, yes. If you want to say is one more toxic than
23 the other, I'm not sure you can do that, so I'd like
24 to ask that you ask me if possible a more specific
25 question.

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1 Q Can you compare the 12.5 micrograms that are
2 contained in a thimerosal-containing vaccine to the
3 doses that were exposed to the people who ate the
4 grain in Iraq and who consumed the fish in Minamata?

5 A No question about it. I now understand your
6 question. I'm sorry. I didn't mean to interrupt you.

7 Q Okay.

8 A My apologies.

9 Q No. That's my question.

10 A Okay. There is no comparison. The amount
11 that was used, the exposure in Iraq was much, much
12 higher.

13 We were talking in the talk I gave earlier
14 in I think it's the Rooney paper explained the
15 differences between a chronic high dose and a chronic
16 low dose. Certainly if you want to talk about chronic
17 doses the exposure of children getting vaccines would
18 be considered to be a chronic low dose whereas the
19 Iraqi people being exposed to the various forms of
20 mercury in the flour that the U.S. Government gave
21 them, that would be considered a chronic high dose.

22 Q Do you agree that the researchers in Iraq
23 and Minamata established a dose/response relationship
24 in their studies?

25 A I've got to be very careful here because the

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1 Minamata studies are so old. My guess is yes, they
2 did, but I just don't remember the particular paper
3 with the particular dosage, but I'm sure Tom Clarkson,
4 knowing how he works, did establish. I would suspect
5 that Tom Clarkson did establish a dose/response curve
6 in Iraq.

7 Q Have you read the 1973 Bakir article,
8 B-A-K-I-R?

9 A Which one? I've read all the Iraqi
10 articles, and some of the names I have difficulty
11 remembering.

12 Was that the one? There was one -- I'm not
13 sure whether Clarkson was the first author or he was
14 -- which showed that depenicillamine was one of the
15 best ways of getting rid of mercury in the blood. Is
16 that the article you're talking about?

17 Q I'm talking about an article that was filed
18 on Petitioners' Master List 178. We can hand you that
19 article if you'd like to see it.

20 A Yes, I would like to see that article,
21 please.

22 (Pause.)

23 A This is a very old article. I'm not sure I
24 remember reading everything about it, but I do
25 remember that when it came out I read it and maybe a

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1 couple times since then, but not recently.

2 What would you like me to address in this
3 article?

4 Q Do you recall the threshold dose of mercury
5 that was observed in Iraq before effects of toxicity
6 were observed?

7 A I don't recall at all.

8 Q I want to refer you then to page 238 of that
9 article.

10 A Page 238.

11 Q Okay. I think it's the top center column.
12 We have it up on the screen as well.

13 A Excuse me. You're talking about Figure 7?

14 Q I'm talking about the paragraph that's
15 highlighted. It should be on your screen, sir.

16 A Oh, I'm sorry.

17 Q It says: Nevertheless, the threshold value
18 of 25 to 40 milligrams of mercury as computed for
19 parasthesis agree remarkably well with the threshold
20 figure of 30 milligrams of mercury computed by the
21 Swedish expert committee from data on the Japanese
22 epidemics.

23 Would you agree then from that article that
24 there was a threshold value of 25 milligrams of methyl
25 mercury?

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1 A I agree that nevertheless, the threshold
2 value of 25 milligrams of mercury was computed for
3 parasthesia agrees remarkably well with the figure of
4 30. Is that what you're asking me?

5 Q Yes.

6 A I have no argument.

7 Q Now, the threshold value of 25 milligrams.

8 A Yes?

9 Q What is that equal to in micrograms?

10 A Twenty-five milligrams would be 25,000
11 micrograms.

12 Q In either one of those epidemics, either in
13 Minamata or in Iraq, was there an increase of autism
14 reported as an outcome of the affected populations?

15 A No one even thought of autism in those days.
16 You should ask Tom Clarkson, who is a fantastically
17 good scientist. People have asked him that, and his
18 response is no one thought about autism in those days.

19 I think most people did not know what autism
20 is. I think most medical students were not taught
21 anything about autism, so it's not surprising that no
22 autism cases turned up.

23 Q Do you know if the clinical effects then
24 that were reported in either the Iraq or Minamata
25 study resembled autism? Even if we didn't know what

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1 autism was, were any of the listed effects clinically
2 significant for the diagnosis of autism?

3 A Well, as I remember, and again it's been a
4 long time since I looked at these studies, but as I
5 remember there were cerebral palsy like effects that
6 they found. You've read the article more recently
7 than I have.

8 There was certainly without any question
9 central nervous effects on young children and children
10 that were born.

11 Q Do these clinical effects resemble autism?

12 A Since I wasn't there and did not examine the
13 children or wasn't there when a physician examined
14 them, I just don't feel comfortable answering that
15 question one way or the other. I would be guessing at
16 it.

17 Q Could you clarify your opinion as it relates
18 to the thimerosal-containing vaccines we're discussing
19 today? Does dose matter in these cases whether
20 thimerosal-containing vaccines cause autism?

21 A Certainly when you consider that a child
22 over a short period of time relatively, it's possible
23 for him or her to get 187 micrograms of mercury.

24 That's a large dose for a child who has a
25 very low body weight so on a per kilogram basis my

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1 scientific assumption, based on the data I have so
2 far, would be that those amounts of thimerosal could
3 cause autism in some children.

4 Q Do you have to get the entire 87.5 (sic)?

5 A Pardon?

6 Q Do you have to get the entire series of
7 shots, the 187.5 micrograms?

8 A I don't know that. Again, it depends upon
9 the susceptibility of the child and the metabolism of
10 the child as to how he or she handles that mercury.

11 When you talk about dose determines the
12 poison as some other people would say, you could also
13 have a child with a small dose or the large dose
14 having the same effect.

15 Q So let's assume that your hypothesis that we
16 have a genetically susceptible child is true. Could
17 12.5 micrograms cause that child to have autism?

18 A If we knew that we would be able to do
19 something, but that specific question in a specific
20 child we don't know the answer to. All we know is
21 there appears to be a relationship between the amount
22 of mercury that children are exposed to via the
23 vaccinations and whether they get autism or not.

24 You heard what was said this morning by the
25 epidemiologist who quite honestly and carefully

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1 debunked many of the epidemiology studies that have
2 been published in the past. It was such a good
3 rendition that I asked him to write a paper just on
4 what he said.

5 Q But you don't know the dose it would
6 require?

7 A Pardon?

8 Q You don't know the dose of ethyl mercury it
9 would require for a child to have autism?

10 A No. I don't think anyone does because each
11 child also would be quite different in his response or
12 her response and there's tremendous variation.

13 MS. RENZI: I'll just have 10 more minutes
14 of questions. Would that be okay?

15 SPECIAL MASTER HASTINGS: All right.

16 BY MS. RENZI:

17 Q Dr. Aposhian, you did not speak about this
18 today, but it is contained in your report, and I would
19 like to discuss some of the aspects of your report.

20 A Which? Today's report?

21 Q The report that you filed for the Court --

22 A Yes.

23 Q -- that we believed was going to be your
24 testimony today.

25 A Do you think I could have a copy?

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1 Q Sure.

2 A Thank you. Thank you very much.

3 SPECIAL MASTER HASTINGS: For the record,
4 that's Exhibit 25, I believe.

5 MS. RENZI: I think it's Exhibit 19.

6 SPECIAL MASTER HASTINGS: Dr. Aposhian's
7 report? Okay. Exhibit 19.

8 BY MS. RENZI:

9 Q Dr. Aposhian, on pages 6 and 7 of your
10 report you discuss four factors that you believe can
11 cause someone to be more susceptible to mercury. Do
12 you have that?

13 A I have the page. Beginning on page 6, No.
14 I, at the bottom.

15 Q Do you mean when you say susceptible to
16 mercury, mercury toxicity?

17 A Pardon?

18 Q When you say susceptible to mercury do you
19 mean mercury toxicity?

20 A I'm sorry. I can't understand you.

21 Q What do you mean by susceptible to mercury?

22 A I don't see the word susceptible at all on
23 this page, on page 6. I've looked for it. In the
24 bottom part that's typed I don't see the word
25 susceptible at all.

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1 Q Okay. We'll call them then factors of
2 vulnerability.

3 A Where are we?

4 Q We won't say susceptibility.

5 A Where are you?

6 Q I'm on page 6.

7 A All right. Many other factors are involved
8 in the vulnerability.

9 Q Okay. I apologize. It was vulnerability.
10 not susceptibility.

11 A Your apology is accepted.

12 Q The first of these four factors of
13 vulnerability that you say --

14 A Could you speak into the microphone? Thank
15 you.

16 Q The first factor that you say increases
17 someone's vulnerability to mercury. Actually, let's
18 go back. Could you define vulnerability to mercury?
19 What do you mean by that?

20 A You're asking me to define the word
21 vulnerability? Is that correct?

22 Q Vulnerability to mercury.

23 A Yes.

24 Q The phrase that you used. Do you mean
25 mercury toxicity? What do you mean?

APOSHIAN - CROSS

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1 A I mean their response to mercury. Their
2 vulnerability to mercury would be their response to
3 mercury.

4 Q And what would the response to mercury be?
5 Would it be a toxic response?

6 A There's wide variation. In some people
7 there would be high levels of mercury in the blood or
8 high levels of mercury in the urine or high levels of
9 mercury in the hair, or some people would have,
10 depending on which species, a tremor.

11 There are all sorts of signs of the
12 vulnerability of an individual to mercury, depending
13 on what the species of mercury is also.

14 Q Okay. The first factor you say increases
15 one's vulnerability to mercury is antibiotics, and
16 that's on page 6 of your report.

17 A Yes. Antibiotics being used when mercury
18 exposure occurs can inhibit mercury excretion and then
19 potentially increase its toxicity.

20 Q And you're referring to the Roland study?
21 Is that correct?

22 A I'm really referring to -- I should have put
23 this down -- Ann Summers at I think it's either the
24 University of Georgia or Georgia State. I don't
25 remember. She went there from Mass General where she

APOSHIAN - CROSS

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1 had a very distinguished career.

2 She has published many papers that show that
3 not only exposure to mercury, but the number of
4 amalgams in your mouth, can affect the amount of
5 mercury that -- I'm sorry. The antibiotics can affect
6 the amount of mercury you're excreting.

7 I think that's in good peer reviewed
8 journals. I want to say proceedings in the National
9 Academy of Science, but I'm not even sure which
10 journal.

11 Q But that's not what you relied on in your
12 report for this?

13 A Again, I'm sorry to bring up a personal
14 matter. This report was written at a time in my life
15 where I could not spend as much time as I usually do.

16 This report was written between 4 a.m. and
17 6 a.m. every morning and so there are shortcomings. I
18 take that responsibility and I apologize to the Court
19 for it.

20 Q Can I just ask you a question? Is the
21 Roland study that you rely on no longer valid? Is
22 that what you're saying?

23 A No, I'm not saying that. I'm saying that
24 there have been more studies since Roland, namely Ann
25 Summers and probably also Fritz Lorscheider. There

APOSHIAN - CROSS

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1 have been other studies that have proven the same
2 thing; that antibiotics will decrease the excretion of
3 mercury.

4 Q And you said with dental amalgams?

5 A Pardon?

6 Q With dental amalgams?

7 A With or without dental amalgams. Wherever
8 the mercury comes from. In many experimental systems
9 they expose them to mercury vapor, and there have been
10 human studies I believe that show the same thing.

11 Q Now, the Roland study was a rat study. Is
12 that correct? A rodent study?

13 A I don't remember the Roland study now. I
14 would suspect it was a rat study, but I'm not
15 positive.

16 Q You don't know the doses of methyl mercury
17 that were administered?

18 A Definitely not. It's things like that you
19 can look up and read in the paper. I don't believe in
20 memorizing things like that.

21 Q We can hand you the paper.

22 A Sure.

23 Q Because I do have some questions on that.

24 A Sure.

25 (Pause.)

APOSHIAN - CROSS

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1 A Thank you. Do you want this one back, or
2 should I keep this one? Thank you.

3 Now, we're looking on The Effects of Diet on
4 Mercury Metabolism and Excretion of Mice Given Methyl
5 Mercury, so it's mice and not rats.

6 Q Okay. Mice.

7 A Thank you for bringing that to my attention.

8 Q On the top of page 402 --

9 A Page 402.

10 Q And we can highlight that. We can put it
11 right up on the screen for you.

12 A I'm on 402, but I don't know what you just
13 said. I'm on page 402.

14 SPECIAL MASTER HASTINGS: Doctor, she has it
15 on the screen.

16 THE WITNESS: Oh, I'm sorry.

17 SPECIAL MASTER HASTINGS: That may be easier
18 for you.

19 THE WITNESS: Much easier. Thank you.

20 BY MS. RENZI:

21 Q Would you agree that the dose was .6
22 milligrams of mercury per kilogram?

23 A All right.

24 Q And wouldn't the dose of mercury be
25 equivalent to 600 micrograms per kilogram of body

APOSHIAN - CROSS

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1 weight?

2 A Six hundred milligrams of mercury per
3 kilogram of body weight. Is that what you asked?
4 Yes.

5 Q And that 600 micrograms per kilogram of body
6 weight would be equal to a 6,000 microgram dose in a
7 10 kilogram child. Is that correct?

8 A Well, they're talking about mice here. I'm
9 not certain that you can just transpose a mouse dose
10 to a human dose that quickly just by changing the
11 weight, so I don't know what your point is.

12 Q My point is the doses are not comparable.
13 Are those doses comparable to the amount of ethyl
14 mercury contained in a thimerosal-containing vaccine?

15 A I don't claim the doses are comparable. I
16 don't claim that's so.

17 Q But you said in your report that based on
18 the Roland paper high doses of methyl mercury in mice
19 inhibit the excretion.

20 A What page are we on now?

21 Q I'm sorry. You said that based on the
22 Roland study that high doses of antibiotics --

23 A What I say, if you're talking about page 6,
24 let's quote it correctly. Antibiotics being used when
25 mercury exposure occurs can inhibit mercury excretion

APOSHIAN - CROSS

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1 and thus potentially increase its toxicity.

2 Q Right. But even with the administration of
3 antibiotics, weren't the doses administered to the
4 mice in this study much larger than the doses that are
5 contained --

6 A I make no claim about dosage in this. All
7 I'm saying -- and I quote the Roland paper here,
8 whatever doses they're uses. That antibiotics being
9 used when mercury exposure occurs can inhibit mercury
10 excretion and thus potentially increase its toxicity.

11 Q So this study has no applicability to what
12 antibiotics can do to a person who's exposed to
13 thimerosal through a thimerosal-containing vaccine?

14 A I think what you've got to understand is
15 science changes. Sometimes it changes the way you
16 want it to change, whether it's you or me, and
17 sometimes it changes a different way. In this case
18 these studies showed that mercury excretion was
19 inhibited by giving an antibiotic.

20 Now, I'm on very weak ground with the
21 following statement, all right? I wish I had known
22 you would ask this. I would have been certain. There
23 may even be some --

24 Q It was in your report.

25 A Pardon?

APOSHIAN - CROSS

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1 Q It was in your report.

2 A No, no. Whether it's in my report or not
3 doesn't matter. I just didn't realize I had to be
4 prepared for this.

5 What I'm trying to say is there may be a
6 study in humans by Ann Summers -- in fact, I'll make a
7 point of calling her tomorrow. Either Ann or someone
8 else did some studies I think showing that when humans
9 were given antibiotics that there was a decrease in
10 mercury excretion. That statement is usually accepted
11 by most toxicologists today.

12 Q Of methyl mercury or ethyl mercury?

13 A I'm just talking about whatever mercury they
14 were using at the time. I don't remember. I'm
15 certain they didn't give methyl mercury to humans in
16 experimental situations to prove that.

17 My guess is they gave it to probably humans
18 that were ill. They gave them an antibiotic, and they
19 also did a fecal excretion and a urinary excretion of
20 mercury -- that's what my guess is -- and probably
21 related it to their mercury exposure. I'm not
22 positive of that, but that's what comes up in the back
23 of my mind.

24 Q So you're not sure?

25 A I'm not sure. I'm telling you the truth

APOSHIAN - CROSS

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1 when I say I'm not certain.

2 Q Now the second factor you list on page 6 of
3 your report. The second factor.

4 A Yes?

5 Q You state a factor may include one's
6 vulnerability. One factor is a combination of genetic
7 predisposition and a stress such as fever may increase
8 the impact of the stress causing agent, and you cite
9 Morton.

10 A And what's your question?

11 Q The Morton article is entitled The Genetic
12 Epidemiology of Hearing Impairment. We can hand you
13 that article if you would like to see it.

14 A You brought up a very good point. I'll go
15 back and see what the story is. It seems ridiculous
16 for me -- no abstract available. It's also possible I
17 have that in my library at home.

18 Q We have that article.

19 A I can't answer any more.

20 Q We have that article. I have it.

21 A Oh, is it in there? Can I see that? Thank
22 you. Is it mentioned? I'll take your word for it.

23 Is it mentioned?

24 Q Well, my question to you is you mentioned
25 the article in your report.

APOSHIAN - CROSS

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1 A Yes, but what I'm asking you is do they
2 mention stress and mercury in this report?

3 Q They make no reference to mercury.

4 A Then my guess is that it was a mistake and
5 it should have been the Mutter paper immediately
6 thereafter because the Mutter paper comments on the
7 article, The Toxicology of Mercury and its Chemical
8 Compounds, or another.

9 I don't know. You have a good point. I
10 concede that point to you.

11 Q So can you cite to a peer reviewed article
12 on the combination of genetic susceptibility and a
13 stress with regards to thimerosal in autism? So a
14 genetic susceptibility, stress, thimerosal leading to
15 autism? Is that the article you did not --

16 A You're talking about No. 3? Is that what
17 you're talking about?

18 Q Right. Can you cite to a peer reviewed
19 article about a combination of genetic susceptibility
20 and stress with regard to thimerosal and autism?

21 A Now, what is your question?

22 Q Can you cite to a peer reviewed article?
23 You said that Morton doesn't apply in this case,
24 correct?

25 SPECIAL MASTER HASTINGS: Doctor, she's

APOSHIAN - CROSS

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1 still on Point 2 at the bottom of page 6.

2 THE WITNESS: I'm at that point, and I don't
3 understand what your question is. I can read the --

4 BY MS. RENZI:

5 Q Okay. If the Morton article doesn't apply,
6 which you just said the Morton article should not have
7 been cited, correct?

8 A You're absolutely correct.

9 Q Okay.

10 A I'm certainly not perfect.

11 Q Okay. Can you cite though to a peer
12 reviewed paper that discusses the combination of
13 genetic susceptibility and stress with regard to
14 thimerosal causing autism?

15 A I'm not certain. Let me just check one
16 thing. All these points refer not to autism, but they
17 refer to the once accepted toxicology axiom that dose
18 determines the poison.

19 Nowhere in that first paragraph on page 6 or
20 on the second or under (1) or (2) do I see the word
21 thimerosal or autism, so I don't understand what the
22 point is, ma'am. I don't mean to be rude. I just
23 don't understand.

24 Q Sir, you put these in your report about what
25 makes people more vulnerable to mercury, and I just

APOSHIAN - CROSS

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1 want to go over this for the basis --

2 A But I don't say anything about thimerosal,
3 and I don't say anything about autism here.

4 Q So these don't apply to thimerosal-
5 containing vaccines?

6 A I don't know that. I'd have to think more
7 about that. I think that these are generally accepted
8 beliefs about the vulnerability of people to mercury.
9 Antibiotics are generally now considered to inhibit
10 mercury excretion.

11 Certainly many people accept the idea that
12 there's a genetic predisposition to mercury toxicity,
13 I think the effects of mercury, and there are a number
14 of papers that prove that now.

15 I haven't said anything about thimerosal and
16 autism in these lines that you're quoting.

17 Q The Palmer study.

18 A Okay. Let's go to the Palmer study. This
19 study has been criticized probably quite well since
20 this paper was published.

21 I'm not even sure. Again, it's been a long
22 time. I'm not even sure they measured the mercury in
23 the air. I just don't remember this paper well
24 enough. If you have that paper I'd love to have it.

25 Q Why did you cite the Palmer study?

APOSHIAN - CROSS

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1 A Pardon?

2 Q Why did you cite the Palmer study?

3 A The Palmer study was cited because, as it
4 says here someplace: The association between an
5 environmentally related mercury, special education and
6 autism rates in Texas was investigated using data from
7 the Texas Education Department and the United States
8 EPA.

9 There was a significant increase in the
10 rates of special education students and autism rates
11 associated with increases in environmentally released
12 mercury. On the average, for each 1,000 pounds of
13 environmentally released mercury there was a 43
14 percent increase in the rate of special education
15 services and a 61 percent increase in the rate of
16 autism.

17 Now, this study has been criticized, and
18 just again it's been so long since I read this
19 article. I don't remember all the criticisms, but the
20 study has been criticized I think for -- I don't
21 remember whether they themselves did the mercury
22 determinations or if any mercury determinations were
23 actually done.

24 Q Doctor, is it your opinion that mercury in
25 the air causes autism?

APOSHIAN - CROSS

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1 A No, but that's not the only exposure that a
2 person may have or a child may have or a mother, a
3 pregnant woman, may have for mercury. It's not just
4 mercury in the air.

5 I think in my slides today I made it very
6 clear that exposure of humans to mercury in the air is
7 not very important.

8 Q The fourth factor that you list in your
9 report --

10 A Let me check the reference first to be
11 certain it's correct. Yes.

12 Q Okay.

13 A This is an excellent book from the new
14 Norberg group. Yes.

15 Q But the fourth factor you say plays a role
16 in someone's vulnerability to poisons is diet. Is
17 that correct? That's on page 7 of your report.

18 A Yes, one of the points.

19 Q And you state in your report that glutamine
20 is low in autistic children. Is that correct?

21 A I guess that's what I say.

22 Q What studies do you rely on for the
23 proposition that glutamine levels are lower in
24 autistic children?

25 A I would suggest -- it's not a very good

APOSHIAN - CROSS

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1 reference -- that the new Norberg text, which is an
2 excellent text that I recommend to anyone who's
3 interested in metals.

4 It was just published in 2007, and there are
5 chapters in there about glutamine, metals and autistic
6 children, as I remember. It's a chapter in the
7 Norberg book. I did not realize before that I did not
8 put the page number down.

9 Q You state on page 7 in your report that
10 glutamine is a precursor of glutathione.

11 A Glutathione is glutamyl, cysteinyl and I've
12 forgotten the other amino acid, but glutamic acid
13 certainly is part of glutathione.

14 Q Is it a direct precursor?

15 A Pardon?

16 Q It's not a direct precursor as you state in
17 your report, is it, sir?

18 A In order to make glutathione, you have to
19 have glutamyl cysteine is one of the precursors. In
20 order to make glutamyl cysteine, you have to have
21 glutamic acid.

22 Q What's the basis for your opinion on that?

23 A Pardon?

24 Q What is the basis for that?

25 A Go to any basic biochemistry textbook.

APOSHIAN - CROSS

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1 Q Well, we're going to pull up the Jill James
2 paper, and that's Jill James 205. It's Petitioners'
3 Master List 7.

4 We'll see from the homocysteine down to the
5 glutathione. I don't see glutamine on there. Is
6 glutamine a precursor to glutathione?

7 A But this is not the only way of making
8 glutathione in the cell. If you look at the structure
9 -- you must have someplace the structure, the chemical
10 formula for glutathione. You'll see glutamyl,
11 cysteinyl, glycine. I think that's what it is. Here
12 we have cystathiomine. We have the cysteine. Let's
13 see.

14 There are other pathways. This is not the
15 only pathway for making glutathione. If you go to an
16 elementary textbook of medical biochemistry you'll
17 find three or four different pathways.

18 Q Assuming glutamine levels are low, are
19 glutamine concentrations rate limiting in glutathione
20 synthesis?

21 A I don't know.

22 Q So the concentration in glutamine doesn't
23 determine the synthesis of glutathione? You don't
24 know?

25 A I don't know.

APOSHIAN - CROSS

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1 Q How much lower are the levels of glutathione
2 in autistic children compared to nonautistic children?

3 A Say that again.

4 Q How much lower are the levels of glutathione
5 in autistic children compared to nonautistic children?

6 A You have a copy of the Jill James paper.
7 It's in there.

8 Q You don't know off the top of your head?
9 No? Okay. That's fine.

10 A The Jill James paper published probably last
11 year or the year before.

12 Q Do you know how low levels of glutathione or
13 glutamine have to be in order to inhibit the excretion
14 of 25 micrograms of ethyl mercury?

15 A I have no idea. I have no idea.

16 Q Does the body have mechanisms other than
17 glutathione to bind to, transport and eliminate ethyl
18 mercury?

19 A If you read Clarkson's articles, which are
20 good review articles on the whole, I think you'll see
21 that the glutathione is considered to be the major
22 pathway.

23 Certainly to get mercury, methyl mercury
24 included, into the bile and into the feces it usually
25 is combined with glutathione as one of the carrier

APOSHIAN - CROSS

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1 mechanisms. It may also be combined with glutathione
2 tied up with other proteins, but they don't know that
3 yet.

4 Q But there are other mechanisms? Is that
5 correct?

6 A There are other mechanisms.

7 Q Could you list some of those mechanisms?

8 A Excuse me?

9 Q Could you list a few of the mechanisms?

10 A No.

11 Q I'll list some, and if you could tell me if
12 I'm correct?

13 A Pardon?

14 Q Would selenium be one thing in the body --

15 A What about selenium?

16 Q -- that would help transport, eliminate and
17 bind to heavy metals such as ethyl mercury?

18 A Now you're getting into a very difficult
19 area because you're going to ask a specific question,
20 so let me ask a specific question if I may that maybe
21 you'd like.

22 Does selenium have anything to do with the
23 excretion of mercury? Off the top of my head I would
24 say no. Does selenium have anything to do with the
25 detoxification of mercury? If you believe most of the

APOSHIAN - CROSS

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1 people who dabble in this sort of thing, they will say
2 that mercury is very reactive with selenium, and a
3 mercury selenide is formed, as I think I mentioned in
4 my testimony.

5 This mercury selenium or mercury selenide is
6 very, very insoluble. I doubt very much. I don't
7 know what the data is, but I doubt very much that
8 mercury selenide comes out in the body as such because
9 it is so insoluble.

10 Does that answer your question at all? I
11 don't want to make things difficult, I assure you.

12 Q That answers my question. I have another
13 question for you.

14 A All right.

15 Q Is metallothionein something in the body
16 that binds, transports and eliminates heavy metals
17 such as ethyl mercury?

18 A Let's first deal with simple mercuric ions,
19 all right? There's no question that mercuric ions
20 have an affinity for metallothionein. Metallothionein
21 is a protein of which I think one-third of the amino
22 acids are cysteines, CYSH, three sulphhydryl groups.

23 Metallothionein is used in the body as a
24 mechanism, number one, for inactivating cadmium.
25 Another metal may be lead and mercuric mercury is one

APOSHIAN - CROSS

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1 of them. I think methyl mercury forms a different
2 complex with metallothionein, and I'm not certain what
3 people feel is the significance of that as far as the
4 excretion.

5 Certainly metallothionein is known to
6 transport certain metals from the liver to the kidney,
7 but whether it does that with mercury I don't
8 remember. It is not considered to be a major pathway.

9 Q I want to move back to glutathione. Does
10 glutathione protect against mercury? Does glutathione
11 only protect against mercury, or does it protect and
12 aid in detoxifying other substances?

13 A The concentration of glutathione in your
14 liver cells is 10 millimole. I mean, that's a lot of
15 glutathione, a tremendous amount of glutathione. It
16 is one of the major detoxifying agents in the body,
17 all right?

18 Does it detoxify other agents? Absolutely.
19 Not only metals, but many other agents. Glutathione
20 is one of the major endogenous detoxifying agents that
21 we have. Ten millimole is no small amount.

22 Q It's a huge amount. Is that correct?

23 A It's huge.

24 Q So if the levels of glutathione are so low
25 as to cause --

APOSHIAN - CROSS

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1 A So low?

2 Q So low hypothetically. If your levels of
3 glutathione are so low that you cannot detoxify the
4 amount of ethyl mercury in a mercury-containing
5 vaccine, how could you detoxify any other substance in
6 your body?

7 A Who says the glutathione level is so low
8 that it cannot detoxify things? I don't know.

9 What you must say is the glutathione level
10 in the plasma is very low. You're quoting Jill James
11 or you're referring to Jill James' work. She did not
12 do liver glutathiones. She did not do brain
13 glutathiones. She did red cell. No, she didn't even
14 do red cell glutathione.

15 She studied plasmic glutathione, and, as I
16 and everyone else have told her, plasma does not have
17 a high level of glutathione. Most glutathione is an
18 intracellular compound. Very little glutathione is
19 found extracellularly. I don't know whether that
20 helps you or not.

21 Q No. It helps me. Thank you.

22 A Thank you.

23 MS. RENZI: I think that I'll break here for
24 today.

25 SPECIAL MASTER HASTINGS: All right. Thank

APOSHIAN - CROSS

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1 you.

2 MS. RENZI: Thank you, Special Master.

3 SPECIAL MASTER HASTINGS: Thank you very
4 much.

5 MS. RENZI: Thank you, Dr. Aposhian.

6 SPECIAL MASTER HASTINGS: Dr. Aposhian,
7 thank you. You're done for the day, but we'll start
8 with you again at 9 a.m. tomorrow morning.

9 THE WITNESS: Okay. Thank you.

10 SPECIAL MASTER HASTINGS: Counsel, before we
11 go off the record is there anything we should talk
12 about before we break for the day?

13 MR. MATANOSKI: Not on the record, sir.

14 MR. POWERS: Nothing for Petitioners.

15 SPECIAL MASTER HASTINGS: Okay. We are done
16 for the record for today for those listening at home.
17 We will start again at 9 a.m. Eastern time tomorrow
18 morning. Thank you all.

19 (Whereupon, at 5:40 p.m., the hearing in the
20 above-entitled matter was adjourned, to reconvene at
21 9:00 a.m. on Tuesday, May 13, 2008.)

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24 //

25 //

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REPORTER'S CERTIFICATE

DOCKET NO.: 03-584-V, 03-215V
CASE TITLE: In Re: Claims for Autism
HEARING DATE: May 12, 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 12, 2008

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