

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. MEAD,)
A MINOR,)

Petitioners,)

v.)

Docket No. 03-215V)

SECRETARY OF HEALTH AND)
HUMAN SERVICES,)

Respondent.)

Pages: 2146 through 2275/2345

Place: Washington, D.C.

Date: May 20, 2008

HERITAGE REPORTING CORPORATION

Official Reporters

1220 L Street, N.W., Suite 600

Washington, D.C. 20005-4018

(202) 628-4888

hrc@concentric.net

IN THE UNITED STATES COURT OF FEDERAL CLAIMS

IN RE: CLAIMS FOR VACCINE)
INJURIES RESULTING IN)
AUTISM SPECTRUM DISORDER,)
OR A SIMILAR)
NEURODEVELOPMENTAL)
DISORDER)
-----)

FRED AND MYLINDA KING,)
PARENTS OF JORDAN KING,)
A MINOR,)

Petitioners,)

v.)

Docket No.: 03-584V

SECRETARY OF HEALTH AND)
HUMAN SERVICES,)

Respondent.)
-----)

GEORGE AND VICTORIA MEAD,)
PARENTS OF WILLIAM P. MEAD,)
A MINOR,)

Petitioners,)

v.)

Docket No. 03-215V

SECRETARY OF HEALTH AND)
HUMAN SERVICES,)

Respondent.)

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

Tuesday,
May 20, 2008

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

2147

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

APPEARANCES:

For the Petitioners:

THOMAS B. POWERS, Esquire
MICHAEL L. WILLIAMS, Esquire
Williams Love O'Leary & Powers, P.C.
9755 S.W. Barnes Road, Suite 450
Portland, Oregon 97225-6681
(503) 295-2924

For the Respondent:

VINCE MATANOSKI, Esquire
LINDA RENZI, Esquire
ALEXIS BABCOCK, Esquire
U.S. Department of Justice
Civil Division, Torts Branch
Ben Franklin Station, P.O. Box 146
Washington, D.C. 20044-0146
(202) 616-4356

2148

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 Respondent:</u>					
L. Jackson Roberts	2153	2187	2195	--	--
Jeff Johnson	2198	2248	2262	--	--

E X H I B I T S

RESPONDENT'S <u>EXHIBITS:</u>	<u>IDENTIFIED</u>	<u>RECEIVED</u>	<u>DESCRIPTION</u>
6	2154	--	L. Jackson Roberts, II slide presentation
7	2197	--	Jeff Johnson slide presentation

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

P R O C E E D I N G S

(9:00 a.m.)

SPECIAL MASTER HASTINGS: Good morning to all. We're here for another day of proceedings in the omnibus autism proceeding, Theory II trial. We've got a couple of matters to talk about, at least one before we go on the record.

(Discussion held off the record.)

SPECIAL MASTER HASTINGS: We have a housekeeping matter that we need to take care of. As you heard the other day, we had some presentations by both parties about how to handle the rebuttal evidence in this case and the issue of how to handle the testimony in the third case and the rebuttal.

Last evening, after the close of proceedings on the record, we did have additional discussion of that. Both counsel for both parties made presentations on that and we discussed it, and Special Master Vowell is going to explain our ruling on those issues.

SPECIAL MASTER VOWELL: Okay. Essentially, our ruling is this. We've asked the Respondent to continue presenting its case in chief on both the Theory A and Theory B of Theory II, the second theory of causation, to put on all of their witnesses now

1 with the exception of the two that we've already
2 discussed. Drs. Clarkson and Magos were not available
3 until July.

4 Petitioner will put on their rebuttal case
5 in this coming week and a half at the conclusion of
6 the government's case to what they've already heard
7 from the government. We are scheduled to have further
8 proceedings then on the Theory II omnibus matters, the
9 general causation matters, and to hear the third test
10 case case-specific information in the third week of
11 July.

12 We will allot two days to testimony on the
13 specific new test case, two days to the government to
14 present the two toxicologists, and whatever is left of
15 the second day that Petitioners have or the beginning
16 of the third day to hear their case-specific. I
17 assume pediatric neurologist, whether it's Dr. Rust or
18 someone else.

19 Friday will be reserved to the Petitioners
20 to provide rebuttal to Drs. Clarkson and Magos, but we
21 will strictly enforce that it has to be rebutting what
22 Drs. Clarkson and Magos testified to, not the gamut of
23 what we've heard or what we will hear in the next week
24 and a half.

25 Does that comport with my recitation of the

1 ruling last evening?

2 MR. POWERS: From Petitioners, that's an
3 accurate recitation, Special Master.

4 SPECIAL MASTER VOWELL: And, Mr. Matanoski,
5 you looked a little confused.

6 MR. MATANOSKI: No, ma'am. Actually, that
7 comports exactly with what I understood the ruling to
8 be when we spoke last evening. I just wanted to, for
9 the record, as far as in another proceeding earlier in
10 this omnibus trial, we had rebuttal close at the end
11 of that proceeding and then there were some written
12 submissions thereafter.

13 I just wanted to make sure that that's not
14 the process that we're adopting here today, but
15 rather, in this process the rebuttal is going to end
16 at the end of this trial.

17 SPECIAL MASTER VOWELL: That is my fervent
18 hope, Mr. Matanoski.

19 MR. MATANOSKI: Thank you.

20 SPECIAL MASTER HASTINGS: All right. Well,
21 with that matter having been discussed, I guess it's
22 time to go to the next government witness. Mr.
23 Matanoski?

24 MR. MATANOSKI: Thank you. At this time,
25 the government is going to call Dr. Jackson Roberts.

ROBERTS - DIRECT

2153

1 SPECIAL MASTER HASTINGS: Dr. Roberts,
2 please have a seat, and we'll ask you to raise your
3 right hand, please.

4 Whereupon,

5 L. JACKSON ROBERTS, II

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

8 SPECIAL MASTER HASTINGS: Please go ahead,
9 Ms. Renzi.

10 MS. RENZI: Thank you. Good morning.

11 DIRECT EXAMINATION

12 BY MS. RENZI:

13 Q Good morning, Dr. Roberts.

14 A Good morning.

15 Q Could you please state your name for the
16 record?

17 A L. Jackson Roberts, II, M.D.

18 SPECIAL MASTER HASTINGS: All right. Dr.
19 Roberts, we wondered if you could, to the extent
20 possible, sit to your right there, please? Don't go
21 off the edge of the podium there, but it would be
22 easier for us to see you. And do keep your voice up
23 so we can hear you.

24 THE WITNESS: Can you hear me now?

25 SPECIAL MASTER HASTINGS: Ms. Renzi, go

ROBERTS - DIRECT

2154

1 ahead.

2 MS. RENZI: I think you're fine.

3 THE WITNESS: Okay.

4 SPECIAL MASTER HASTINGS: Now, I notice that
5 we've just been given a handout to go with Dr.
6 Roberts' testimony. We should mark that, I assume, as
7 Respondent's Trial Exhibit 6, Ms. Renzi?

8 MS. RENZI: Yes.

9 SPECIAL MASTER HASTINGS: All right.

10 (The document referred to was
11 marked for identification as
12 Respondent's Trial Exhibit
13 No. 6.)

14 BY MS. RENZI:

15 Q Dr. Roberts, could you briefly describe your
16 educational background starting with your Bachelor's
17 degree?

18 A I got a B.A. degree from Cornell College in
19 1969, and then I went on to the University of Iowa
20 where I got an M.D. degree. I subsequently went on to
21 Washington University in St. Louis where I did
22 internal medicine residency and was board-certified in
23 internal medicine.

24 And then I went to Vanderbilt University to
25 take a fellowship in clinical pharmacology where I've

ROBERTS - DIRECT

2155

1 remained since.

2 Q When did you become a full professor at
3 Vanderbilt?

4 A I think it was around 1986.

5 Q And then in 2006 you became a T. Edwin
6 Rogers Professor of Pharmacology. Could you please
7 explain what that is?

8 A That's an endowed chair that was given to me
9 by the university. Endowed chairs give money to
10 particular professors who had a long track record of
11 accomplishments to give them some latitude, so it's a
12 very prestigious thing.

13 SPECIAL MASTER HASTINGS: Dr. Roberts, if
14 you could do your best to speak up.

15 THE WITNESS: Okay.

16 SPECIAL MASTER HASTINGS: Perhaps a little
17 slower, too. We're having a little tough difficulty
18 hearing you. Speak up as loud as you can, please.

19 THE WITNESS: Okay.

20 BY MS. RENZI:

21 Q And, Dr. Roberts, I'm going to put on the
22 screen, it's right there in front of you, a portion of
23 your curriculum vitae that was filed as Respondent's
24 Exhibit DD, and this section is called the academic
25 and professional honors. Could you please describe

ROBERTS - DIRECT

2156

1 your awards?

2 (Away from microphone.)

3 A Well, when I was in medical school I was
4 elected in Alpha Omega Alpha, which is AOA, Society,
5 which is like Phi Beta Kappa in normal universities.
6 In 1983, I received the Burles Open Scholar award in
7 clinical pharmacology, and then in 2001 I received a
8 Sidney Kolowick faculty research award from
9 Vanderbilt.

10 Then I was elected to two of the sort of
11 prestigious societies in medicine, and you have to be
12 elected, which is the American Society for Clinical
13 Investigation and Association of American Physicians.
14 2001 I received a merit award from the National
15 Institutes of Health. That's a very, very prestigious
16 award.

17 They only give out a few of those, and they
18 give them out to certain scientists who have had a
19 long track record of very successful funding and
20 accomplishments to allow them normal research grants.
21 The maximum you can have is five years, so this goes
22 for 10 years and it doesn't have to be renewed after
23 five years, you just tell them what you're going to
24 do.

25 So they're putting their confidence that

ROBERTS - DIRECT

2157

1 because of your track record they give you this
2 latitude for 10 years of funding. Then in 2006 I got
3 the Discovery award from the Society for Free Radical
4 Biology in Medicine. This is basically for our
5 discovery, which I think we'll talk about a little bit
6 later, compounds of liquid oxidation called
7 isoprostanes.

8 Then the same year I received the Earl
9 Sutherland prize for achievement in research in
10 Vanderbilt University. This is not just a medical
11 school competition, it's universitywide. It's a very,
12 very prestigious award. Then we talked about
13 receiving the T. Edwin Rogers chair in pharmacology.

14 Then last year I also received a
15 distinguished alumni award from the University of Iowa
16 School of Medicine.

17 Q Thank you. And, Dr. Roberts, do you
18 currently sit on any editorial boards?

19 A I'm associate editor of the journal called
20 *Free Radical Biology in Medicine*.

21 Q And what are your duties as the associate
22 editor?

23 A Well, journals have editorial boards,
24 particular individuals who will usually agree to
25 review papers. The editors sort of sit above the

ROBERTS - DIRECT

2158

1 editorial boards. When somebody submits a paper for
2 publication it comes in to the journal, and it's
3 assigned to, I think we have four associate editors,
4 one of the associate editors.

5 So it comes to me, I take a look at it, I
6 decide a couple of very excellent potential reviewers
7 to review this paper, including myself looking at the
8 paper, we send it out for review, we get the reviews
9 back from experts, I look at those reviews and my
10 opinion about the paper and I make the ultimate
11 decision whether this paper should be published or
12 rejected.

13 Q Now, Dr. Roberts, we're going to show you a
14 slide up on the screen. This is Slide 2, and it's a
15 list of your current funding and grants. Could you
16 please go through those?

17 A The first grant is a very large grant that's
18 been going on in our division with Jason Morrow, who
19 is head of our division. He's the principal
20 investigator. You know, it's been going on for about
21 25, 28 years now I believe. So there's multiple
22 investigators involved in this and I have one project
23 in that.

24 The next grant, that 5R37 GM40256, that's my
25 merit award, which I've already discussed. The next

ROBERTS - DIRECT

2159

1 one is a grant from National Institute of Aging and
2 that's another grant where I'm principal investigator
3 in that. I'm dealing with investigating the role of
4 oxidative injury in Alzheimer's disease.

5 The third one I'm also principal
6 investigator on and that involves investigating the
7 role of oxidative damage in cardiac arrhythmias. The
8 last two are just grants from other people in which
9 I'm sort of a coinvestigator on.

10 Q And the amounts on that funding chart, are
11 those annual amounts?

12 A Yes.

13 Q And next to the annual amounts we see 1.2
14 calendar months, six calendar months. What do those
15 numbers represent?

16 A Those are sort of if you add up, for
17 example, if you look at the second one, six calendar
18 months means that I'm spending half of my time a year
19 on that grant and then it's split up by 1.2, et
20 cetera, et cetera, et cetera.

21 Q Okay. And do you run a lab at Vanderbilt?

22 A Yeah.

23 Q And do you supervise people in your lab?

24 A Yes.

25 Q How many?

ROBERTS - DIRECT

2160

1 A I've got four research assistants, I'm also
2 mentoring a junior faculty member and one Ph.D.
3 student.

4 Q You also hold several patents, which are
5 listed on pages 6 and 7 of your CV. I think we're
6 going to bring up another slide, which is Slide 3.
7 Could you briefly describe just the patents that are
8 related or relevant to your testimony today?

9 A Well, these are all sort of general titles
10 but they all have to do with specific patents related
11 to oxidative stress/injury.

12 Q And, Dr. Roberts, you've published over 340
13 peer-reviewed articles, abstracts and book chapters,
14 is that correct?

15 A Correct.

16 Q And of these papers and book chapters,
17 approximately 180 are in the area of oxidative stress?

18 A Correct.

19 Q And since 1990 have all your papers been or
20 almost all your papers been in the area of oxidative
21 stress?

22 A Correct.

23 Q And do you give presentations on the topic
24 of oxidative stress and oxidative injury?

25 A Many.

ROBERTS - DIRECT

2161

1 Q Could you just describe where you've been
2 asked to present?

3 A I've been asked to present at several
4 international meetings regarding oxidative stress.
5 About four years ago I was also the keynote speaker on
6 the first European workshop on isoprostanes, which is
7 in France. We have annual meetings for the Society of
8 Free Radical Biology in Medicine. I've presented
9 there numerous times.

10 Q Now, prior to you exclusively studying
11 oxidative stress, your research focused primarily on
12 prostaglandins. I'd like you just to tell us how your
13 research in prostaglandins led you into the area of
14 oxidative stress.

15 A Well, to describe a prostaglandin though,
16 prostaglandins are small lipid molecules.
17 Prostaglandins are made by the enzyme that's inhibited
18 by drugs, like aspirin. We had discovered that one
19 prostaglandin called prostaglandin D2 is metabolized
20 to prostaglandin, what we call an *F* type ringer,
21 *F* type prostaglandin.

22 For various reasons there should be several
23 different isomers of these. When we were looking and
24 trying to analyze for these, these *F* ring metabolized
25 to prostaglandin D2 by mass spectrometry in normal

ROBERTS - DIRECT

2162

1 humans. The levels consistently, drawing blood from
2 several people in the lab or whatever, were
3 consistently around 30 picograms per ML.

4 We happened to take a plasma from a normal
5 person that had been in our -20 freezer for several
6 months. Of note that at -20 freezer things are not
7 solid ice, and chemical reactions can happen even in
8 the freezer. What we saw with mass spectrometry, we
9 saw the identical same compounds by mass spectrometry
10 but now the levels were in the thousands.

11 This was, what in the world is going on
12 here? And so we were running around the department
13 getting samples from the freezers and they were always
14 in the thousands, but consistently if we drew blood
15 from normal people they were always around 30 or 40
16 picograms.

17 To make a long story short, I even submitted
18 a grant to the NIH with a rational hypothesis to
19 explain this still related to prostaglandins, thinking
20 these were still prostaglandins. That turned out not
21 to be the right hypothesis, but we did figure it out.
22 What we figured out was what was happening in the
23 freezer was simple oxidation of the precursor, which
24 is a lipid arachidonic acid.

25 So we were generating these prostaglandin-

ROBERTS - DIRECT

2163

1 like compounds in the freezer without this
2 psychooxygenase enzyme that normally makes these that
3 drugs, like aspirin, inhibit. So basically this was
4 just a free radical oxidation of the arachidonic acid
5 going on in the freezer.

6 So then the obvious question is is this
7 happening in our body? What we subsequently showed,
8 yes in fact it is. So at that point I sort of looked
9 back on the prostaglandin field, looked ahead in the
10 oxidative free radical field. I said, the free
11 radical field, it looks more interesting and it's
12 probably more relevant to human disease, so I switched
13 fields.

14 Q And during that process is when you
15 discovered the isoprostanes, correct?

16 A That's what these compounds that we termed
17 -- yeah.

18 Q And what has been the impact of your
19 discovery on the area of oxidative stress and the
20 research that has followed?

21 A I think it's been pretty profound in that at
22 the time -- let me get the glass of water. So sort of
23 about the time that we made this discovery, people in
24 the free radical field, a lot of chemists were in the
25 free radical field trying to understand in a test tube

ROBERTS - DIRECT

2164

1 all of these chemical reactions that free radicals can
2 do.

3 It's a lot of elegant chemistry. Then
4 people started asking the question: does this
5 chemistry happen in humans, and is it involved in the
6 pathogenesis of various and sundry human diseases? So
7 people developed certain analytical methods to assess
8 that, and the problem is at the time most of these
9 methods were very unreliable or nonspecific.

10 So there was a problem at that time with
11 translating all of this elegant chemistry to see
12 whether it actually happens in the body, and secondly
13 is that it plays a role in the cause of any human
14 disease.

15 So when we discovered these compounds, these
16 F2 isoprostanes, for the first few years after this
17 discovery it sort of became and it appeared that maybe
18 measuring these compounds appeared to be probably the
19 most reliable way to assess oxidative stress status or
20 oxidative injury in the body.

21 It was about four years ago it was
22 published, so this was then independently confirmed.
23 We actually asked National Institutes of Environmental
24 Health Sciences. They set up an independent sort of
25 study which they called the BOSS study, biomarkers of

ROBERTS - DIRECT

2165

1 oxidative stress status, where essentially they set up
2 a very well-accepted model of very, very, very severe
3 oxidative injury to the liver in vivo.

4 They took samples of liver, et cetera, and
5 plasma and sent these around to investigators all
6 around the country who all had different methods of
7 assays to assess oxidative stress. What came out of
8 that study clearly was that measuring these F2
9 isoprostanes is far and away the most reliable way to
10 assess oxidative stress status.

11 Some of these sort of assays that people had
12 been using, such as what's called the TBARS assay -- I
13 mean, this is a Hiroshima bomb model of oxidative
14 injury, so the F2 isoprostanes in this model go up
15 like 80 fold. Some of these other assays that people
16 had been using, they didn't go up at all and a couple,
17 as I remember, even decreased.

18 So basically I think what this discovery of
19 these F2 isoprostanes was is it really helped move the
20 field from the test tube to what's going on in humans
21 and what's going on. Is oxidative injury really
22 playing a role in human disease?

23 Q Now, doctor, you don't consider yourself to
24 be an expert in mercury toxicity or the diagnosis or
25 treatment of autism, is that correct?

ROBERTS - DIRECT

2166

1 A Right.

2 Q And do you consider yourself to be an expert
3 in the area of oxidative stress and oxidative damage
4 as it relates to various diseases?

5 A Yes.

6 Q Now, in addition to your report filed as
7 Respondent's Exhibit CC, you also listened to the
8 testimony of Dr. Deth that was presented to this Court
9 on May 13?

10 A Yes.

11 Q Now, I want to move on to if you could just
12 explain in simple terms, and we have some slides,
13 about just what oxidative stress is?

14 A Well, we've heard that term so I thought it
15 might be helpful to actually sort of define what is
16 the concept of oxidation. I'll start with just saying
17 molecules are made up of several different atoms.

18 SPECIAL MASTER HASTINGS: Doctor, let me
19 interrupt here.

20 THE WITNESS: Sure.

21 SPECIAL MASTER HASTINGS: I think we're on
22 Slide No. 4 here, so as we go from slide to slide
23 let's record the number. Also, as we get into the
24 substance of your testimony do bear in mind that
25 you're talking to laypeople here. When we get into

ROBERTS - DIRECT

2167

1 difficult terms or terms that laypeople may not
2 understand, make sure you explain them to us.

3 These words that are new to us, pronounce
4 them as precisely as you can so we can understand and
5 follow what's going on. Go ahead, Ms. Renzi.

6 SPECIAL MASTER VOWELL: If I could add to
7 that, if you would slow down just a little bit it
8 would help me.

9 THE WITNESS: Okay. I'm a fast talker. So
10 I tried to make this concept of oxidation, which we've
11 heard of during these trials, exactly what it is, why
12 it happens and what's going on. So I think everybody
13 knows what molecules are. Molecules are made up of
14 atoms, okay?

15 So there's electrons that orbit the nucleus
16 of atoms and they orbit them in pairs. One is
17 spinning one way, one is spinning the other way, and
18 so everything is happy because everything is balanced.
19 Now, if something comes along and extracts a single
20 electron from an atom, that's termed oxidation. So
21 extraction of electron is termed oxidation.

22 So what that leaves behind is one unpaired
23 electron and that electron now is not happy because
24 its lost its partner. So what it's going to do is try
25 and find another electron somewhere. It's very, very

ROBERTS - DIRECT

2168

1 unstable when you have an unpaired electron. Very,
2 very unstable, and these compounds are very reactive.
3 They really want to go find another electron.

4 So they'll go find, extract an electron from
5 another atom or atom in another molecule and that
6 actually causes a chain reaction that propagates the
7 further oxidation, and it just keeps going, and going
8 and going.

9 BY MS. RENZI:

10 Q Yes. And a free radical then is a molecule
11 that only has one electron, the other one is gone?

12 A Exactly.

13 Q Now, your next slide, which is going to be
14 Slide No. 5, is on free radical produced lipid
15 peroxidation and the mechanisms for oxidative damage,
16 is that correct?

17 A That's correct.

18 Q And could you please go through that?

19 A So this just sort of depicts what I have
20 just said. The *L* here is a lipid, and an *H* is a
21 hydrogen atom and the *R* is a radical. So this radical
22 will extract this hydrogen, which is an electron, from
23 the lipid and so that will make an RH. What's left
24 behind now is a lipid radical that doctored the
25 radical, an unpaired electron.

ROBERTS - DIRECT

2169

1 There's a lot of oxygen around in the body
2 so that L. or that lipid with an unpaired electron
3 will immediately react with oxygen. That still leaves
4 a radical. It's LOO. So that LOO., now it's still
5 trying to find another electron so what it will do is
6 oxidize like another lipid, so that makes LOOH.
7 That's okay, but what it leaves behind is another L.,
8 which we can see. Then you start back up here again.
9 So this just keeps propagating itself until something
10 stops it.

11 Q And how do you stop this chain reaction?

12 A I think we go to the next slide.

13 Q And we're on Slide 6.

14 A So how do we stop this process? Because
15 it's just a chain reaction. And so the way this can
16 be terminated is by donation of an electron, which is
17 termed reduction. So oxidation is taking an electron
18 away, reduction is donating an electron from, for
19 example, an antioxidant molecule.

20 So you might think, well, that's just going
21 to set up continued propagation. But that's not the
22 case because antioxidant molecules have very unique
23 properties in that the unpaired electron remaining
24 after donating electrons in the antioxidant molecules
25 is not highly reactive and therefore will not extract

ROBERTS - DIRECT

2170

1 another electron from another molecule.

2 So there, the chain reaction is stopped by
3 this antioxidant. So accordingly, the REDOX status,
4 we've heard that term in these proceedings before,
5 really represents the balance between reduction and
6 oxidation and it's a balance and where you are in that
7 balance. So oxidative stress is defined as an
8 imbalance between oxidation and reduction in favor of
9 the former.

10 Q Thank you. Now, every human being undergoes
11 oxidative stress, is that correct?

12 A Right. Our normal process of metabolism,
13 everything, we have a certain amount of oxidative
14 stress, but the damage caused by that is kept in
15 check.

16 Q And what are some examples that will elicit
17 oxidative stress?

18 A Well, several things. I mean, you bruise
19 your finger, you're going to have oxidative stress in
20 your finger until that's repaired. Exercise is even
21 associated. That's well-known to actually cause a
22 modest oxidative stress. Actually, a modest oxidative
23 stress can be actually beneficial because what we
24 have, we're balancing things, like I said, between the
25 amount of oxidation and the amount of reduction.

ROBERTS - DIRECT

2171

1 We have a battery of protective mechanisms,
2 which we call antioxidant enzymes, and superoxidate --
3 catylates (phonetic) through the found peroxidates.

4 SPECIAL MASTER HASTINGS: Can you say that
5 again? You really started to go fast in that last
6 part of the answer.

7 THE WITNESS: Okay. So we have a balance,
8 you know, there's a certain amount of oxidative stress
9 always going on. So why doesn't that just go rampant,
10 because we have a battery of protective antioxidant
11 enzymes that keep that in check at a certain level. I
12 can name these enzymes. So it's how much oxidation is
13 going on and how much of this protective mechanism.

14 That's why we don't just oxidize ourselves
15 to death. We have this constant low-level degree of
16 oxidation going on but we have these incredible
17 antioxidant defense mechanisms to keep that at bay.
18 Does that make sense?

19 MS. RENZI: Yes.

20 THE WITNESS: Okay.

21 BY MS. RENZI:

22 Q So if exercise causes oxidative stress it
23 doesn't mean I shouldn't go running when it stops
24 raining this afternoon?

25 A No. I mean, most people think that's what

ROBERTS - DIRECT

2172

1 is behind the beneficial effects of exercise. It's a
2 modest oxidative stress which then leads to
3 upregulation of all these antioxidant defenses so that
4 then if you have some oxidant going on you're already
5 more than prepared to take care of that.

6 Q So you're saying basically that oxidative
7 stress can have a protective effect?

8 A Well, in a modest degree.

9 Q Then we'll move on to Slide 7. Now,
10 oxidative stress does not necessarily mean no
11 oxidative damage, is that correct?

12 A That's correct.

13 Q And if you could just go through this slide,
14 please?

15 A So you have to say oxidative stress and
16 oxidative damage are two different things.

17 SPECIAL MASTER HASTINGS: Can you say that
18 one again?

19 THE WITNESS: So oxidative stress doesn't
20 necessarily equate to oxidative damage. Your body
21 senses that this REDOX status is altered and what it's
22 trying to do is keep important molecules from becoming
23 oxidatively damages, so it will upregulate these
24 defenses to keep this at bay.

25 So there's ways you can assess oxidative

ROBERTS - DIRECT

2173

1 stress, but that doesn't necessarily equate to
2 oxidative damage, per se, or it will be a minimal
3 damage that can be readily repaired. So the second
4 one is the fact that moderate levels can be
5 protective, when the body senses, it upregulates to
6 synthesis enumerant antioxidant enzymes which can
7 prevent oxidative damage to --

8 SPECIAL MASTER HASTINGS: Doctor, when you
9 start pointing at the screen and reading your voice
10 doubles in speed and we can't get any of it, so when
11 you get to that part slow down.

12 THE WITNESS: Okay. So I actually think
13 I've just covered these things on the slide.

14 BY MS. RENZI:

15 Q Okay. Does the finding of oxidative stress
16 in the periphery, the plasma, indicate that there's
17 oxidative stress in the brain?

18 A No.

19 Q And why is that?

20 A You know, the damage done by free radicals
21 happens where they're generated. As I said, free
22 radicals are very, very reactive. They don't travel
23 around the body and go to the brain. They're going to
24 try to get this electron from what's next door and
25 they will get it. They don't travel around because

ROBERTS - DIRECT

2174

1 they're very, very extremely reactive.

2 So there's all kinds of diseases which we
3 and others have, you know, well-documented: severe
4 sort of oxidative injury in peripheral organs, you
5 know, and these people don't have any central nervous
6 system abnormalities.

7 You know, we even looked at graduate
8 students who have elevated cholesterol levels. These
9 are 20-year-old kids who have cholesterol levels above
10 200. They have higher levels of isoprostanes for
11 another reason. Obviously they're in graduate school,
12 they don't have any problems thinking.

13 Q And if there is oxidative stress in the
14 brain, can that be detected by measuring oxidative
15 stress in the periphery?

16 A No, it can't, and for the same reasons I
17 said before. These free radicals don't move around.
18 They're going to react locally with other
19 macromolecules. In fact, we've done a lot of research
20 into the role of oxidative injury and Alzheimer's
21 disease.

22 We can detect this by looking at brains
23 taken from patients with Alzheimer's disease at
24 autopsy or we can see this elevation in these
25 isoprostanes in cerebral spinal fluid taken from the

ROBERTS - DIRECT

2175

1 lumbar spine which is draining the brain. We've
2 published this as well, that we cannot pick up this
3 oxidative injury that's happening in the brain when we
4 measure isoprostanes in plasma or urine.

5 I've got ongoing studies with some people in
6 Dallas where we're looking at people who have very,
7 very severe, traumatic brain injury. Indeed, the
8 amount of oxidation going in the brain and the spinal
9 fluid that's draining the brain is enormous in these
10 patients, and we cannot pick that up in the periphery.

11 We're also studying patients with
12 subarachnoid hemorrhage where they bleed into their
13 brain. The amount of oxidation there we can pick up
14 in the cerebral spinal fluid is very high, and we
15 cannot pick that up in the periphery.

16 Q Now, Petitioners and Petitioners' experts
17 here have talked a lot about various biomarkers that
18 they say indicate ongoing oxidative stress. I just
19 want to ask you a few questions about some of those
20 tests, well, of some of the indicators of oxidative
21 stress.

22 The first is the glutathione and oxidized
23 glutathione balance. Could you just explain what
24 glutathione is? I think it's referred to as GSH?

25 A Yeah, GSH. And so, GSH, if you remember

ROBERTS - DIRECT

2176

1 back on my first slide, if you extract electrons from
2 GSH, that H, that hydrogen, you're left with GS.
3 that's an unpaired electron. So that then, if you've
4 got two GS.'s, they will combine and form GSSG. I
5 think Dean Jones who is going to testify will get into
6 this in more detail. So the ratio of GSH to GSSG is
7 the ratio of oxidized glutathione to reduced
8 glutathione.

9 Q And in this case, the altered GSH and GSSG
10 ratios have been used to argue that children with
11 autism have chronic oxidative stress, which
12 Petitioners have causally implicated in the etiology
13 of autism. Can these altered ratios be indicative of
14 oxidative stress?

15 A They can be indicative of oxidative stress,
16 but they're not necessarily indicative of oxidative
17 damage. Furthermore, these measurements were done in
18 plasma, which I've said what's going on in the
19 periphery doesn't have any relevance, very little
20 relevance, to what's going on in the brain.

21 Q I think you've talked about this earlier on
22 when you were talking about your research and what led
23 you to the discovery of the isoprostanes but what is
24 the most accurate way then to measure oxidative
25 injury?

ROBERTS - DIRECT

2177

1 A I mentioned this before, that this
2 independent study by National Institutes of
3 Environmental Health Sciences essentially sort of
4 evaluated the validity of almost every method that's
5 ever been developed to assess oxidative injury, and
6 the analysis of F2 isoprostanes far exceeded other
7 things.

8 I mean, some of these assays, like I've said
9 before, you know, the isoprostanes went up like 80
10 fold in this well-established animal model of
11 oxidative injury. In some of these other methods that
12 had been developed, I mean, they went up 20 percent or
13 something like that.

14 Q And so, again, if you did find an elevated
15 level of these F2 isoprostanes in the plasma, would
16 that reflect anything that's going on in the brain?

17 A No.

18 Q And were there oxidative damage in the
19 brain, could that be detected by measurements in the
20 periphery?

21 A No.

22 Q Now, in your expert report you reviewed some
23 of the papers relied upon by Dr. Deth that proved that
24 there was oxidative stress going on.

25 A Yes.

ROBERTS - DIRECT

2178

1 Q And I would just like to go through a couple
2 of those with you.

3 A Okay.

4 Q The first is the Chahan 2004, which was
5 Petitioners' Master List 481. The authors of that
6 paper measured levels of MDA and plasma by TBARS
7 assay. I'd like you just to describe that process and
8 let me know if that's a reliable test to determine
9 oxidative damage.

10 A It's totally unreliable, and there's two
11 reasons for it.

12 SPECIAL MASTER VOWELL: I'm sorry, you're
13 going to have to repeat that. I cannot pick that up.

14 THE WITNESS: Okay. It's totally
15 unreliable. The reason for that is MDA, or
16 malondialdehyde, is not a specific product of lipid
17 peroxidation, and the TBARS assay used to measure MDA
18 is not specific for MDA. There's a real problem with
19 using the TBARS assay in plasma. The reason for that
20 is so TBARS measures malondialdehyde and some other
21 things.

22 SPECIAL MASTER VOWELL: Measured? What was
23 that word?

24 THE WITNESS: TBARS.

25 SPECIAL MASTER VOWELL: TBARS measure

ROBERTS - DIRECT

2179

1 something?

2 THE WITNESS: Measures MDA, but some other
3 things as well. It's not specific for measuring MDA.

4 SPECIAL MASTER VOWELL: Okay.

5 THE WITNESS: Okay? Malondialdehyde.

6 SPECIAL MASTER VOWELL: That was the word I
7 couldn't pick up.

8 SPECIAL MASTER HASTINGS: That's the word,
9 and that's what?

10 MS. RENZI: MDA.

11 SPECIAL MASTER HASTINGS: That's MDA. Okay.

12 THE WITNESS: MDA is malondialdehyde, right.
13 And the other problem is they measured this in plasma.
14 I'm going to try and make you understand this because
15 it may get a little complicated, but I'll go through
16 it as slow as I can. So does everybody know what
17 platelets are?

18 SPECIAL MASTER VOWELL: Yes.

19 THE WITNESS: Okay. When you draw blood to
20 isolate plasma you cannot draw blood without
21 activating platelets, okay? It just happens. There's
22 little platelets, and, you know, they come squeezing
23 through the needle, and they don't like that, they get
24 aggravated. So one problem is there's this enzyme in
25 platelets called thromboxane synthase.

ROBERTS - DIRECT

2180

1 So when you activate platelets they start
2 making thromboxane by this enzyme. The problem is for
3 every molecule of thromboxane that this enzyme makes,
4 it also makes one molecule of MDA. Has nothing to do
5 with oxidation. It's an enzymatic product of this
6 enzyme and platelets which is activated when you draw
7 the blood.

8 So, as I said, measuring MDA in plasma, if
9 you had a very, very specific assay for MDA, would not
10 be reliable as a measure of oxidative stress. The
11 TBARS is not even reliable to measure MDA. So there's
12 big problems with measuring the TBARS assay in plasma.
13 Totally unreliable.

14 BY MS. RENZI:

15 Q And the other study that you reviewed was
16 Ming 2005, which is Petitioners' Master List 124.
17 This also is relied upon by Dr. Deth. In that Ming
18 test they measured F2 isoprostanes with immunoassays
19 as evidence of oxidative damage in autistic children.
20 If you could just go through the type of test that was
21 performed and whether that is reliable?

22 A Well, we do our analyses for isoprostane by
23 mass spectrometry. I'm sure there's many people who
24 don't know what mass spectrometry is. It requires a
25 very sophisticated instrument which costs several

ROBERTS - DIRECT

2181

1 hundred thousand dollars, but it's the most accurate
2 way to probably measure anything.

3 So immunoassays is where somebody develops
4 an antibody against some analyte, whatever that is,
5 usually it's proteins, and that binds to it. So you
6 can measure certain compounds using an immunoassay.
7 This gets back to, as I said, these isoprostanes are
8 small lipid molecules. They're not big proteins.

9 Antibodies against big proteins are usually
10 much more specific than trying to make antibodies to
11 small molecules, such as lipids. These isoprostanes
12 are lipids. So when I was in the prostaglandin field
13 they developed immunoassays for prostaglandins.
14 Remember, the isoprostanes are prostaglandinlike
15 compounds.

16 SPECIAL MASTER HASTINGS: Would you say that
17 last again?

18 THE WITNESS: Okay.

19 SPECIAL MASTER VOWELL: I think if we could
20 just take a short recess here. We're going to try to
21 swap out your mic, doctor. We're getting feedback,
22 which is also interfering with our hearing. So if we
23 can go off the record for five minutes or so.

24 (Whereupon, a short recess was taken.)

25 SPECIAL MASTER HASTINGS: I'll just ask

ROBERTS - DIRECT

2182

1 again, doctor, please try to slow down. We know
2 you're giving us some important testimony here. We
3 want to actually understand it.

4 THE WITNESS: Okay. Do my best. So we were
5 talking about immunoassays for isoprostanes. So when
6 I started this I wanted to make it clear, I hope I
7 made it clear, that isoprostanes are prostaglandinlike
8 compounds, okay, which are very small lipid molecules.

9 So when you have immunoassays you have an
10 antibody, and it binds to a certain analyte, and you
11 can measure how much the binding is, and therefore,
12 quantitate whatever you're trying to measure with an
13 antibody. Most antibodies are against things, big
14 molecules, such as proteins or something.

15 So but isoprostanes are small lipids, very
16 small molecular weight. When I was in the
17 prostaglandin field people tried for years and years
18 to try to develop a reliable, accurate measure
19 immunoassay for measuring prostaglandins, and
20 essentially it never happened.

21 They tried all kinds of distortions and all
22 kinds of ways to do this. Sometimes they would
23 extract samples, and sometimes that made it worse,
24 sometimes it made it better. So there's a lot of
25 interfering substances and biological fluids, such as

ROBERTS - DIRECT

2183

1 plasma and urine, which can interfere with this
2 antibody binding.

3 So basically companies sell these
4 immunoassay kits because they make money, but their
5 reliability is very, very questionable. Aside from
6 that, given the fact, which I've talked about before,
7 measuring something in the plasma tells you nothing
8 about what's going on in the brain.

9 So even if this immunoassay that they used
10 measuring isoprostanes in the plasma was reliable --
11 which it probably, I won't say it wasn't because I
12 don't know for sure, but most immunoassays for small
13 lipids and isoprostanes that have been developed, and
14 we've shown that, are not reliable -- that tells you
15 nothing about what's going on in the brain.

16 BY MS. RENZI:

17 Q Thank you. Have you done in vitro studies
18 on oxidative stress?

19 A Yes.

20 Q And you've also done animal studies on
21 oxidative stress?

22 A Yes.

23 Q And human studies?

24 A Yes.

25 Q And do you have an opinion on the value of

ROBERTS - DIRECT

2184

1 extrapolating in vitro data to what occurs in vivo?

2 A It's very, very, very difficult. I think
3 we've already heard that at this is you can use cell
4 culture systems as an initial hint of whether you
5 might want to do something else, but you can't
6 extrapolate. These cells in culture are already
7 transformed.

8 You know, if you took a cell out of your
9 brain, a neuron, and put it in a culture, it's going
10 to die. So these are not normal cells and the culture
11 conditions are not normal. So if you're extrapolating
12 what you might find in a cell culture system to what
13 happens in vivo, you can't. It's just initial hint,
14 should we look further or not?

15 So, you know, that's a lead. Then usually,
16 you know, you will go, if you've had animal model --
17 for instance, in some disease we'll set up an animal
18 model of that disease -- a lot of animal models in
19 disease don't actually accurately mimic, at least in
20 toto, what's going on in a human disease, and that's
21 known to be problem.

22 So that's a stepwise sort of fashion. Then
23 you sort of evaluate if there is one in an animal
24 model if that's human disease. If things look
25 positive, then what you really absolutely in the end

ROBERTS - DIRECT

2185

1 need to do is look at humans. I'm sort of a
2 translational scientist, I do very basic research, but
3 I go to humans as fast as I possibly can because
4 that's where the real answer is.

5 Q In your opinion, do the studies relied upon
6 by Dr. Deth show more likely than not that autistic
7 children have oxidative stress in the brain?

8 A No.

9 Q So even if Dr. Deth and Dr. Mumper are
10 correct, namely that there is evidence of oxidative
11 stress in children with autism with finding in the
12 periphery, is there any way to discern the cause of
13 that stress?

14 A No.

15 Q Why is that?

16 A As I said, I mean, it can happen from all
17 kinds of different things, such as even modest
18 exercise. And so all we can say is in these kids, and
19 it may be poor nutrition, these children aren't normal
20 children. I can imagine their dietary habits or
21 intake is not completely normal.

22 They get up from the table, and they go
23 somewhere and, you know, it could be -- we have to
24 take in certain small antioxidant enzymes such as
25 we've all heard about, vitamin C, vitamin E.

ROBERTS - DIRECT

2186

1 We have to take these in from our diet. And
2 so it's conceivable, it's all speculation, that maybe
3 some of these children, their nutrition is not
4 adequate, so their amount of vitamin C, vitamin E and
5 other antioxidants they have to ingest may not be
6 normal.

7 Q And is oxidative stress indicative of
8 oxidative injury?

9 A No. What I might say is that, you know, an
10 oxidative stress may cause a minimal amount of
11 oxidative injury, but that can be protected because
12 then that leads to this upregulation of all these
13 antioxidant defense enzymes and mechanisms that keep
14 this whole process in check from getting out of hand.

15 Q And would that finding tell you anything
16 about what is going on in the brain?

17 A No.

18 Q Are there any specific biomarkers for
19 mercury-induced oxidative stress?

20 A Not that I know of.

21 Q And finally, doctor, in your 20 years of
22 experience working in the field of oxidative stress,
23 in your opinion, is there reliable evidence to
24 conclude that autism is caused by oxidative stress?

25 A I see none.

ROBERTS - CROSS

2187

1 Q In your opinion here today, do you believe
2 that reflects what's generally accepted by researchers
3 in the area of oxidative stress?

4 A Yeah. I mean, our sort of Free Radical
5 Society and Society for Free Radical Biology in
6 Medicine, I can't even remember, I can't say that
7 there wasn't some abstract submitted on that, but it's
8 certainly not something that's even discussed in
9 people in the field.

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

12 SPECIAL MASTER HASTINGS: Petitioners have
13 any questions here?

14 MR. WILLIAMS: Very few.

15 SPECIAL MASTER HASTINGS: Please go ahead.

16 CROSS-EXAMINATION

17 BY MR. WILLIAMS:

18 Q Good morning, Dr. Johnson.

19 A Roberts.

20 Q Let me ask you, is there any way that
21 researchers trying to treat autism could measure
22 oxidative stress in the periphery to see if it was
23 going on in the brain?

24 A No.

25 Q No way to do it at all?

ROBERTS - CROSS

2188

1 A (Nonverbal response.)

2 Q Spinal fluid maybe?

3 A Yes.

4 Q Do you understand that the general theory
5 that Dr. Kinsbourne presented here is that the
6 persistence of inorganic mercury in the brain of these
7 children leads to active chronic neuroinflammation
8 which then can explain the symptoms of autism
9 according to a number of published papers? Do you
10 agree that neuroinflammation can explain the symptoms
11 of autism?

12 MR. MATANOSKI: I want to object. This is
13 beyond his scope of his direct. He is offering
14 opinion on Dr. Deth's testimony.

15 SPECIAL MASTER HASTINGS: Mr. Williams?

16 MR. WILLIAMS: Well, let me withdraw the
17 question then.

18 BY MR. WILLIAMS:

19 Q Can neuroinflammation in the brain cause
20 oxidative stress?

21 A Yes, it can, up to a certain extent. It
22 depends how severe the inflammation is, and, you know,
23 that doesn't this oxidative stress may not, depending
24 on the severity. There's a gradation, as I've tried
25 to explain, and we have defense mechanisms that may

ROBERTS - CROSS

2189

1 not necessarily translate into oxidative damage.

2 Q And oxidative damage could be a loss of
3 function, not just cell death, correct?

4 A Yes.

5 Q Would inorganic mercury inside neurons cause
6 oxidative stress in those neurons?

7 MR. MATANOSKI: Again, beyond the scope of
8 his direct, and also, he said that he's not an expert
9 in mercury.

10 SPECIAL MASTER HASTINGS: Well, that
11 question, let's see if he can answer. If he can't
12 answer it then he'll tell us that.

13 THE WITNESS: So repeat your question, sir.

14 MR. WILLIAMS: Can inorganic mercury inside
15 neurons cause oxidative stress to the neuron?

16 THE WITNESS: I don't know that.

17 BY MR. WILLIAMS:

18 Q Okay. You mentioned autopsy studies of
19 Alzheimer's patients which do show oxidative stress in
20 those people, correct?

21 A And oxidative damage.

22 Q And oxidative damage. Have you reviewed any
23 of the autopsy studies of autistics?

24 A No.

25 MR. WILLIAMS: Thank you. That's all I

ROBERTS - CROSS

2190

1 have.

2 SPECIAL MASTER HASTINGS: Any redirect for
3 this witness?

4 MS. RENZI: No. Thank you.

5 SPECIAL MASTER HASTINGS: All right. Dr.
6 Roberts, we're sorry we stuck you with a bad
7 microphone for the beginning of your testimony. I
8 thank Special Master Vowell for figuring that out. I
9 didn't. We thank you very much for your testimony.
10 You're excused at this time.

11 I'm sorry, I'm sorry, you're not excused. My
12 mistake. Special Master Campbell-Smith?

13 SPECIAL MASTER CAMPBELL-SMITH: Dr. Roberts,
14 I did have a question. I heard you testify on cross
15 that neuroinflammation can cause oxidative stress, and
16 your testimony was depending on the level of
17 neuroinflammation?

18 THE WITNESS: Uh-huh. Yes.

19 SPECIAL MASTER CAMPBELL-SMITH: Can you give
20 some general, without perhaps specific numbers, but
21 when you say depending on the level, would that have
22 to be substantial neuroinflammation that would cause
23 oxidative stress?

24 THE WITNESS: I mean, it's a continuum of
25 things where a small amount can be protective. The

ROBERTS - CROSS

2191

1 only way to answer that question would be if you had
2 absolutely firm evidence that there was oxidative
3 damage at some level of inflammation because, you
4 know, leukocytes try to kill bugs by making hydrogen
5 peroxide.

6 SPECIAL MASTER HASTINGS: Can you say that
7 sentence again?

8 THE WITNESS: Okay. So when you have
9 inflammation, like leukocytes, I mean, they try to
10 kill bacteria by making oxidants, like hydrogen
11 peroxide, but the point I tried to make across,
12 there's a continuum of all this. So your question is
13 I think by and large a little bit unanswerable because
14 where does this amount of inflammation turn into
15 oxidative damage rather than not?

16 SPECIAL MASTER CAMPBELL-SMITH: Well, you're
17 anticipating a question, and maybe you're thinking a
18 step ahead of me. What we've been hearing is there is
19 a chronic level of neuroinflammation --

20 THE WITNESS: Right.

21 SPECIAL MASTER CAMPBELL-SMITH: -- that
22 leads to oxidative stress, oxidative stress that is
23 sufficient to cause damage that looks like a loss of
24 cell function as opposed to cell death.

25 I've heard you testify that there is a

ROBERTS - CROSS

2192

1 chronic level of oxidative stress that exists at all
2 times that can be handled by upregulated antioxidants,
3 and that does not necessarily translate into damage
4 which would be, in your definition damage is
5 alteration of cell function and cell death?

6 Because it appeared when you said that you
7 can cause damage but if the body can handle it and the
8 cell protective mechanisms can repair it you don't
9 really regard that as a damage.

10 THE WITNESS: that's correct.

11 SPECIAL MASTER CAMPBELL-SMITH: Okay. So I
12 think you might have been anticipating my next
13 question. I recognize it may be unanswerable but
14 we're floating in a level of where is the difference
15 between just what is oxidative stress that the body's
16 own system is able to handle and when do we begin to
17 veer into what you would regard as damage.

18 THE WITNESS: Well, the only way to know
19 where you're on that curve is to actually measure and
20 quantify the level of oxidative damage. So you don't
21 know, and it may vary between one person or another
22 person -- so there's a continuum, and you don't know
23 where you are on that continuum unless you measure a
24 product of oxidative damage.

25 It's too hypothetical to know where you're on

ROBERTS - CROSS

2193

1 this curve. Does that make sense?

2 SPECIAL MASTER CAMPBELL-SMITH: It does.

3 THE WITNESS: Okay.

4 SPECIAL MASTER CAMPBELL-SMITH: It does.

5 Okay.

6 THE WITNESS: You know, you have to see, is
7 there oxidative damage and actually actively quantify
8 the level of oxidative damage and see if it's
9 increased. You don't know where you are on that curve
10 because how much in this person, your antioxidant
11 defenses are upregulated because of this low level of
12 stress. You don't know. The only way you'd know
13 where you are on that curve is to measure how much
14 damage is being done.

15 SPECIAL MASTER CAMPBELL-SMITH: And you
16 cannot do that in the periphery and get an
17 understanding of what's happening in the brain?

18 THE WITNESS: That's correct.

19 SPECIAL MASTER CAMPBELL-SMITH: Thank you.

20 SPECIAL MASTER HASTINGS: No. Wait a
21 minute, doctor.

22 MR. WILLIAMS: Well --

23 SPECIAL MASTER HASTINGS: Yes, please.

24 MR. WILLIAMS: One more quick line of
25 questions.

ROBERTS - REDIRECT

2194

1 BY MR. WILLIAMS:

2 Q When you speak of oxidative damage in the
3 brain, there's been evidence here that monkeys exposed
4 to inorganic mercury leads to neuroinflammation and
5 astrocyte death. If astrocytes die as a result of
6 neuroinflammation, can that lead, as Dr. Deth told us,
7 to a lowering of glutathione in the brain?

8 MR. MATANOSKI: I'm going to object again
9 because it's beyond the scope of his direct and I
10 think it's beyond the scope of the questions from the
11 bench as well.

12 SPECIAL MASTER HASTINGS: Well, I'm going to
13 let him. Why don't you ask the question again. I'll
14 let him answer that.

15 MR. WILLIAMS: Okay. One of the things Dr.
16 Deth testified to was that neuroinflammation in the
17 brain can lead to dysfunction, even death, of
18 astrocytes. Dysfunction and death of astrocytes can
19 lead to a lowering of glutathione, which then leads to
20 a chronic inability to restore the REDOX balance in
21 the brain.

22 My question to you is do you agree that that
23 is a plausible mechanism?

24 THE WITNESS: Well, I would ask do we know
25 what caused the cell death? Is it really oxidative

ROBERTS - REDIRECT

2195

1 damage? You know that cells are dying in the brains
2 of these children with autism but do you know the
3 mechanism?

4 MR. WILLIAMS: Well, I'm asking you.

5 THE WITNESS: You would have to have
6 measurements of oxidative injury in those brains.

7 BY MR. WILLIAMS:

8 Q And you haven't reviewed the autopsy
9 studies?

10 A No.

11 MR. WILLIAMS: Okay.

12 SPECIAL MASTER HASTINGS: Anything further,
13 Ms. Renzi?

14 MS. RENZI: Just one question.

15 SPECIAL MASTER HASTINGS: Please go ahead.
16 Doctor, you stay there until we tell you. Each time
17 one of us asks a question that means the rest get to
18 respond to that.

19 THE WITNESS: That's fine.

20 REDIRECT EXAMINATION

21 BY MS. RENZI:

22 Q I'll make this very short. Is there a
23 difference between oxidative stress, oxidative damage
24 and oxidative damage that has consequences?

25 A Yes. As I said, I mean, these isoprostanes,

ROBERTS - REDIRECT

2196

1 which are indicative of oxidative damage to lipids, I
2 can measure those in your plasma and there's a normal
3 level of oxidative damage to all of our
4 macromolecules, proteins and everything else, but
5 that's kept at a level that doesn't hurt us.

6 It's only when we can't keep it at that
7 level and it starts to sort of fly away, then we get
8 more damage and that's when you can get into trouble
9 with cells dying, et cetera, et cetera.

10 MS. RENZI: Thank you.

11 SPECIAL MASTER HASTINGS: Mr. Williams,
12 anything further?

13 MR. WILLIAMS: No. I'm finished.

14 SPECIAL MASTER HASTINGS: Special Masters,
15 anything?

16 THE WITNESS: Can I leave?

17 SPECIAL MASTER HASTINGS: Going once. Going
18 twice. Doctor, thank you again.

19 (Witness excused.)

20 SPECIAL MASTER HASTINGS: All right. Is the
21 government ready to call its next witness?

22 MR. MATANOSKI: They're in the building, as
23 I understand, they're just not in the courtroom right
24 now. If we had about a 10-minute break and switch out
25 here.

1 SPECIAL MASTER HASTINGS: Let's take a
2 10-minute break.

3 (Whereupon, a short recess was taken.)

4 SPECIAL MASTER HASTINGS: I imagine we have
5 Dr. Johnson on the stand here. Ms. Babcock, when
6 you're ready, please go ahead.

7 MS. BABCOCK: Good morning.

8 MR. JOHNSON: Good morning.

9 MS. BABCOCK: Could you please state your
10 name for the record?

11 MR. JOHNSON: Jeff Johnson.

12 MS. BABCOCK: I suppose we should start by
13 saying we have a slide exhibit.

14 SPECIAL MASTER HASTINGS: All right. Yes.

15 MS. BABCOCK: Should we identify it as the
16 Trial Exhibit 7?

17 SPECIAL MASTER HASTINGS: Yes.

18 MS. BABCOCK: Take a moment.

19 (The document referred to was
20 marked for identification as
21 Respondent's Trial Exhibit
22 No. 7.)

23 SPECIAL MASTER HASTINGS: Thank you.

24 MS. BABCOCK: I'm sorry. Special Master,
25 did you want to swear the witness in?

JOHNSON - DIRECT

2198

1 SPECIAL MASTER HASTINGS: Yes. Dr. Johnson,
2 would you raise your right hand, please?

3 Whereupon,

4 JEFF JOHNSON

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

7 SPECIAL MASTER HASTINGS: Please do speak
8 up. Go ahead, Ms. Babcock.

9 DIRECT EXAMINATION

10 BY MS. BABCOCK:

11 Q Could you please state your name for the
12 record?

13 A Jeff Johnson.

14 Q And what is your profession?

15 A I am a Professor in the School of Pharmacy
16 at the University of Wisconsin in Madison.

17 Q And could you briefly describe your
18 collegiate and graduate education?

19 A I received my bachelor's of science degree
20 in biology with minors in chemistry and philosophy
21 from the University of Minnesota in Duluth. I
22 received a master's in pharmacology from the
23 University of Minnesota in Duluth. Then I moved on to
24 a Ph.D. at the University of Wisconsin in
25 environmental toxicology.

JOHNSON - DIRECT

2199

1 I did a postdoctorate fellowship at the
2 University of Washington, the other U-dub, for about
3 three years, and there I worked on molecular
4 neuroscience and single transduction.

5 Q And do you hold teaching positions at the
6 University of Wisconsin?

7 A Yes, I do teach at the University of
8 Wisconsin. I'm a Professor there, yes.

9 Q You teach both graduates and undergraduates?

10 A Yes, I teach both graduates and
11 undergraduates and also professional students in the
12 pharm-D program.

13 Q And you also have a laboratory at the
14 University of Wisconsin?

15 A Yes.

16 Q And what is the primary focus of your
17 research?

18 A The primary focus of my research is
19 neurodegenerative diseases, so we work on Alzheimer's,
20 Parkinson's, ALS and Huntington's disease.
21 Specifically, we're interested in ways to protect from
22 cell loss and neuronal cell death in those diseases.

23 Q And have you published on topics in the
24 field of your research?

25 A Yes, many times.

JOHNSON - DIRECT

2200

1 Q And are you a reviewer for any publications?

2 A Yeah. In fact, I just got an email this
3 morning to review an article while I was in my hotel
4 room, so I get asked about every week to review an
5 article from, I can't even -- there's, you know, 20,
6 30 different journals.

7 Q Pardon me. Did I cut you --

8 A No. That's okay.

9 Q Okay. Sorry.

10 A Did you want me to recite the 20 or 30? I
11 don't want to.

12 Q I think for the sake of brevity this morning
13 we will let your CV, which has been filed into the
14 record.

15 A Okay.

16 Q Have you received any significant honors for
17 your work?

18 A Well, one of the ones that I received early
19 in my career was the Burroughs Welcome award, which is
20 a new investigator of toxicology award. Why I
21 consider that an honor is it's a very competitive
22 award.

23 Essentially every institution in the United
24 States that does research, like the University of
25 Wisconsin, picks one candidate from their institution

JOHNSON - DIRECT

2201

1 that's an assistant professor and they're allowed to
2 submit one application. So you can imagine there's
3 probably 50 to 100 applications on one of those rounds
4 and they select four of the top people in their field
5 that get that award, and I was that.

6 The other one that I'm proud of recently was
7 I was given the Community Humanitarian award by the
8 Huntington's disease Society of America. That came
9 from my research which got a bunch of publicity. I
10 got involved in, you know, groups, and family groups
11 and things like that.

12 So I'll go and speak to family groups, and,
13 you know, groups with ALS and things like that to talk
14 to them about what we're doing in research-wise.
15 That's been, actually, a very rewarding part of my
16 research that's come out in the past couple of years.

17 Q And did you review the expert reports and
18 literature in this case as it related to your area of
19 expertise?

20 A Yes, I did.

21 Q You've also prepared an expert report which
22 has been filed in this case?

23 A Yes.

24 Q And were you present in Court last week to
25 hear some of the expert testimony?

JOHNSON - DIRECT

2202

1 A Yes, I was.

2 Q And as part of your research you study
3 neurodegenerative diseases, correct?

4 A That is correct, yes.

5 Q Now, comparing the general symptoms of
6 neurodegenerative diseases and the ultimate end point,
7 does autism bear any resemblance to the diseases that
8 you study?

9 A No. If it did, we'd be studying it. Again,
10 in the case of neurodegenerative diseases, the
11 outcomes are essentially neuro death and the patients
12 die, and so that would be my focus. If that was
13 occurring in autism, it would probably be under that
14 list of research areas that I gave you at the
15 beginning.

16 Q And in general, do most neurodegenerative
17 diseases occur much later in life?

18 A In general, yes. At least the ones I've
19 listed begin later in life. They can begin early in
20 life depending on the genetic components that are made
21 up of that. For example, Huntington's disease is a
22 genetic disease which can occur earlier in life.

23 Q Have you ever been a reviewer for the
24 National Institutes of Health?

25 A Yeah. I served on study section for five

JOHNSON - DIRECT

2203

1 years.

2 Q And study section is the group of academics
3 and researchers who review grant applications,
4 correct?

5 A Correct, yeah. So when I submit, the same
6 happens to me. It's like peer review of a manuscript,
7 only it's peer review of a grant.

8 Q And study sections have particular focuses?
9 You know, is your study section based on your area of
10 expertise?

11 A Yeah. My study section was titled
12 Neurotoxicology and Alcohol, so it basically dealt
13 with the neurological effects of alcohol in the brain
14 as well as neurotoxicology.

15 Q Now, when you review grant applications for
16 your study section are decisions based on the
17 scientific validity of the proposed study or potential
18 political policy considerations?

19 A We don't consider politics and political
20 considerations. The reviews, and as specifically, I
21 can comment on this in response to something that Dr.
22 Deth was saying in his testimony, our study section
23 actually reviewed a Deth grant in 2003 and my
24 recollection of that grant review was that it was a
25 weak hypothesis, preliminary data didn't support it

JOHNSON - DIRECT

2204

1 and there was not a good experimental design set up in
2 the grant.

3 And so the reason that grants and study
4 sections don't get funded, or get rejected, or get low
5 scores is not due to the politics, it's due to the
6 scientific merit of the application. Absolutely.

7 Q Now, in your review of Dr. Deth's expert
8 report you identified a number of concerns. I wanted
9 to just talk about a few of them here. I think we're
10 switching to Slide 2 now. In general, did you
11 encounter instances where Dr. Deth used in vitro
12 laboratory work to extrapolate to the in vivo
13 situation?

14 A Yeah. In his expert report he did that I
15 think over and over.

16 Q Now, are there complications that can arise
17 from in vitro studies?

18 A There's complications and there's dramatic
19 limitations. I mean, in vitro studies are in vitro
20 studies. I mean, I tell the people in my laboratory
21 and postdocs and grad students if you're working with
22 a cell line, the interpretation that you can make on
23 the data that you generate in that cell line, it has
24 to be held within that cell line.

25 I mean, you can form hypotheses based on

JOHNSON - DIRECT

2205

1 maybe what you get from the cell line, but you can't
2 extrapolate that data without actually doing
3 experiments.

4 Q Now, are there protective mechanisms that
5 happen in vivo that are not present in vitro?

6 A Once you take out the cell and put it into,
7 you know, an environment that's not natural, a lot of
8 things change, and so, yeah, you're changing all kinds
9 of aspects of that, so you don't have the cell/cell
10 communication anymore and you also are looking at, you
11 know, different things that are occurring in the cell,
12 so things are completely different. You can't even
13 compare it.

14 Q And the particular cells used sometimes have
15 an effect. This is Slide 3.

16 A Yeah. I put this slide up to try to, again,
17 help clarify what the cell line is and how we look at
18 a cell line. So a neuroblastoma cell line is
19 basically a self-renewing cell line that grows
20 spontaneously and they're usually from tumors. They
21 often have avert numbers of chromosomes. They don't
22 have the normal number of chromosomes.

23 They also contain in a number of situations
24 multiple genetic mutations because of the way the
25 tumors are growing, and self-renewing cells tend to,

JOHNSON - DIRECT

2206

1 you know, have mutations that they carry through.
2 Again, as I've mentioned earlier, they're constantly
3 expanding and dividing and they have uncontrolled
4 growth.

5 If you transplant them into mice they form
6 tumors. In most situations, especially when we're
7 talking about neuroblastoma cells, and I think this is
8 a real critical point, is that we get what we call a
9 dedifferentiation. So, for example, the neuroblastoma
10 cells that are being used in most of these studies is
11 they also have characteristics of glial cells.

12 So they don't have just the neuronal
13 proteins in them anymore, they also express glial
14 proteins, and they have glial characteristics and you
15 can see all these other kinds of things. So they
16 almost take a step back away from this differentiated
17 state that we see in vivo to more of a primordial
18 state where they have different proteins turned on
19 that are not normally there in neurons.

20 That's I think a major issue that people
21 need to understand is these are not like neurons,
22 differentiated neurons. The reason they're used is
23 because they're easy to use and they're cheap, and so
24 you can do a lot of experiments, you know, fast in
25 them, but you do have to remember that their

JOHNSON - DIRECT

2207

1 interpretation, it's impossible to extrapolate to
2 humans.

3 The other system that I want to talk about
4 briefly in vitro was this primary neuronal cultures.
5 In this situation they're very different.

6 SPECIAL MASTER HASTINGS: Can you say that
7 again? The what?

8 THE WITNESS: Primary neuronal cultures.
9 They're very different because what you do in that
10 situation is you remove the brains from mice and
11 you're able to dissociate and plate them out in a
12 dish, and they are terminal basically. They
13 differentiate, like you would in vivo.

14 So if you look at the culture, they have
15 markers of glial cells in the glial culture and the
16 neurons don't have those glial markers and so on. SO
17 they do maintain, "a little more of their phenotype",
18 in that kind of context.

19 So the next step, at least what we've done,
20 is if you find something in a blastoma cell or a cell
21 line, we instantly move it into a primary culture
22 system because it's more representative of what's the
23 in vivo situation is. Again, because it's not in the
24 context of the brain, its extrapolation is limited.

25 You can't just say what's happening there

JOHNSON - DIRECT

2208

1 will happen in vivo, but at least they're normal
2 cells, although they may not be, you know, in this
3 context of the brain, but they do have normal
4 phenotypes, and so they're a better thing to use in a
5 dish than a cell line for sure.

6 They give you a little bit more insight and
7 they maintain much more of the normal function of the
8 individual cells you're trying to study.

9 MS. BABCOCK: Now, on page 3 of his report
10 in the second full paragraph Dr. Deth states that
11 thimerosal is toxic to human cortical neurons in
12 neuronal cells grown in culture. Is it okay if I just
13 generally describe where that is? Do you need me to
14 give you a more pinpoint identification of the
15 location?

16 SPECIAL MASTER HASTINGS: No, that's fine.

17 MS. BABCOCK: Okay. He cites to three
18 references, which I believe are Herman, Baskin and
19 Perrin.

20 THE WITNESS: Yes.

21 MS. BABCOCK: Were these in vitro studies?

22 THE WITNESS: Yes, they were.

23 BY MS. BABCOCK:

24 Q And what type of cells were used in these --

25 A Cell lines. They were the neuroblastoma

JOHNSON - DIRECT

2209

1 cell lines, and they were not the primary cultures.

2 Q So they -- I'm sorry.

3 A Yeah. This again bothers me because when
4 people talk about cell lines and they use the word
5 "neuronal" that infers to people that are looking at
6 it or that are reading it that it's actually neurons
7 and they are not. So there is a distinct
8 misrepresentation of using that kind of terminology,
9 cortical neurons or neuronal, when you're looking at
10 neuro cell lines.

11 Again, if a student gives me a paper that
12 they're working on and they use the word "neuronal"
13 and they don't use the word "neuroblastoma," it's
14 changed, it's wrong. It's just a misrepresentation.
15 It's misleading to say that.

16 Q And were the doses used in these studies
17 similar to what's used in vaccinations?

18 A Oh, no. You know, based on the couple of
19 papers that have looked in mouse and primate at, you
20 know, this mimicking this vaccination schedule, the
21 Berman paper and then the Burbacher paper, but I
22 looked at those papers just to kind of get a dose of
23 what would be in the brain.

24 Q And let me be clear, I'm not asking you to
25 go into specific toxicology of mercury because that's

JOHNSON - DIRECT

2210

1 not --

2 A That's not my area, no.

3 Q -- what you're here to talk about.

4 A All I did was look at those and say, okay,
5 here's what they're saying is a dose or a level in the
6 brains of these animals. As it's been presented
7 before, that's in an animal arrange. So when I looked
8 at the papers then of course they were micromolar
9 range, and so that to me said that they were much,
10 much higher than what would be at least in those two
11 studies.

12 Q Now, Dr. Deth also cites a paper by Mady
13 Hornig in support of his arguments, correct?

14 A Yes.

15 Q I believe that's PML 15. Now, you
16 mentioned, this is in your expert, that the mouse
17 strain Dr. Hornig used was selected because it had a
18 stronger immune response.

19 A Right.

20 Q But took issue with Dr. Deth's explanation
21 of the rationale behind the use of the strain,
22 correct?

23 A Right.

24 Q And I believe he stated that hers was a
25 mouse strain harboring genetic deficits and REDOX-

JOHNSON - DIRECT

2211

1 related enzymes. This is from page 4, the first
2 sentence of the paragraph preceding the bolded effects
3 of methylation. What strain of mouse was used?

4 A That was an SJLJ mouse. The interpretation
5 of that or the way that that was written by Dr. Deth
6 in his report was inferring that there is a REDOX
7 enzyme differential or some kind of differential, and
8 that's absolutely not true. I mean, the mice have
9 this increased immune response and that's why the mice
10 were selected.

11 They've been used in these studies a lot by
12 other groups. So there is absolutely no data
13 supporting the fact that there is a REDOX enzyme
14 differential. Now, I can understand the reason it's
15 in there is because it supports his hypothesis in the
16 sensitivity, but that's not an accurate representation
17 of the mice.

18 MS. BABCOCK: And in general, do you have
19 confidence in Dr. Hornig's reported results? Here,
20 actually we're switching to Slide 4. I apologize. We
21 inadvertently switched Slide 4 and Slide 5, so really
22 what we mean to be switching to is what is marked in
23 the trial exhibit as Slide 5.

24 SPECIAL MASTER HASTINGS: All right.

25 THE WITNESS: Will you repeat that?

JOHNSON - DIRECT

2212

1 MS. BABCOCK: If you have confidence in Dr.
2 Hornig's reported results?

3 THE WITNESS: No.

4 BY MS. BABCOCK:

5 Q And part of that has to do with the
6 hippocampus section, correct?

7 A Yeah. I mean, the quality. I mean, I don't
8 know if I can point this out but if you look at these
9 images on the right side of this slide --

10 Q Again, they are the sections from the Hornig
11 paper.

12 A Yeah, these are from the Hornig paper.
13 These are the vehicle and this is the thimerosal
14 treated mouse.

15 SPECIAL MASTER VOWELL: Which ones were your
16 referring to when you --

17 THE WITNESS: This. The upper right and the
18 lower right are the two images from the Hornig paper.
19 The A is the vehicle and the B is the thimerosal.

20 BY MS. BABCOCK:

21 Q And what do you mean by vehicle?

22 A Vehicle in this case, whatever they were
23 dissolving the vaccine that they were giving in. So
24 it's basically the same solution, same volume, without
25 the thimerosal in it, all right? what you can see

JOHNSON - DIRECT

2213

1 when you look at these images is to me these images
2 are absolutely awful.

3 Now, the staining here is hematoxylin and
4 eosin, and it's supposed to stain for architecture,
5 and cell integrity and a variety of other things. The
6 tissues are very diffuse, there's not clear neuronal
7 fields. Right here there are deep staining.

8 Q You're pointing to the top slide.

9 A Yeah, top slide. If you look at those
10 images, the cells that are dark right there, those are
11 the neuronal fields. The quality is just extremely
12 low.

13 SPECIAL MASTER HASTINGS: I'm not sure what
14 you mean. The quality of the photography is low?

15 THE WITNESS: No, no. The quality of the
16 sections themselves is really -- in the next slide
17 I'll specifically talk about what I think, you know?
18 Put it this way. I've seen this in my lab before,
19 I've seen people come to me with images like this or
20 with sections and stains like this and I'll say
21 something's wrong, okay, the tissue wasn't prepared
22 right.

23 There's something that's definitely wrong
24 with this because these do not maintain the nice
25 cellular architecture that you should see if the

JOHNSON - DIRECT

2214

1 experiment is done right and the tissue is harvested
2 correctly.

3 BY MS. BABCOCK:

4 Q So it's fair to say that problems with these
5 slides and these sections caused you to question the
6 ultimate finding of the --

7 A Absolutely, yeah.

8 Q And has the recent paper in fact refuted Dr.
9 Hornig's finding?

10 A Yeah. We've talked about the Berman paper.
11 That's come up in the Berman paper. These sections on
12 the left side of this slide, the upper and lower
13 sections, are comparable sections from the Berman
14 paper and, I mean, to me they're absolutely beautiful.

15 When you look at the cellular architecture
16 and the structure of the hippocampus, which is this
17 region, the cells look very nice. The stain is
18 different, that's cresyl-violet, but that wouldn't
19 make any difference. You're still looking at the cell
20 structure, the cell architecture and the way that the
21 tissue was prepared, and it looks very, very, very
22 good.

23 Q Now, strictly discussing dose, what dose of
24 thimerosal was used in the Dr. Berman paper?

25 A Well, Dr. Berman did the same dose that was

JOHNSON - DIRECT

2215

1 used in the Hornig study but then that group also did
2 a dose that was 10 times higher. In both situations
3 there was absolutely no pathological outcome with
4 regard to the dosing with thimerosal.

5 Q And did both papers use antibodies on brain
6 tissues?

7 A Yes, and this adds another factor that I
8 wanted to point out. Yes, staying with antibodies.
9 So antibodies, now, what antibodies do is they stain
10 specific proteins in the tissue sections. What I want
11 to point out here is the distinct difference between
12 the Berman paper sections and the Hornig paper
13 sections using the same antibody. Now, this is
14 exactly the same staining and the same antibody.

15 SPECIAL MASTER HASTINGS: Now we're moving
16 back to Slide 4?

17 THE WITNESS: Back to Slide 4, right.

18 MS. BABCOCK: What was, yes, originally
19 identified as Slide 4. I apologize.

20 THE WITNESS: So, again, what I want to
21 point out is if you look at the architecture of the
22 tissue, it's really nice in the Berman study and you
23 see this nice staining in the hippocampus which is
24 validated, which has basically been shown in many,
25 many other papers prior to this, this type of staining

JOHNSON - DIRECT

2216

1 where you see --

2 MS. BABCOCK: If I can stop you for a
3 moment. I'm sorry. I think we need to clarify.

4 SPECIAL MASTER VOWELL: Right. Dr. Johnson,
5 I'm going to be listening --

6 THE WITNESS: But you can't see. Okay.

7 SPECIAL MASTER VOWELL: -- or reading your
8 testimony again and I'm not going to be able to see
9 where you're pointing. You have to tell me.

10 THE WITNESS: All right. So the Berman
11 sections are the two panels on the left side of the
12 slide, here and here, and then the comparable little
13 boxes in those panels on the left side are enhanced on
14 the lower portion of the right side of slide. So
15 these little squares are put down here.

16 BY MS. BABCOCK:

17 Q And this is the bottom right-hand --

18 A At the bottom right hand corner.

19 Q The two bottom panels.

20 A The two bottom panels. Again, they're
21 labeled vehicle and thimerosal plus vaccine. What you
22 can see is there's very nice staining in the field.
23 The neuronal field, which are the neurons -- the clear
24 layer that goes through that section, those are the
25 neurons, and they are not staining intensely but the

JOHNSON - DIRECT

2217

1 cells around that field are staining very intensely.

2 Again, that's been published multiple times
3 by other groups, that pattern. Now, if you'd look at
4 the upper four panels on the right side, these are the
5 similar, comparable panels from the Hornig study. The
6 first thing that I want to point out is if you look at
7 the tissue it's full of holes.

8 So if you look at this enhanced image right
9 here, the bottom two panels, C and D, from the Hornig
10 study, you can see that the tissue almost looks like
11 it's disintegrating. It's breaking down. There's
12 holes all over in the tissue. Now, I know from
13 experience that when you see tissue like this the
14 amount of nonspecific staining with antibodies could
15 be intense.

16 Basically, if somebody came to me with this
17 kind of staining or this kind of tissue in my
18 laboratory, I would say go back and do the whole
19 experiment again because: (1) these are unpublishable
20 to me; and (2) the potential for artifactual data
21 generated from this kind of degenerated tissue is
22 extremely high.

23 And so they would need to go back and redo
24 these studies to ensure that they were doing the
25 tissue preparation correctly. I mean, this is very

JOHNSON - DIRECT

2218

1 important, especially when you're trying to do
2 histological section and making conclusions from
3 histological data like this.

4 You know, you can do whatever you want after
5 you have the tissue, but it's the process of getting
6 the tissue to the point where the tissue quality is
7 extremely good, then you can make the correct
8 interpretations. In this situation, I don't see that.

9 Q And is it fair to say that you do see that
10 in the Berman tissue --

11 A Yeah. The Berman tissues look absolutely
12 perfect. It looks like their preparation is done
13 extremely well and the sections are beautiful.

14 Q And as a result, do you place more weight on
15 the Berman finding?

16 A Yeah. Absolutely.

17 Q Now, Dr. Deth also relies heavily on the
18 2004 Waly paper which has already been the topic of
19 some of our expert testimony, PML 257. Do you also
20 share concerns about this paper?

21 A Yeah.

22 Q And what are dose curves, and how are they
23 important here?

24 A Well, dose curves are critical to understand
25 the differential sensitivity of different toxins that

JOHNSON - DIRECT

2219

1 you're actually using so you have to lend dose curves
2 to make sure that you're running in the range where
3 you're seeing the effects that you want.

4 If you're trying to compare between
5 different toxicants, I mean, you have to have dose
6 curves so that you know the differential sensitivity
7 of the toxicants with regard to what you're measuring.

8 Q And Dr. Deth, did he use dose curves?

9 A No, he did not.

10 Q And what type of methionine synthase was
11 being measured, and how is that significant? This is
12 Slide 6.

13 A And this is Deth Slide 15. The type of
14 methionine synthase in the SH-SY5Y cells is actually a
15 mutated form of methionine synthase that lacks this
16 blue domain in the upper left-hand corner of the
17 slide, as he pointed out.

18 Q And you're circling the area with the X.

19 A Yeah, with the X through it. This goes back
20 to the point of cell lines. I mean, cell lines are
21 normal, so if you look in normal cells, and normal
22 neurons and normal astrocytes you don't see this form
23 of methionine synthase. This methionine synthase is a
24 result of this tumor transformed to a cell line that's
25 being used in these studies.

JOHNSON - DIRECT

2220

1 Now, how that infects the interpretation of
2 the amount of methionine synthase data remains to be
3 determined, but clearly, you can't assume that the
4 data that's generated with regard to methionine
5 synthase in this cell line is going to represent
6 what's going on even in the dish with the normal
7 neuron because the protein's different.

8 Q Now, how is the reported MAP 3 kinase and PI
9 3 kinase inhibition significant? Why do you doubt the
10 results reported in the Waly paper?

11 A Well, again, Dr. Melman talked about this
12 quite about, too, is that there are a lot of things
13 that you can do. For example, what was used in the
14 paper were chemical inhibitors. Chemical inhibitors
15 are not specific, they're selective. By that I mean
16 is that they can inhibit lots of different things at
17 different doses if you're not careful with how they're
18 used.

19 So today, in this age when we have a variety
20 of other new novel techniques where we can selectively
21 target and knock out specific proteins -- so, for
22 example, in addition to using a chemical inhibitor we
23 often use, you know, a technology called SRNA
24 technology where you can say, okay, IRP 1, or this one
25 protein, this one kinase we think is doing this. We

JOHNSON - DIRECT

2221

1 have an inhibitor but it inhibits like 10 kinases.

2 We want to just see if that one, okay, if we
3 can inhibit that one or take that one out of the cell,
4 do we block what's going on? So what you can do is
5 you can actually do that with these new technologies.
6 You can go in and selectively target specific proteins
7 and get rid of them in the cell and then come back and
8 show that the effect that you're looking for is gone
9 or eliminated.

10 So good, quality papers really combine
11 almost at least two, if not three, different kinds of
12 techniques and they use the pharmacological inhibitors
13 as long as molecular approaches to validate everything
14 so it all fits together. In cell lines that's very
15 easy to do. Cell lines are very conducive or very
16 accepting of these kinds of techniques.

17 So without those kinds of validations it's
18 very difficult to make, you know, conclusions on the
19 specific kinases that might be involved in the
20 pathway.

21 Q Now, I wanted to move on to a discussion
22 about some of the unpublished data. Now, Dr. Deth in
23 his report cited to a manuscript in preparation,
24 correct?

25 A Right.

JOHNSON - DIRECT

2222

1 Q I believe, for the record, that's Reference
2 No. 24, which he specifically cites at the bottom of
3 the first paragraph on page 5. Have we ever seen a
4 copy of this? Has a copy ever been provided to you or
5 to the Court, to your knowledge?

6 A No.

7 Q But Dr. Deth does discuss this unpublished
8 work in his expert report?

9 A Yes.

10 Q Setting aside for a moment the fact that it
11 is unpublished, do the numbers discussed in his report
12 raise questions when compared to other research
13 involving thimerosal, just, again, generally in your
14 review?

15 A Right. Again, the doses that are presented
16 in the report are implying that there are low
17 nanomolar doses that are doing the, generating the
18 effects that Dr. Deth is saying, and in almost all of
19 the other literature in fact even in other people
20 using the same cells that Dr. Deth uses, they're
21 showing, you know, effects in the micromolar range.

22 My comment on that I think is that, you
23 know, a cell line is used for a number of reasons. In
24 this case the SH-SY5Y cell line was used, but this
25 cell line is available commercially from a called ATTC

JOHNSON - DIRECT

2223

1 who banks these cells.

2 So one of the nice things about a cell line,
3 if there are 10 investigators across the country, and
4 they all order the cell line from this company and
5 they grow it in their incubators, then the theory is,
6 or at least, you know, what we find is that there can
7 be consistency between the different labs.

8 So if you treat the cells the same way with
9 drugs or whatever you see relatively consistent
10 results between the different groups and the different
11 labs that are doing this. You know, there can be some
12 variation between groups, you know, whether the cells
13 are in California or in New York. They could have
14 different, you know, environmental exposures or air.

15 You know, they have different air
16 concentrations and stuff like that. In general, you
17 know, we could maybe attribute that at very small
18 different, you know, changes. Maybe four or five,
19 maybe 10 fold at the most differentials in
20 sensitivity.

21 Two or three orders of magnitude, I just
22 can't understand or I can't understand how that would
23 happen outside of just some technical kind of
24 differences or if the cells are really, really sick.

25 Q So the reported results are substantially

JOHNSON - DIRECT

2224

1 lower, 100 to 1,000 times?

2 A Yes, and it's the only report that shows
3 that.

4 Q Any indication that this has been peer-
5 reviewed or tested?

6 A No.

7 Q Now, Dr. Deth also discussed quite a bit of
8 unpublished data in his presentation last week.
9 You've just sort of talked about some of the general
10 issues you have with, you know, some of the
11 unpublished data we've seen as it related to Deth
12 Reference No. 24.

13 My next questions sort of relate generally
14 to that and also what he presented in his testimony.
15 The data that he presented last week as well, in
16 addition to Reference 24, has any indication that
17 that's ever been peer-reviewed?

18 A No.

19 Q Not published?

20 A No.

21 Q Tested?

22 A No.

23 Q We just don't know?

24 A No. We just don't know.

25 Q Now, were you present during the testimony?

JOHNSON - DIRECT

2225

1 A Yes, I was.

2 Q You've had an opportunity to review the
3 slide presentation. Obviously you've incorporated
4 some here already.

5 A Yes.

6 Q And now I know you wanted slap comment on
7 Slide 17, which is Slide No. 7 in your presentation.

8 A Yes.

9 Q Why did Dr. Deth discuss this slide?

10 A Well, I think what Dr. Deth was trying to
11 say here was that the levels of cystathionine and his
12 pathway is on the next page, and I'll show you that
13 briefly, were markedly higher in the human cortex than
14 in other species. So, you know, this slide looks at
15 the human brain and a variety of other animals,
16 including --

17 Q You've switched quickly to Slide 8.

18 A -- duck. So what he used this data to do
19 was to justify this statement here that the
20 increase --

21 SPECIAL MASTER HASTINGS: Which statement?

22 THE WITNESS: The statement in the middle
23 that's highlighted in the light green.

24 MS. BABCOCK: Or blue.

25 THE WITNESS: Or blue, or whatever. I'm not

JOHNSON - DIRECT

2226

1 colorblind but I just don't know colors. My daughter
2 would be able to tell me that's aqua something,
3 something, you know?

4 MS. BABCOCK: I'm sure we could come up with
5 at least five numbers of what that color should be but
6 I'll call it light blue.

7 THE WITNESS: So he's using that to justify
8 this statement that the conversion of cystathionine to
9 cystine is compromised, and, again, here's the word
10 "neuronal cells." That's not true. This is SH-SY5Y
11 cell. Basically, that's impossible to conclude
12 because there's no measurement of cystine or there's
13 no measurement of glutathione.

14 Maybe the human brain just has more of the
15 cystathionine, but they actually maybe have more of
16 the cystine and the glutathione as well, and without
17 knowing that you can't make any conclusion that
18 there's a partial dysfunction in that pathway.

19 In fact, if you look at human tissues, and
20 you look at mouse tissues and you look at these other
21 tissues, except for duck, I've never looked at duck,
22 the glutathione levels in the brains of these animals
23 are not different or they, well, they range, but
24 they're certainly within a very close window of
25 concentration. And the duck thing, I kept thinking

JOHNSON - DIRECT

2227

1 about the duck.

2 BY MS. BABCOCK:

3 Q Let me get you there. Was there a citation
4 to the source of this data?

5 A No. Actually, Dr. Deth had no citation.

6 Q Slide 9.

7 A When I walked away from this I assumed that
8 he had generated this data himself. Like I said, the
9 duck kept bothering me. I kept thinking about this,
10 and so what I did in this day and age is we Google.
11 So I Googled duck and cystathionine and the top hit
12 was a paper published in 1958 by Harris, et al. who
13 actually measured cystathionine levels in duck.

14 What I was really surprised to see was that
15 the data that Dr. Deth presented was basically the
16 same table that was published in 1958 but he didn't
17 reference it.

18 Q Scientifically, do you have a problem with
19 this?

20 A I have a major problem with this because as
21 scientists, you know, if we're using somebody else's
22 work, we reference it. This brings into question, I
23 mean, you know, the scientific integrity of somebody
24 that's going to be, you know, taking somebody else's
25 data and using it but not actually giving the

JOHNSON - DIRECT

2228

1 reference of where they received it, where they got it
2 from.

3 Q Now, did you also review Dr. Deth's Slides
4 24 and 28, also, the unpublished data?

5 A Yeah, this was also the unpublished data.
6 Yes, I did.

7 Q What would your concerns be as someone who
8 looked over this, Slide 10?

9 A Well, again, you know, I looked at these
10 slides when they were presented, this Slide 24 and
11 Slide 28, and the image that's up here from Slide 28
12 is a partial, is just looking at the glutathione
13 component, which is a big part. Half of that whole
14 slide.

15 One of the things that jumped out at me
16 right away when I saw these slides is the
17 concentration of glutathione. So the basal level of
18 glutathione that he shows in the panel on the left,
19 Slide 24, just at the zero point on the curve is 700
20 nanomoles per milligram protein in the SH-SY5Y cells.
21 Then in Slide 28 it's the same cells. Here, the
22 nanomole per milligram protein of glutathione is over
23 1,500.

24 I thought this was extremely high based on
25 my experience, and so I went into the literature and I

JOHNSON - DIRECT

2229

1 actually looked at about 10 papers that used SH-SY5Y
2 cells and measured glutathione in the same units,
3 nanomoles per milligram protein. And it turns out
4 that all 10 of those papers, the basal glutathione in
5 the SH-SY5Y cells is between 12 and 30 nanomoles per
6 milligram protein.

7 So, again, this could be a calculation
8 error. It's not an intentional misrepresentation, but
9 it goes to the point that this data was not carefully
10 evaluated as far as the units and the numbers that
11 were used.

12 Again, it just has a careless nature about
13 it because if you know the literature and you
14 understand the glutathione concentrations in the
15 cells, you would have noticed that these numbers are
16 extremely high and far off base.

17 Q Now, moving on to Slide 11, I know you had a
18 comment about, you know, glutathione measurement and
19 time.

20 A Yeah. This, again, is another instance of,
21 you know, basically picking the time that you want to
22 show your effect. In all of Dr. Deth's studies in the
23 previous slides the time after the treatment was one
24 hour. So he's looking at a very, very acute depletion
25 of glutathione in these cells.

JOHNSON - DIRECT

2230

1 We have experience and a number of other
2 labs have shown that if you actually deplete
3 glutathione in a cell, like in a cell unlike this, and
4 you get a significantly, like maybe down to 70 or 80
5 percent, what happens is the cell senses that the
6 glutathione is reduced and the cell compensates so it
7 changes.

8 What it does is it actually makes the
9 proteins and the enzymes that synthesize glutathione.
10 If you look at the same cells that were 80 percent
11 depleted at four hours, as shown in this slide on the
12 lower right hypothetical data set, if you look at
13 those same cells at 24 and 48 hours, you may actually
14 have two or three times the level of glutathione in
15 those cells.

16 Those cells would actually be more resistant
17 to toxicity if you actually at that point put a toxin
18 on. So it's a dose and it's a time issue. You really
19 have to run the full spectrum I think of both dose and
20 time to make the right kinds of interpretations about
21 this data. So what this really is showing here or
22 describing is what we call almost like a
23 preconditioning response.

24 So a little bit of stress is good because a
25 little bit of stress causes you to have this

JOHNSON - DIRECT

2231

1 compensatory mechanism that then makes you more
2 resistant to more stress, okay? So this is a very
3 important concept in toxicology in preconditioning
4 response and the way that cells respond to these kinds
5 of issues.

6 Q Now, what is carbon 14 labeled THS?

7 A Carbon 14 labeled tetrahydrofolate.

8 Q Slide 12.

9 A So I don't want to make this complicated.
10 This is more of a question I think. I didn't quite
11 understand this, but I wanted to understand the
12 methionine synthase assay. You know, Dr. Deth spent a
13 lot of time talking about methionine synthase. So
14 methionine synthase is this enzyme he says that's
15 inhibited, and he has an assay that he uses to measure
16 this.

17 I want you to understand this assay, okay?
18 So I'm not going to try to be very complicated with
19 this, I'm going to be very straight. So if you look
20 at this slide, look at the red, okay? So the red in
21 the upper right-hand, the CH₃, okay, that's the radio
22 label.

23 SPECIAL MASTER HASTINGS: That's the what?

24 THE WITNESS: Radio label. Radioactive. So
25 in the end this is what you measure. So that thing,

JOHNSON - DIRECT

2232

1 that red CH₃, has to be on the methionine at that
2 point so that you can actually put it into a machine
3 and the machine tells you how much radioactivity is
4 there, okay?

5 SPECIAL MASTER VOWELL: And the amount of
6 radioactivity would tell you how much --

7 THE WITNESS: How much activity the enzyme
8 has, right.

9 SPECIAL MASTER VOWELL: Okay.

10 THE WITNESS: And so the traditional, I went
11 back and found the methods in enzymology paper that
12 actually uses this assay. The way that this is done
13 is you have this methyl group that's radioactive, so
14 you could measure the enzyme, but what happens is this
15 tetrahydrofolate donates this to the hydroxo-B12, so
16 then what happens is this B12 carries that label,
17 okay?

18 Then that label is transferred to methionine
19 by methionine synthase. So in the end of this
20 experiment what you have is you have this radio
21 labeled red thing that moves through this assay and
22 ends up on what you want to measure and gives you some
23 measure of enzymatic activity.

24 Now, when you go to the next slide, and
25 we'll go to the next slide and want to come back, but

JOHNSON - DIRECT

2233

1 when you go to the next slide what you're seeing here
2 is, and this is D Slide 28 and it's my Slide 13, is
3 you'll see that there's hydroxo-B12, which is referred
4 to in the red lines of all these graphs, and then we
5 have the methyl B12, which is the blue lines in all
6 these graphs.

7 Now, the question I have is if you're adding
8 methyl B12 -- so if you can go back to the other slide
9 -- if you're adding this to the assay, which goes
10 right to here with this, but the methyl B12 doesn't
11 have the radioactivity on it that you put into the
12 assay, how can you measure enzymatic activity?

13 You can't because this is going to be
14 sitting there, you're going to have tons of this
15 around that doesn't have the label on there and all
16 this unlabeled stuff is going to be going into the
17 assay.

18 SPECIAL MASTER VOWELL: Doctor, I'm going to
19 ask you to run back through that again. Instead of
20 saying this and pointing, tell us what it is.

21 THE WITNESS: Okay. So the methyl B12
22 that's shown here that's radioactive.

23 SPECIAL MASTER VOWELL: Okay. And when you
24 say here, you're referring to the CH3 and B12 on the
25 left side?

JOHNSON - DIRECT

2234

1 THE WITNESS: B12, right. The CH3 B12 in
2 this assay, in this case, when you're looking at this
3 diagram, the way the assay is run is what ends up
4 transferring that radio label to the CH3 methionine.
5 You can measure that.

6 But if you're adding CH3 B12 where the CH3
7 is not radioactive, you basically can't measure the
8 methionine synthase activity because you get a CH3
9 methionine that doesn't have any radio label on it.
10 This is why peer review is important because we don't
11 know what he did. We don't know what the assay was,
12 we don't know how this works.

13 Then, if you flip to the next slide, it
14 shows that all of the assays where you use this methyl
15 B12, they're all higher than they are with the
16 conventional assay. So I just can't figure it out.
17 This, again, the reason I do this is because I want to
18 point out this is the kind of thing that a peer
19 reviewer would actually want to address.

20 They'd want to know how this was done. We'd
21 need to see the methods and so on. So I don't want to
22 do this to confuse you, but I'm trying to just make
23 the point that these are the kinds of issues with
24 unpublished data and a lack of peer review. I spent a
25 lot of time looking at this and it got me really

JOHNSON - DIRECT

2235

1 frustrated.

2 BY MS. BABCOCK:

3 Q Now, Slide 34, it was more unpublished data
4 involving an experiment with PCR.

5 A Right.

6 Q Is PCR a technique your laboratory uses?

7 A Yes. We do quantitative PCR all the time.

8 Q As I think the Court indicated yesterday and
9 I'm also acutely aware, we're somewhat informed on the
10 issue of PCR already so we're not going to go into a
11 big description of that, but just generally, looking
12 at a PCR assay like this, what sort of concerns or
13 questions would you need to have answered in order to
14 place any scientific weight on this?

15 A Well, first off, I mean, there's no
16 indication of how many samples were analyzed, we don't
17 now how the assay was run. I mean, was there equal
18 amount of RNAs in the assay. How is the assay
19 standardized? Conventionally when we standardize a
20 PCR reaction we actually do a housekeeping gene or
21 another gene that's not going to change, so you can
22 actually control for that to make sure --

23 SPECIAL MASTER HASTINGS: Let me stop you ad
24 go back because I'm not following on this at all.

25 THE WITNESS: Yeah, that's fine.

JOHNSON - DIRECT

2236

1 SPECIAL MASTER HASTINGS: First of all,
2 we're on your Slide 14.

3 THE WITNESS: Yeah, and we're talking about
4 D Slide 24.

5 SPECIAL MASTER HASTINGS: Yes.

6 MS. BABCOCK: Thirty-four.

7 THE WITNESS: Thirty-four. Sorry. My
8 fault.

9 SPECIAL MASTER HASTINGS: We're talking
10 about the Deth Slide 34, and D Slide 34, refresh my
11 memory. That is another one of his slides describing
12 his original research over the last year.

13 THE WITNESS: Right. Yes.

14 SPECIAL MASTER HASTINGS: That had not yet
15 been published.

16 THE WITNESS: Right.

17 SPECIAL MASTER HASTINGS: And Slide 34
18 describes what? Tell us what it described before you
19 --

20 THE WITNESS: So what Slide 34 describes is
21 it's describing the loss of methionine synthase
22 expression or the loss of RNA in autistic patients
23 versus control patients.

24 SPECIAL MASTER HASTINGS: It describes a
25 test that he did.

JOHNSON - DIRECT

2237

1 THE WITNESS: Yes. It shows the results of
2 a test that he did that in autistic patients this
3 enzyme, this methionine synthase enzyme expression, is
4 significantly lower in autistic patients than in
5 control patients. The problem with the data is that
6 there's no indication of how the data was
7 standardized. The RNA quality is a major problem.

8 I mean, if there's any RNA breakdown in the
9 samples before you run this assay it can completely
10 mess up what you're trying to interpret. The reason I
11 brought this up is because we have tried for a long
12 time to get reliable RNA to do PCR from Down syndrome
13 patients, postmortem kind of tissue, and we have had
14 an impossible time to get a good yield of high-quality
15 RNA to the point that we feel comfortable actually
16 running the PCR at all.

17 We haven't even been able to get RNA that we
18 think we're able to run an assay. So without having
19 RNA gels and RNA analysis to find out if the RNA is
20 good to begin with you can't even run these assays.

21 So the reason I thought this was important
22 is this is a finding that needs to be, you need to
23 see, we need to see in a peer review situation that
24 the RNA preparations and that all the stuff that you
25 need to get before you even do this is of good

JOHNSON - DIRECT

2238

1 quality. None of that is indicated in here. So
2 that's why I wanted to make sure that I pointed this
3 out.

4 SPECIAL MASTER HASTINGS: All right. Go
5 ahead.

6 BY MS. BABCOCK:

7 Q Now, as we've already heard this week a good
8 scientific method involves hypothesis generation and
9 then an effort to try and disprove a hypothesis via
10 testing to see if you can replicate or validate the
11 results, correct?

12 A Correct.

13 Q Is there any indication that Dr. Deth's
14 unpublished data has undergone this process?

15 A No. In fact, it would appear more likely
16 that what Dr. Deth's preliminary data is doing is
17 trying to prove his hypothesis. We had a nice talk
18 from Dr. Melman about this. I'll tell you, the first
19 thing I do when I get a new grad student or postdoc in
20 my lab and they come into my office and they sit down
21 in front of me and I say what's your hypothesis? What
22 are you trying to test?

23 They'll say, well, I think this is the
24 hypothesis and this is the result, you know, this is
25 the results that I think we should get. I looked

JOHNSON - DIRECT

2239

1 right at them and I said what I'd want you to do is I
2 want you to think about this. I want you to think
3 about the hypothesis.

4 I know there are 100 experiments that you
5 could do that you could try to prove this, but what I
6 want you to do is I want you to think of the easiest,
7 the most straightforward and the simplest experiment
8 that if it didn't work would refute your hypothesis
9 and defeat it, okay. And do that one first because
10 you could spend four years of your graduate school,
11 you know, working to try to prove your hypothesis and
12 then do that experiment at the end and the whole thing
13 goes up in smoke.

14 We don't want that. What we want is we want
15 this to be critical from the very beginning, and for
16 the exact same reasons that Dr. Melman explained, this
17 is a critical, critical experiment, even to the point
18 if the data is so important we'll actually ask other
19 people in other labs to try to validate that data even
20 before we publish it.

21 Q And there's no indication that other labs
22 have been able to validate this, correct?

23 A No.

24 Q Do we have any information about the known
25 or potential rate of error with this research?

JOHNSON - DIRECT

2240

1 A I mean, it could be huge. I mean, we don't
2 know.

3 Q And based on your knowledge of this area and
4 the scientific literature, is there any indication
5 that this hypothesis is accepted by the general
6 medical or scientific community?

7 A No.

8 Q And the idea that TCVs could have a role in
9 autism isn't a new or novel one, is it?

10 A No. It's been around since 2000.

11 Q Now, were you here for the testimony of Dr.
12 Kinsbourne last week?

13 A I was here, yeah, for the direct and part of
14 the cross.

15 Q And as a neurotoxicologist, does some of
16 your laboratory work involve the same mechanisms in
17 the brain that Dr. Kinsbourne discusses?

18 A Yes.

19 Q Now, as I understand it, Dr. Kinsbourne
20 posits a theory that in part relies on astrocytes
21 dying or malfunctioning, unable to properly fulfill
22 their role in the brain.

23 A Yes, that's in general what he was saying.

24 Q Now, did you understand Dr. Kinsbourne to be
25 saying that his model of causation was resulting in

JOHNSON - DIRECT

2241

1 neuronal death?

2 A No.

3 Q And can activation of microglia actually be
4 beneficial?

5 A Absolutely. Yeah. There are a number of
6 situations where microglial activation can be
7 beneficial. This, again, is one of these areas where,
8 you know, sitting in the Court and listening to these
9 conversations has been a bit frustrating because I
10 think it's been an oversimplified process. What I'd
11 like to do, if I could, would be to step back.

12 So when I teach I try to involve my class in
13 doing things, and so there's really three cells
14 involved here. It's the astrocyte, the neuron and the
15 microglia. At least that's what we've been talking
16 about. So, Special Master Campbell-Smith, you will be
17 an astrocyte; Special Master Hastings, you will be a
18 neuron; and you get to be the microglia.

19 SPECIAL MASTER VOWELL: Macrophages.

20 THE WITNESS: So in a normal state, you
21 know, the three of you are existing in perfect
22 harmony, and, you know, you're functioning fine, and
23 actually your role is to be kind of this barrier
24 between Special Master Vowell and Special Master
25 Hastings, at least between the microglia and the

JOHNSON - DIRECT

2242

1 neuron.

2 So in my context the astrocyte is actually a
3 very positive component in the brain that maintains
4 kind of this dynamic. It communicates with both the
5 microglia and the neuron and tries to maintain this
6 homeostatic state.

7 So in the context of what we've been talking
8 about with the bad effects of microglia, what happens
9 is, for example, the astrocyte in this situation would
10 fall asleep during my testimony, which I hope doesn't
11 happen, by dysfunctional and that would allow the
12 microglia to jump on and kill the neuron.

13 Not that that would happen either in the
14 courtroom, but, you know, we're trying. So in that
15 case it would be a negative effect. That's kind of
16 what we've been talking about this whole time. Now,
17 on the other situation, there are times and examples,
18 both in vivo, where you, as a neuron, would be
19 damaged.

20 The ability to repair your damage is not
21 dependent upon the astrocytes but is actually
22 dependent upon the microglia. So the microglia and
23 activation of the microglia in that damage situation
24 is actually very important for you to become back to a
25 normally functioning neuron.

JOHNSON - DIRECT

2243

1 We need to understand that neuroinflammation
2 as a term is not astroglia and microglia. It's really
3 a combination of the microglia and the astroglia and
4 how they communicate with each other and how you are
5 suppressing the negative effects, and you're able to,
6 as a microglia, have positive effects in the brain,
7 too.

8 So microglia are not always negative,
9 they're positive. They can be negative in certain
10 kinds of contexts as well. It's a very dynamic system
11 and you can't just generalize by saying, you know,
12 specific things. Go ahead.

13 BY MS. BABCOCK:

14 Q I'm sorry. Did you want to finish?

15 A No, that's fine. That's okay.

16 Q Do microglia release both proinflammatory
17 and antiinflammatory agents?

18 A Yes.

19 Q Now, moving on to proliferation of
20 astrocytes, is this what's known as gliosis?

21 A Yes, the gliosis.

22 Q Now, Dr. Kinsbourne mentioned that glial
23 scars are formed from astrocytes dying. Do you agree?

24 A No, I do not agree with that. Glial
25 scarring actually is a result of activated astrocytes

JOHNSON - DIRECT

2244

1 moving into the region of damage and actually
2 secreting proteins that lay down a matrices that form
3 the scar. Astrocytes in and of themselves aren't
4 dying to form the scar. That's, again, I think a
5 misrepresentation.

6 I talked to colleagues about this that do
7 this work and they completely agree with that is that
8 the astrocytes in a glial scar are not dying to form
9 the glial scar. What they're doing is they're
10 secreting factors, and proteins and matrices that lay
11 down that form the scar.

12 Q So gliosis does not result in astrocytic
13 death? Is that a fair statement?

14 A No. Actually, gliosis results in increased
15 astrocytes.

16 Q Okay. And can death itself affect what you
17 see in astrocytes?

18 A Death itself?

19 Q The process of dying. If, God forbid, I
20 walk out after today's testimony, and I'm crossing
21 15th Street and I'm hit by a bus, is the fact that I'm
22 hit by a bus and then I unfortunately die, could that
23 affect what you see regarding astrocytes?

24 A Absolutely. I mean, if you're hit by the
25 bus, you fall and your head hits the pavement, I mean,

JOHNSON - DIRECT

2245

1 that's going to cause dramatic trauma to the brain.

2 Again, depending on if you're not killed, I
3 mean, I don't want to kill you, but say you're killed
4 instantly and they take your brain out within a matter
5 of an hour, though I don't know why they would take
6 your brain out but let's just say that for example,
7 you may see, you know, inflammatory responses
8 occurring.

9 Say they put you on a respirator or say that
10 you were in the hospital after this head trauma for
11 three days before you died. If they took your brain
12 out at that time you would see massive probably
13 microglial activation and astrogliosis as well
14 associated with the damage.

15 So the time between an insult and the cell
16 death and the time between when you're looking at the
17 brain is very, very critical I think, yes.

18 Q And in animal studies, can the manner in
19 which the animal is sacrificed affect what you see in
20 the brain?

21 A Yeah. Again, very much so. You have to be
22 very careful in how you handle and how you harvest
23 tissues in animals to make sure that you're not
24 causing effects in the brains of animals or whatever
25 you're studying that are due to the way that you knock

JOHNSON - DIRECT

2246

1 the animals out. And harvest the tissues and prepare
2 the tissues because you don't want to generate an
3 effect which is something that you're looking for but
4 that's due to, you know, an artifact of your
5 preparation.

6 Q Now, if astrocytes are failing to reuptake
7 glutamate, what are the short-term and long-term
8 effects?

9 A Well, the short-term effects of not
10 reuptaking glutamate are probably you're going to have
11 an excitatory amino acid. Your glutamate is going to
12 increase in the synapse, it's going to be binding to
13 the receptors and the neuron that's on the
14 postsynaptic side is going to be hyperactive.

15 In the long term, what's going to happen
16 with the increased glutamate excitation is the neurons
17 are going to die. In fact, in vitro and in vivo there
18 are very well-established models using glutamate and
19 glutamate agonists to basically kill neurons.

20 Q Now, if you see a significant long-term
21 decrease in astrocytes, what would you expect to
22 happen to neurons?

23 A They would die.

24 Q And what if instead of dying astrocytes were
25 dysfunctional? What would you expect to happen to

JOHNSON - DIRECT

2247

1 neurons?

2 A They would die.

3 Q And if this was chronic dysfunction?

4 A They would die.

5 Q And in your study of a neurodegenerative
6 diseases, once you see symptoms, what happens?

7 A Well, once you see physical symptoms of
8 somebody having neurodegenerative disease the disease
9 progresses and you get neuronal cell death like, for
10 example, Alzheimer's or whatever, in the region where
11 the cells are stressed that propagates and expands to
12 include the whole brain and eventually kills all this,
13 it kills the cells and you die.

14 Q And is there ever a plateau?

15 A No.

16 Q So does it make sense for Dr. Kinsbourne to
17 say that there is chronic steady cell destruction via
18 the astrocytes without meaning progressive disease and
19 cell death?

20 A No.

21 Q So overall, based on your clinical
22 experience, and your research and your knowledge of
23 the reports and the literature relating to your area
24 of expertise, what is your conclusion regarding Dr.
25 Deth's hypothesis in this case?

JOHNSON - CROSS

2248

1 A It's not valid.

2 Q And what is your opinion about Dr.
3 Kinsbourne's hypothesis involving the astrocytes and
4 neuroinflammation?

5 A Well, the astrocytes and neuroinflammation,
6 but, I mean, how that affects, it's not valid with
7 regard to autism.

8 Q Now, you hold these opinions to a reasonable
9 degree of scientific certainty?

10 A Yes.

11 MS. BABCOCK: I have nothing further.

12 SPECIAL MASTER HASTINGS: Mr. Williams, do
13 you have any questions for this witness?

14 MR. WILLIAMS: I do.

15 CROSS-EXAMINATION

16 BY MR. WILLIAMS:

17 Q I want to find out first, are you
18 disagreeing with the folks at Johns Hopkins and
19 elsewhere that think that at least some autistic
20 people have neuroinflammation as the primary
21 underlying disease process?

22 MR. MATANOSKI: I object to that
23 characterization of the work. That is not what the
24 Vargas article, if that's what you're referring to,
25 states.

JOHNSON - CROSS

2249

1 MR. WILLIAMS: I'd like to hear the witness.

2 SPECIAL MASTER HASTINGS: Well, did you
3 understand the question?

4 THE WITNESS: Yes, sir, I did. He needs to
5 restate it I think for me.

6 BY MR. WILLIAMS:

7 Q What is your understanding of the role of
8 neuroinflammation in autism?

9 A I don't think neuroinflammation contributes
10 to autism.

11 Q You don't?

12 A No.

13 SPECIAL MASTER VOWELL: Did you say triggers
14 or produces?

15 THE WITNESS: Doesn't contribute to it.

16 SPECIAL MASTER VOWELL: Doesn't contribute.
17 Okay.

18 THE WITNESS: I think it doesn't. That's
19 just my opinion.

20 //

21 BY MR. WILLIAMS:

22 Q And have you reviewed the autopsy studies on
23 the autistic brains?

24 A Which ones are you referring to?

25 Q Lopez-Hurtado, for example.

JOHNSON - CROSS

2250

1 A I looked at it. I didn't review it.

2 Q By the way, in the autopsy studies, as well
3 as in the adult monkeys studies and the infant monkey
4 studies, they had controls who were also sacrificed,
5 or killed by drowning, or trauma, right?

6 A I mean, I just made a general comment about
7 harvesting tissues. I wasn't specifically referring
8 to any study.

9 Q So you're not criticizing the autopsy
10 studies that have found differences in the brains of
11 autistics versus controls, let's stop there, are you?

12 A I mean, I've never done autistic versus
13 controlled comparisons with postmortem tissues. I
14 mean, you can look at the papers, but I really can't,
15 I mean, I really don't, it's really not what I do, so,
16 I mean, my focus is mainly neurodegenerative diseases,
17 and so we really don't look at autism, per se.

18 So all I'm saying is that the hypothesized
19 neuroinflammation, the neuroinflammation in
20 neurodegenerative diseases is clearly leads to
21 pathogenic processes that progress cell death and
22 eventual patient death.

23 Q And I'll get to that in a minute but what
24 I'm trying to find out now is just when you're talking
25 about the trauma of death leading to brain damage that

JOHNSON - CROSS

2251

1 could, you know, make it more difficult to see what
2 was going on, isn't using a controls a way to handle
3 that problem?

4 A Absolutely. Yeah. You have to age matched
5 controls, and controls that have the same postmortem
6 time and things like that, sure.

7 Q And that's also true of the monkey studies,
8 right?

9 A Absolutely. Yeah. Any study has to have
10 controls. If you don't have controls, it's not a
11 study.

12 Q Now, one question about the monkey studies.
13 I want to throw them up here because we spent a lot of
14 time the other day when Dr. Brent was testifying, and
15 that may have been yesterday. We saw levels of
16 inorganic mercury in the brain of the adult monkeys as
17 low as 100 parts per billion, 100 nanograms per
18 milliliter.

19 A I don't work on mercury stuff, so, I mean, I
20 don't think my --

21 Q Well, but you were saying that you thought
22 that --

23 A Let me just clarify. The only reason I
24 looked at those papers was to get at what they said in
25 those papers was the dose of mercury in the brains or

JOHNSON - CROSS

2252

1 the level of mercury in the brains so that I could
2 compare it to the in vitro studies. That's all I
3 looked at that for. I didn't look at it to interpret
4 other data.

5 Q But you expressed your surprise that Dr.
6 Deth could get results in the nanomolar range when you
7 thought everybody else was only getting results in the
8 micromolar range.

9 A That's all in vitro studies, yes. I mean,
10 to have that kind of a differential in an in vitro
11 study, as I've already stated, when people are using
12 the exact same cell lines, I mean, I've never seen
13 that big of a differential before, so that's all I was
14 saying. It had nothing to do with the mercury in the
15 primates.

16 Q But the in vivo studies that we looked at,
17 these adult monkey studies, they were getting
18 activated microglia and astrocyte death in the
19 nanomolar range, weren't they?

20 A No, I disagree. I mean, we just talked
21 about this astrocyte death. Astrocytic death is
22 probably not occurring in this process.

23 Q It's not occurring in the adult monkey
24 studies?

25 A I don't recall. I mean, what adult monkeys

JOHNSON - CROSS

2253

1 studies are you referring to?

2 Q I'm referring to the five studies that came
3 out of the mid-1990s.

4 A You know, again, those seemed irrelevant to
5 me as far as what we're talking about today, so I
6 really didn't focus on analyzing that data.

7 Q Let's look at one of the autopsy studies on
8 autistics, if we could. This will be Petitioners'
9 Master Reference List 446. I've got a copy to give
10 you. Here's a copy for you. Is that one of the
11 papers that you looked at?

12 A I glanced at it I think while it was being
13 discussed in Court.

14 MR. WILLIAMS: We've blown up the title
15 there. It's called *A Microscopic Study of Language-*
16 *Related Cortex in Autism*. Then I just briefly show
17 you the abstracts here. If you can pull that up.
18 They were looking at three different brain areas here
19 that they had hypothesized might be related to some of
20 the symptoms of autism.

21 Without worrying about that problem, what I
22 wanted to show you is where they talk about the
23 density of glial cells. It's in about the middle of
24 the abstract. It says the mean density of glial
25 cells. Yeah, that's right, Scott.

JOHNSON - CROSS

2254

1 THE WITNESS: Yes.

2 BY MR. WILLIAMS:

3 Q The density of glial cells was greater, the
4 density of neurons was lesser in autism Area 22 and
5 another area of the brain, and then they also found
6 greater numbers of lipofuscin-containing cells. Now,
7 do you know what lipofuscin is?

8 A It's some kind of deposits in neurons I
9 think. It occurs with aging.

10 Q And they say the results are consistent with
11 accelerated neuronal death in association with
12 gliosis. They go on to say that production of
13 lipofuscin is accelerated, which is a matrix of
14 oxidized lipid and cross-linked protein more commonly
15 associated with neurodegenerative disease, and that's
16 accelerated under conditions of oxidative stress.

17 Now, if there's chronic neuroinflammation in
18 the brains of autistic patients, wouldn't that lead to
19 oxidative stress in their brains?

20 A Well, I mean, you're asking me a question, I
21 haven't looked at the paper. I mean, I, as a
22 scientist, don't read an abstract and make conclusions
23 based on data in a paper.

24 SPECIAL MASTER HASTINGS: Can you say that
25 again?

JOHNSON - CROSS

2255

1 THE WITNESS: I said I cannot just look at a
2 statement in an abstract of a paper and make any
3 conclusions based on what's being done. I mean, I
4 would have to read the whole paper and come back with
5 a critical evaluation of the paper. I'm not going to
6 comment on some highlighted section of the text where
7 I'm asked to make an opinion on that and I have no
8 background for it. I just don't do that.

9 BY MR. WILLIAMS:

10 Q Well, I understand that, but you didn't read
11 this before you came in even though you were going to
12 discuss neurodegeneration in the brains of autistics.

13 A No, I wasn't discussing neurodegeneration in
14 the brains of autistics. I was talking
15 neurodegeneration in what we study. I was just saying
16 that the autistics patients don't have the end result
17 where in chronic neuroinflammation, in chronic
18 astrocytic microglial activation you have progression,
19 neuronal cell death and eventual death of the
20 patients.

21 I mean, I've seen the word plateau used in
22 almost all the time in autistic patients. Plateau.
23 That doesn't happen. In a chronic neuroinflammatory
24 disease or a neurodegenerative disease that I study,
25 all the time you see chronic inflammation, or you see

JOHNSON - CROSS

2256

1 astrocytic activation, microglial activation, neuronal
2 cell death, progresses to death of the patient.

3 Q Is the lifespan of autistic people the same
4 as normal people?

5 A I have no idea.

6 Q You have no idea?

7 A Well, I mean, how long do autistic patients
8 live?

9 Q Yeah, that's my question.

10 A I don't know.

11 Q You never looked at that?

12 A No. I have no reason. I don't study
13 autism.

14 Q Are you aware that the Johns Hopkins group
15 that has published some of these papers we've looked
16 at, Dr. Vargas, and Dr. Zimmerman and others, that
17 they've actually applied for grants to find therapies
18 to treat neuroinflammation as a way to try to treat
19 autism?

20 A No.

21 Q Do you think that's a silly idea because
22 neuroinflammation can't explain autism?

23 A I mean, I really can't comment on that. I
24 have to read the review of the grant and see what
25 their preliminary data say. As we talked about this

JOHNSON - CROSS

2257

1 earlier, as a study section member, what you do is you
2 look at the hypothesis, you critically evaluate the
3 preliminary data and see if the experimental design
4 justifies, you know, the funding of the grant.

5 So, again, I mean, you're asking me to
6 comment on things when I don't have the background or
7 the understanding of what their proposal is actually
8 trying to do.

9 Q Okay. Let me ask you one question about the
10 Berman mouse study.

11 A Sure.

12 Q One difference that I understood they used
13 in their methods compared to what Dr. Hornig's group
14 had done is that they randomized the mice to treatment
15 or nontreatment with thimerosal within a litter as
16 opposed to having, as Hornig did, have the entire
17 litter treated or having the entire litter untreated.

18 A Right.

19 Q And they knew they were taking a risk of
20 cross-contamination because they said in the paper
21 they had done a pilot study to see if there was a
22 problem with cross-contamination. Do you know why
23 they decided to take that risk?

24 A Explain what you mean by risk of cross-
25 contamination.

JOHNSON - CROSS

2258

1 Q Don't mice eat each other's feces when
2 they're young?

3 A You need to explain that to me a little bit
4 better because it's very standard practice to avoid
5 bias by randomizing pups from different litters for
6 your studies.

7 SPECIAL MASTER HASTINGS: We lost you in the
8 middle of that sentence.

9 THE WITNESS: It's very common practice to
10 randomize your litters so that you avoid litter bias
11 in your experiments.

12 So what I mean by that is if I'm doing an
13 experiment in my lab what we would do is if we're
14 going to treat with two different things, let's say,
15 like vehicle and something else, if we need 10
16 animals, we'll take one animal from each litter,
17 different litters, and make that one group and then
18 take an individual animal, another animal, from the 10
19 litters and make that a different group.

20 So the randomization is actually a way to
21 avoid bias in experimental design. That's, actually,
22 I think a very positive thing.

23 BY MR. WILLIAMS:

24 Q We've had testimony that thimerosal, ethyl
25 mercury, is primarily excreted in the feces not the

JOHNSON - CROSS

2259

1 urine, and that's true in the animals. If that's
2 true, and if it's also true that young mice eat each
3 other's feces, isn't that a risk of cross-
4 contamination in a thimerosal experiment?

5 A Well, I mean, my understanding of litter
6 randomization is that you randomize the litters and
7 then you do the dosing, so you don't mix the groups
8 together like in one cage that have been treated with
9 one thing or the other for one thing. You don't do
10 that. My understanding of what they did is they
11 randomized the litters for treatment.

12 They didn't mix the litters together. I
13 think you're misinterpreting what's being said in the
14 paper. I really do. That's being cautious.

15 So the problem, and let's go back to the
16 Hornig paper, if what you said is true, is where they
17 take all of one litter and they treat that with
18 something and they take all of another litter and they
19 treat that with something, then what you could have is
20 you could have a differential between the two litters
21 that are litter bias that has nothing to do with your
22 treatment.

23 So that's why you do the litter
24 randomization. It makes perfect scientific sense to
25 do litter randomization so that you don't bias

JOHNSON - CROSS

2260

1 yourself in interpretation data. If there's something
2 wrong with the one litter, say the mom's not nursing
3 as much, I mean, you're going to cause stress in the
4 animal.

5 That could bias your litter so that that
6 whole litter is biased because they're not nursing as
7 well. It's very standard scientific protocol to
8 randomize your litters. So I think you should
9 probably look at that

10 Q Randomize within litters, you mean?

11 A No, randomize the cross-litters. Yeah,
12 because, no.

13 Q Let's just make sure we're understanding
14 each other because what I understood the Berman paper
15 to do was that they say there were eight mice, eight
16 pups, in the litter and they injected four of those
17 pups with thimerosal and four and up, right?

18 A Right.

19 Q But they knew they were taking a risk of
20 cross-contamination because they went to do this pilot
21 study to check.

22 A No. I think that what they're controlling
23 therefore is litter bias, and I think that's much more
24 important than what you're trying to infer from this.
25 So if you're trying to control for difference

JOHNSON - CROSS

2261

1 responses in different litters by doing it that way.
2 I agree with that 100 percent.

3 Q It's not that expensive to do mice. Why
4 couldn't they do the experiment both ways and see if
5 it makes a difference?

6 A Well, I mean, I can't tell you why they
7 didn't do that, but I'm just saying that the way that
8 it was done, at least the way that you're describing
9 it to me, sounds like pretty good standard design
10 experiments.

11 Q I wanted to ask you the question about
12 inorganic mercury in neurons. Is that good, bad or
13 ugly?

14 A Good, bad or ugly if inorganic mercury is in
15 neurons?

16 Q Yes.

17 A Like I said, I mean, I really don't feel
18 comfortable commenting a lot on mercury because we
19 really don't work with mercury. I'm more interested
20 in the oxidative stress components and the pathologic
21 process that we see in the disease. From a toxicology
22 standpoint, I would say it probably isn't good. It
23 probably isn't good having inorganic mercury anywhere.

24 MR. WILLIAMS: That's all I have. Thanks.

25 MS. BABCOCK: I have one quick followup.

JOHNSON - REDIRECT

2262

1 SPECIAL MASTER HASTINGS: Please go ahead.

2 REDIRECT EXAMINATION

3 BY MS. BABCOCK:

4 Q Now, on your cross, they put up the Lopez-
5 Hurtado paper and I'm not going to ask you to comment
6 specifically on the results. We know it's not
7 something you're comfortable doing. We did note that
8 what was highlighted there noted neuronal loss.

9 A Right.

10 Q And you saw that line that they highlighted?

11 A Right.

12 Q Assuming that these results are correct, is
13 that consistent with what Dr. Kinsbourne has
14 hypothesized about sedisate of astrocyte death and
15 dysfunction without progressive disease process?

16 A No.

17 MS. BABCOCK: Nothing further.

18 SPECIAL MASTER HASTINGS: Any questions for
19 this witness?

20 (No response.)

21 SPECIAL MASTER HASTINGS: Mr. Williams,
22 anything further for this witness?

23 MR. WILLIAMS: Nothing further.

24 SPECIAL MASTER HASTINGS: All right. Dr.
25 Johnson, we're done with you. Thank you very much.

JOHNSON - REDIRECT

2263

1 THE WITNESS: Thank you.

2 (Witness excused.)

3 SPECIAL MASTER HASTINGS: Well, counsel,
4 it's unexpectedly early in the day. Do you have any
5 more witnesses you've planned to call today for the
6 government?

7 MR. MATANOSKI: No, sir.

8 SPECIAL MASTER HASTINGS: All right. Let me
9 raise an issue then while we're here. We had talked
10 last week about Respondent's Exhibit LL, the Pardo.

11 MR. MATANOSKI: Yes, sir.

12 SPECIAL MASTER HASTINGS: And we had talked
13 about whether we needed to talk further about that
14 exhibit.

15 MR. MATANOSKI: That's correct. I can tell
16 you right now that Dr. Pardo, my last information was
17 that he is not in the country until the 21st. So I
18 have not been able to inquire of him any further about
19 whether he'd be available to answer written questions,
20 whether he'd be available to come and testify.

21 I know that my last conversation with him he
22 was not willing to testify, and I haven't been able to
23 have a conversation with him since then since he's
24 been out of the country.

25 I know we've discussed some other matters

1 perhaps that might help with respect to further seeing
2 his views, and I, frankly, would be anxious, if
3 Respondent's will be willing to, to have those further
4 views in front of the Court because I think they
5 expand upon --

6 SPECIAL MASTER HASTINGS: Speak up.

7 MR. MATANOSKI: I'm sorry. I think they
8 expand upon and in fact make even more apparent the
9 limitations he believes that can be placed upon his
10 work, at least for the interpretations or
11 extrapolations that are being drawn from it by the
12 Petitioners right now.

13 I have not been able to speak to him since
14 actually before the trial before I even received the
15 letter from him, and I understand that he's not back
16 in this country until I believe the 21st.

17 SPECIAL MASTER VOWELL: Of this month?

18 MR. MATANOSKI: Of this month, which is
19 tomorrow.

20 SPECIAL MASTER HASTINGS: Tomorrow. So you
21 hope to have a chance to talk with him tomorrow at
22 some point?

23 MR. MATANOSKI: I'm not sure when he gets
24 back in the country tomorrow. That was the date I was
25 given. Yes, as soon as he came back we were hoping to

1 get in touch with him to discuss whether he'd be
2 available in some fashion to elaborate on the comments
3 that he had in his letter.

4 SPECIAL MASTER HASTINGS: And if I recall
5 correctly, the Petitioners, when the Respondent filed
6 Exhibit LL, Mr. Powers, your response to it was that
7 we would like to cross-examine him?

8 MR. POWERS: Yes, Special Master. The
9 letter actually turned out to be something a little
10 bit different than what I had expected to see. My
11 understanding initially was that this was something
12 that was being given by Dr. Pardo to Respondent, and
13 when one looks at the letter, it's correspondence
14 between Dr. Kemper and Dr. Pardo.

15 So I was thinking that it would be something
16 akin to an expert report or a commentary that would
17 resemble an expert report that would be given to
18 Respondent and be filed in, but it's correspondence
19 between nonparties here. So to that extent, we're
20 prepared to use that letter in cross-examination of
21 witnesses since it's been filed in the case to explore
22 the areas that are raised in there.

23 So we're prepared to use it in cross-
24 examination. On the other hand, if there's any -- and
25 it sounds as if what Mr. Matanoski's further

1 characterization of what Dr. Pardo might believe, if
2 this is going to be a surrogate for an expert report
3 that they're relying on, then we certainly would want
4 to cross-examine.

5 We completely understand that under the
6 program an expert report, for example, can be
7 submitted and no cross-examination is had, but what we
8 see in this case is nothing that even resembles an
9 expert report at this point.

10 SPECIAL MASTER VOWELL: Well, we frequently
11 consider letters, do we not? For example, a letter
12 from one expert physician to the primary care
13 physician saying I think X and this is why I think it.
14 You submit those as exhibits all the time.

15 MR. POWERS: Correct, and that's why I'm
16 saying that if this is correspondence, then, yeah, you
17 take it at face value, cross-examine to explore the
18 underlying basis for what's being said and the context
19 from which its emerged, and we're totally prepared to
20 do that.

21 All I'm saying is that if this letter is
22 something that is eventually going to be reduced to a
23 form like an expert report stating an opinion being
24 filed on behalf of the Respondent in support of their
25 case, then we would want an opportunity to cross-

1 examine Dr. Pardo.

2 At this point it looks like the letter is
3 like any other correspondence that might come in, and
4 we're prepared to use it in cross-examination at this
5 point.

6 MR. MATANOSKI: The letter obviously was
7 written to one of our witnesses, and, as such, I agree
8 with Mr. Powers, he can cross-examine the witness as
9 to those matters. The letter gives him a little bit
10 of a heads up of what Dr. Pardo has relayed to Dr.
11 Kemper. So I expect we are going to hear some things
12 from Dr. Kemper about what Dr. Pardo and his
13 colleagues have found in those autopsy studies.

14 The letter is not submitted as an expert
15 report. Dr. Pardo is explaining what his study --
16 he's almost like a fact witness, if you will. His
17 study has been looked at and relied on heavily by
18 Petitioners at this point. He's seen that it's been
19 relied on by them and he's trying to explain the
20 limits that one can place on his work, at least as far
21 as the interpretations or extrapolations therefrom.

22 We saw something similar in the last trial
23 when Dr. Oldstone's work was being characterized in
24 certain fashion by witnesses, and Dr. Oldstone came in
25 and said these are the limits of what I think you can

1 take from my work. I think that's what Dr. Pardo, up
2 to this point at least with respect to the
3 correspondence, has done in this case.

4 SPECIAL MASTER HASTINGS: With that
5 understanding of what the government's purpose in
6 introducing the letter, are you comfortable, Mr.
7 Powers, with its admittance?

8 MR. POWERS: Certainly, Special Master. As
9 I said, just on its face right now we're comfortable
10 with it being in the record, and we're completely
11 prepared to use it in cross-examination and explore
12 the issues that are raised in that letter.

13 SPECIAL MASTER HASTINGS: Let's take a five-
14 minute break here. I want to confer with my
15 colleagues about scheduling very briefly and then
16 we'll get back and presumably we'll be done for the
17 day and we'll make a plan for tomorrow. Let's take a
18 five minute break here.

19 (Whereupon, a short recess was taken.)

20 SPECIAL MASTER HASTINGS: During our recess,
21 Mr. Powers noted to us off the record that he would
22 like to make a brief statement of explanation of
23 something, so go ahead, Mr. Powers, and address that.

24 MR. POWERS: Thank you, Special Masters. I
25 appreciate the opportunity just to take a quick moment

1 to clarify, particularly for the sake of people who
2 may be listening in outside of the courtroom, relating
3 to Dr. Mumper's testimony. Dr. Mumper described two
4 young adults in her testimony.

5 One of them is a young man who lives in
6 Maryland and was involved in litigation, and she was
7 involved in that litigation. That was Mr. Blackwell.
8 There was another young man that was a patient of
9 hers, and she was treating him and he died while in
10 her care.

11 There apparently has been confusion among
12 some people that these are the same person. Dr.
13 Mumper has requested, and the families of those folks
14 have requested, that we just made clear that Mr.
15 Blackwell fortunately is alive and well and is not
16 involved in Dr. Mumper's care, and that the young man
17 who died in, while he was treating with Dr. Mumper
18 that she testified about is a different person.

19 So these were two different young men, and
20 the young man who died is not involved in this
21 litigation. That's the young man that she was
22 describing the family has made his brain tissue
23 available for research via autopsy and allowing
24 scientific researchers to work with it.

25 So she was just requesting that we make it

1 clear that those are two very different young men. I
2 appreciate the opportunity to do that.

3 SPECIAL MASTER HASTINGS: All right. Thank
4 you, Mr. Powers. The other matter is we were
5 surprised this morning that the testimony of the two
6 witnesses scheduled today was concluded so quickly.
7 Particularly, the direct turned out to be under an
8 hour for each of them.

9 We just want to make the point that, you
10 know, we want to make the full use of the time we
11 have. If you're in a situation in the future where
12 you realize, you know, we've got two witnesses
13 scheduled but we only expect our direct of each of
14 them is going to be less than two hours that you would
15 let us know and we would perhaps consider the
16 possibility of bringing in a third witness.

17 With that in mind, I don't know if you have
18 other witnesses today, if you might consider taking a
19 lunch break and doing another witness today? Mr.
20 Matanoski?

21 MR. MATANOSKI: Unfortunately, sir, I don't
22 believe that we'd be ready with any other witnesses
23 today. I will look ahead at the upcoming witnesses
24 and see if this situation might develop in the future
25 with our trial schedule. If it looks like it will,

1 then I'll try to move witnesses around in some fashion
2 that makes sense.

3 Most of them are not local, so with the
4 schedules, their travel schedules as well, there may
5 have to be some movement on that so that we would use
6 the full day and then have as much flexibility and
7 time towards the end of the trial as possible, or if
8 that frees up a day in the middle of it, at least it's
9 a full day and we can go about our other tasks without
10 coming in here and having, you know, just a half a
11 day.

12 Unfortunately today, I apologize. It did
13 surprise us a little bit. I mean, it became a little
14 bit more apparent as we were running up to today that
15 our direct would be shorter than we had anticipated at
16 first.

17 SPECIAL MASTER HASTINGS: Then, Mr. Powers,
18 did you want to say something?

19 MR. POWERS: Yes. I have just two things,
20 both related to scheduling. One, if there's going to
21 be a change in the schedule we certainly would want to
22 know really early because it's one thing to prepare
23 for direct, it's another thing to prepare for cross.
24 They're two different animals.

25 So the farthest in advance notice we could

1 get of a change would be appreciated. I also wanted
2 to let the Special Masters, and, again, we've talked
3 about this earlier with Respondent, know about what we
4 anticipate for scheduling so far with rebuttal next
5 week.

6 SPECIAL MASTER HASTINGS: All right.

7 MR. POWERS: We have confirmed Dr. Deth's
8 availability on Thursday. I guess that's the 29th.

9 SPECIAL MASTER HASTINGS: All right.

10 MR. POWERS: Dr. Greenland is going to be
11 available, and he would likely be available by
12 telephone. He's in Los Angeles. Particularly for how
13 brief we would anticipate his rebuttal, flying him
14 back and forth across the country, seemed better to do
15 it by phone.

16 We've discussed the scheduling with Dr.
17 Mumper. She has a full day of patient care that she
18 cannot reschedule on Thursday, but she is available
19 Friday. So we anticipate Dr. Mumper being here
20 Friday. Dr. Kinsbourne, it sounds as if at least with
21 one of the witnesses today is raising issues related
22 to Dr. Kinsbourne's testimony.

23 So if he is in the mix for rebuttal, we will
24 work on his availability for one of those two days,
25 but that's not determined yet. That's where we stand

1 right now with Dr. Deth confirmed for Thursday, Dr.
2 Mumper confirmed for Friday, Sandra Greenland
3 available by phone. Do you know what day?

4 MR. WILLIAMS: I don't know which day.

5 SPECIAL MASTER HASTINGS: Okay.

6 MR. POWERS: And then Dr. Kinsbourne
7 possibly on either one of those days.

8 SPECIAL MASTER HASTINGS: All right. Thank
9 you.

10 SPECIAL MASTER VOWELL: We've just been
11 informed by our technological people that we can do
12 phone testimony but that would preclude people
13 listening in on that date because we only have one
14 phone line. However, because we have the digital
15 audio files that we can post, people can listen to the
16 testimony, it just won't be a live listening.

17 So I think it would be more important to
18 avoid having Dr. Greenland fly across country for what
19 may be just a few moments of testimony.

20 MR. POWERS: And Petitioners absolutely
21 agree with that. That makes sense.

22 SPECIAL MASTER HASTINGS: All right. Any
23 other scheduling matters we should talk about?

24 MR. MATANOSKI: No, sir.

25 SPECIAL MASTER HASTINGS: If not, then we're

1 done for the day, and we're going to start at 10:00
2 a.m. Eastern time tomorrow with Dr. Rust's testimony.

3 MR. MATANOSKI: Yes, sir.

4 SPECIAL MASTER HASTINGS: All right. Thank
5 you very much. We'll see you tomorrow. We're
6 adjourned.

7 (Whereupon, at 11:43 a.m., the hearing in
8 the above-entitled matter was adjourned, to reconvene
9 at 10:00 a.m. on Wednesday, May 21, 2008.)

10 //

11 //

12 //

13 //

14 //

15 //

16 //

17 //

18 //

19 //

20 //

21 //

22 //

23 //

24 //

25 //

2275/2345

REPORTER'S CERTIFICATE

DOCKET NO.: 03-584V and 03-215V
CASE TITLE: Claims for Vaccine Injuries
HEARING DATE: May 20, 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 20, 2008

Christina Chesley
Official Reporter
Heritage Reporting Corporation
Suite 600
1220 L Street, N.W.
Washington, D.C. 20005-4018