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: 4101 through 4374

Place: Washington, D.C.

Date: May 30, 2008

IN THE UNITED STATES COURT OF FEDERAL CLAIMS
OFFICE OF SPECIAL MASTERS

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SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	)	

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

Friday,
May 30, 2008

The parties met, pursuant to adjournment, at 9:03 a.m.

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

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C O N T E N T S

E X H I B I T S

PETITIONERS' EXHIBITS:	IDENTIFIED	RECEIVED	DESCRIPTION
12	4108	--	Marcel Kinsbourne settlement documents
13	4118	--	NIMH study on riluzole
14	4190	--	Three-slide component of Elizabeth Mumper
15	4213	--	Jordan King video
16	4213	--	William Mead video
17	4270	--	Letter

P R O C E E D I N G S

(9:03 a.m.)

SPECIAL MASTER VOWELL: Good morning. Please be seated. We are back on the record for another day of proceedings on the second theory for the omnibus autism proceeding. We are taking rebuttal testimony. Are there any matters that counsel would like to address on the record before we begin today?

MR. POWERS: No, Special Master, not for Petitioners.

SPECIAL MASTER VOWELL: Thank you.

MR. MATANOSKI: No, ma'am.

SPECIAL MASTER VOWELL: Thank you. Mr. Powers, to call your next rebuttal witness.

MR. POWERS: Yes. Thank you, Special Masters. The Petitioners, at this time, would like to call in rebuttal Dr. Marcel Kinsbourne.

SPECIAL MASTER VOWELL: Thank you. Good morning, Dr. Kinsbourne, please be seated. You will continue under the oath that you were administered and took earlier in the proceeding.

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Whereupon,

MARCEL KINSBOURNE, M.D.

having been previously sworn, was recalled as a witness herein and was examined and testified further as follows:

DIRECT EXAMINATION RESUMED

BY MR. POWERS:

Q Good morning, Dr. Kinsbourne.

A Good morning.

Q And since we are making an audio record here, I'll reintroduce myself. I'm Tom Powers, and, as you know, I represent the Mead and King families, as well as Petitioners' Steering Committee.

Now, Dr. Kinsbourne, you were called to testify during the first week of this hearing. Correct?

A Yes, sir.

Q And in the subsequent days of the hearing, after your appearance in that first week, other witnesses appeared that, based on your review of the record of the proceedings, addressed some of the specific points that you raised in your direct testimony in your report. Correct?

A Yes.

Q So, this morning, what we're going to do

primarily is focus on the specific testimony that you now would like to respond to, and that is testimony that we heard from the government's side of the case in the days after your first appearance here. Correct?

A Yes.

Q Now, before we go into that, there was a matter that you might recall from the cross-examination following your direct examination during the first week of this proceeding. Do you recall, in cross-examination, questions regarding your employment status at the University of Toronto some 31 years ago?

A I do.

Q Do you recall, in that line of questioning, you were asked whether you had been terminated from the university and discussion of the grounds of your termination? Do you recall that?

A I do.

Q What was your response, at that point, to the document that you saw, which was a Grievance Committee report?

A I didn't actually see the document, so I don't exactly know who sent it to whom. I don't think it was a formal report. But in terms of the issues involved, I pointed out that there had been some

allegations made. I filed a grievance. The grievance prevailed, that all allegations and charges were withdrawn, and that the protective order was issued about the whole matter.

I have to say, in these 30-some years, nobody until now has violated that protective order.

Q And you indicated that there might be further information about this matter that might be available and that you were going to see if you could track that information down and find it. Did you, in fact, do that?

A I did. I looked in my file and found a copy of the settlement with the university, which I sent to you, and --

MR. POWERS: Let me interrupt you for just a second, Dr. Kinsbourne.

We're going to mark the settlement documents as Petitioners' Trial Exhibit 12, and I have given a copy to Respondent's counsel before we began a little while ago this morning. I'm going to provide copies to the Special Masters here.

(The documents referred to were marked for identification as Petitioners' Exhibit No. 12.)

BY MR. POWERS:

Q Dr. Kinsbourne, on the screen in front of you, and on the table in front of you, you see a document. Could you just describe for the Special Masters that that document is?

A Yes. This is the outcome of the grievance proceedings, and this document was drawn up by the attorneys for the university and Mr. Jeffrey Sach, who represented my interests and who currently is, I believe, general counsel to the faculty at the university.

By the way, I did talk to Mr. Sach, and he will be available for any questions that the Court might have to follow up on this.

At any rate, this settlement made it clear that all charges were withdrawn and that I was not, in fact, terminated.

Q And, in fact, you had represented, under cross-examination, that you, in fact, resigned voluntarily and were given an opportunity to then seek another teaching position. Is that statement also reflected in this settlement?

A I'm not sure that it's in that document, but I've certainly got more papers to make that point, should the Court require.

Q The document will speak for itself, but I just wanted to give you an opportunity to let the Special Masters know that, under cross-examination, when you referred to additional documentation and a settlement, that this, in fact, is what you were referring to.

A Yes, sir.

Q Okay. So we're going to move on from this and talk about some of the testimony that addressed both your expert report and your direct testimony.

Do you recall Dr. Rutter's, Sir Michael Rutter's, testimony?

A I do.

Q And in a portion of Dr. Rudder's testimony, he had critiques of your mechanistic model of neuroinflammation and overactivation. Do you recall some of those critiques?

A I do.

Q One theme of the critique seemed to be that your model and your analysis lacked scientific rigor. "Scientific rigor," I think, was a term used, a lack of scientific certainty.

So my question for you, Dr. Kinsbourne, is how you would respond to that critique and explain to the Special Masters even whether you were attempting

to state an opinion to a degree of scientific certainty or not.

A Yes, sir. Dr. Rutter described himself accurately as a neuroscientist. He is, and I have a high regard for his work. Certainly, as I, in fact, made clear in my report, I was not presenting, as it were, a scientific discovery, which I could prove to be the case, and I did not think that that was my role in these proceedings to do.

What I'm presenting is a reasonable medical mechanism by which this could have happened, and Dr. Rutter really didn't address the actual purpose and role of my proposal. When neuroscientists use the word "speculation," what they are really saying is that, whether there is evidence or not, if one draws a conclusion before the evidence is complete -- speculated. I, however, was not drawing a conclusion; I was offering a possible mechanism.

Q And that possible mechanism, as you described it; in your opinion, is that mechanism biologically plausible?

A It is biologically plausible, and it is grounded in contemporary scientific literature, as is reflected in my report.

Q And, in fact, there was a specific portion

of the model that Dr. Rutter addressed, and he seemed to take issue with the glutamate-mediated, overactivation model that you described. Do you recall his testimony on that issue?

A Actually, not exactly in those terms. I don't think Dr. Rutter purports to be a neurologist or a neuroscientist. I think he is very careful to stay within his discipline, child psychiatry, and I'm not sure that he actually critiqued the neurobiological aspect.

What he took exception to was the more global interpretation of the hyperglutamanergic, hyper-arousal model as a viable model for autistic behavior.

Q And how would you respond, in general, to that critique of Dr. Rutter?

A Well, it seemed to me that he was critiquing something from his memory of many years ago, which perhaps has not survived. It certainly hasn't, in my memory, but he wasn't really talking about what I presented. He talked about some notion that autistic children are overly emotional or overly reactive, which is not, in those words, accurate. That's not at all what I'm presenting.

In fact, although the over-arousal model did

have earlier origins, the first studies that presented it were EEG studies. They ran studies of children's emotional behavior. There was evidence presented that the brain of these children was overactive, as based on the EEG findings as were available and construed at that time.

Now, this overarousal model has survived, and it has significant support at this time, and, in my report, I reference the important document by Rubenstein and Merzenich, which adopts that model, and other articles which, in fact, give evidence of this overarousal in psychophysiological terms.

Q And, in addition to that, there is contemporary scientific evidence supporting the idea that the role of excess glutamate contributing to this overarousal, there is contemporary support in the scientific literature for that aspect of your model. Isn't that correct?

A Right. Again, as with the overarousal model, the hyperglutamanergic idea is not my idea. It was presented for -- I proposed it, and, again, I mention some of the origins in my report, and I could provide the Court with more documentation of that fact.

My role has been to consider the literature

on glutamate excess in neuroinflammation, consider the literature on glutamate excess in neuroinflammation in autistic individuals, put it together with the evidence for overarousal in autistic children, and combine the neurobiology and the behavior in what I take to be a coherent fashion.

Q Now, Dr. Kinsbourne, let's talk specifically about some of the more contemporary scientific literature that supports a couple of the aspects that Dr. Rutter is criticizing.

First, let's talk about glutamate, and the first article we're going to refer to is Petitioners' master --

MR. MATANOSKI: I just want to clarify. I think the witness has already stated that Dr. Rutter was not criticizing the portion of his data that had to do with glutamanergic response.

MR. POWERS: Well, we're talking about the glutamanergic response as triggering the overactivation, and if we want to parse it out, I can pretend that he is addressing Dr. Rustferti.

BY MR. POWERS:

Q So, Dr. Kinsbourne, do you recall that Dr. Rust described a specific critique of you positing the idea that the glutamanergic response was not

contributory to the appearance of autistic symptoms?

A Yes, sir.

Q Okay. Let's talk about some of the contemporary scientific literature that addresses that issue. This will be Petitioners' Master Reference List 570. I know the screen is hard to read, Dr. Kinsbourne, so I'm going to leave the stand here and give you a paper copy of this article.

A Thank you.

Q So, Dr. Kinsbourne, if you look at the document in front of you -- this is Reference List No. 570 -- is this an article by Dr. Aschner that talks about glutamate and reactive oxygen species and methyl mercury neurotoxicity?

A Yes, sir.

Q So I would like to just briefly direct your attention to page 2 of the exhibit, and if you look at the right-hand column, about half-way down, there is a highlighted section, if we could focus on that.

A I could if it were highlighted.

Q Well, on the screen, it should be.

A I see, yes. Okay.

Q We're trying to coordinate highlighting multiple paper copies and the electronic, but on the electronic, you should see it there.

A I was just reading a spy novel where the highlighting magically disappears.

Q What is the point of the highlighted section there? We don't need to read it aloud because the Special Masters, obviously, can read the article. What do you think the significance of that highlighted portion is?

A It encapsulates a major part of my proposal, and, indeed, this is one of the sources of my proposal.

Q And this is a 2007 article. Correct?

A Right. I'm saying, this is a recent -- of Dr. Aschner's vary distinguished research program, and I also refer to other articles from his group.

Q We're also going to take a look at Petitioners' Master Reference List No. 567, and, Dr. Kinsbourne, is that an article by Dr. Purcell and others that discusses post-mortem brain abnormalities of, again, the glutamate neurotransmitter system and autism?

A That's correct.

Q I would like to draw your attention to what is the exhibit page number 9, and if you look at the right-hand column, what I'm going to highlight for you is, in the first third of that top paragraph, there is

a sentence that begins, "If the increase in GFAP," all the say down to Footnote 31. Again, the Special Masters have the study, and they can read it, but what is the significance of this particular discussion in Dr. Purcell's paper for your theory?

A I think the relevance is that GFAP is a protein which is released by astrocytes under stress, and the article patients out that there may be reactive gliosis. In other words, there may be a proliferation of astrocytes in response to that stress, and that proliferation may contribute to autism pathophysiology. In other words, it may contribute to the mechanism by which an individual becomes autistic.

Q And at the very bottom of that page, again, on the right-hand column, the sentence that begins, "Disrupted," and it will continue on to page 10 of the exhibit, so we'll give our folks to get the entire thing highlighted for you, going from one page to another.

A The first sentence, beginning with "Disrupted," encapsulates the point that I'm trying to make for mechanism, that disruptive glutamate transmission could account for a constellation of the cognitive deficits of autism. I would just add, in my

case, cognitive and behavioral deficits in autism.

Q And if you continue on to the next page, then, it actually starts to talk about the symptoms, particularly, that are related to glutamate.

A Correct. These are relevant symptoms, which I do believe can be explained in terms of disruptive glutamate transmission, and, indeed, as the group points out, that people have taken this seriously, and are, in fact, currently, trying to determine whether drugs that block glutamate receptors might alleviate autistic symptoms, and, in fact, there are several ongoing studies using two agents that I could mention funded by the NIH and by a foundation which is, in fact, finding out whether glutamate receptor antagonists could help autistic children.

MR. POWERS: In fact, we have what we're going to mark as Petitioners' Trial Exhibit No. 13 a brief report of a clinical trial, I think, involving one of the drugs that you're talking about.

(The document referred to was marked for identification as Petitioners' Exhibit No. 13.)

BY MR. POWERS:

Q And, Dr. Kinsbourne, Exhibit 13 that you have in front of you and is now up on the screen;

could you describe to the Special Masters what this document is?

A Yes. This is a study which has been funded by the NIMH, the Mental Health Institute, with the following rationale.

Riluzole is a glutamate blocker. It has been shown to be effective in childhood obsessive-compulsive disorder. Now, we're going to try to see the effects of riluzole glutamate blocking also, as well as in childhood OCD, in children with autism-spectrum disorders.

Now, an important point is that, as I discuss at length in my report, the neuroinflammation, which was discovered by the Vargas/Pardo group, is, in my opinion, more likely harmful to the brain than helpful, but some people have objected that actually it might be helpful or protective of the brain function.

If anybody seriously believed that, this study would never have been funded. Children would have been put at risk if it was a protective mechanism that was being blocked.

So I think that highly responsible scientists from Johns Hopkins and from the study group at NIMH have felt that it was appropriate to attempt

to diminish glutamate transmission in autistic children.

Q And we're actually going to take a quick look at page 3 of this exhibit -- it's page 3 of 5 -- and at the very top of that page, the first full sentence that begins, "Glutamate plays," we're just going to highlight that sentence. What this clinical trial description says is that glutamate plays a crucial role in the regulation of excitatory activity within this circuit and may be involved in the idiopathogenesis of OCD, which is obsessive-compulsive disorder.

Is this statement about glutamate's role in the regulation of excitatory activity; is that consistent with the central theme of your opinion in this case?

A That's correct, yes.

Q We can pull that down from the screen.

Briefly, back to Dr. Rutter and his description of your model of overactivation or overarousal as being somehow historically relevant, are you aware of contemporary scientific discussion of this very theory?

A Yes, indeed.

Q And would that include discussions by Dr.

Casanova, who is one of the Respondent's witnesses who submitted an expert report but did not appear and testify?

A Correct.

Q So I'm going to put up on the screen Petitioners' Master Reference List No. 274, and if we could highlight just the title so that Dr. Kinsbourne can identify it for the Special Masters and for the record.

And, Dr. Kinsbourne, I do have a paper copy, so I'm providing it for you.

So, Dr. Kinsbourne, you have in front of you a Science Journal article called "Mini-column Nerve Pathology in Autism" by Dr. Casanova and others. Is that correct?

A Yes, it's an important document.

Q Let's go ahead and look at the very last page of text in that article, which would be, in terms of the exhibit -- I believe it's page 4 of the exhibit -- and I would like to highlight for you the last full paragraph in that article.

Now, in this highlighted section, is it fair to say that Dr. Casanova is discussing the arousal model in the brain as related to autism spectrum disorders? Is that the general thrust of this

paragraph?

A It's quite specific, yes.

Q He goes on to say, in about the third sentence in this, that the arousal theory is of some interest because it is consistent with the reduction of inhibitory into neuronal activity.

So the arousal theory is certainly interesting enough to Dr. Casanova to discuss it in this article. Correct?

A Yes.

Q And his discussion is on the flip side of the coin of the glutamate homeostasis, which is the inhibitory process, GABA.

A Correct. Still addressing the excitation-inhibition balance.

Q And the excitation-inhibition balance, as you've already testified, is a core concept in your model that you've described?

A It is, and it is a core concept in brain functioning.

Q So it's a functional model, but is there also some possible implication in recent science that the excitation and neuroinflammation and glial activation might actually be causally related to brain pathology?

A A number of sources have raised that question.

Q I'm going to show you what's been filed here as Petitioners' Master Reference List No. 104 coming over with a paper copy, and we'll get that on the screen.

Now, Dr. Kinsbourne, this is an article by Dr. Courchesne and his group, and it's an article that's referred to quite often in these proceedings that's called "Autism at the Beginning." Is that what you see in front of you?

A It is.

Q I would like to turn, and, unfortunately, I don't have my exhibit pages marked, but it's page 590 of your copy, Dr. Kinsbourne; 590 is the journal page number.

SPECIAL MASTER VOWELL: Which, for the record, is page 14.

MR. POWERS: I was just counting, and you're much quicker than I. I appreciate it. It's page 14 of the exhibit.

What I would like to do, there is a section highlighted there, but before even talking about that one, in the left-hand column, the last full paragraph, there is a sentence that begins, "Glial cells," and I

would just like to highlight that first full sentence of the last paragraph on the left-hand column.

Now, this sounds that glial cells play key roles in brain organization during development, as well as in neuroinflammatory reactions. Correct?

A Yes.

Q So the bulk of your report describes the role of glial cells in neuroinflammatory reactions. Correct?

A Could.

Q So Dr. Courchesne is acknowledging that role of glial but also mentioning a little bit new, which is that it plays a role in actually organizing the brain. Correct?

A Yes. Actually, it isn't even new. I think it's part of what we know about neurodevelopment that glial cells actually provide the scaffolding by which neurons move to their appointed locations.

Q Now, you've heard testimony of neuropathologists, including Dr. Kemper, how have argued apparently that pathological abnormalities in the brain cause neuroinflammatory responses in some cases. They have hypothesized that. Correct?

A That's correct.

Q What they haven't discussed is the notion

that glial disruption or glial dysfunction might itself be the cause of the underlying pathology. Do you recall them discussing that issue at all?

A No. That didn't come up.

Q Well, let's go ahead and look at the right-hand column and the first full paragraph, and let's highlight the first half of that paragraph, ending at the word "cerebellum."

Now, what Dr. Courchesne is talking about here is that excess glial production of excess glial activation actually has the potential to produce any or all of the previously described, microstructural findings. Correct?

A Yes.

Q So he is talking about glial disruption affecting the physical architecture of the developing brain.

A Correct. In a manner so as to generate the kind of abnormalities that, in fact, have been reported neuropathologically in brains of autistic individuals.

Q Including the minicolumn abnormalities that Dr. Casanova -- in fact, there is a specific discussion of frontal minicolumn abnormalities. Correct?

A Correct.

Q And that would be in reference to Dr. Casanova's work with minicolumns.

A Yes, it would.

Q So would you characterize the current scientific literature as supporting the notion in your report and in your testimony that glial activation can cause neuroinflammation leading to the symptoms of autism, but also that glial overactivation can actually cause changes to the developing brain's structure?

A Yes. There is support for these propositions.

Q And the support is described in some of the articles that we just took a look at. Correct?

A Yes, sir.

Q Now, Dr. Rust also had some comments on your testimony, and one of the issues that you raise is that, in a couple of places, you misrepresented the cited articles. Do you remember some of his testimony on that?

A I do.

Q And one of those points was, in looking at articles by -- I think it's Dr. Friedman. Dr. Friedman is the lead author on one on the other with

Dr. Petropolous, and he is the second author on the other, with Dr. Petropolous.

We're going to take a look at those, and, in particular, we're going to start off with Physician's Master Reference No. 320. This is the article where Dr. Petropolous is the first author, and Dr. Friedman is the second author.

Q So could you describe for the Special Masters and for the record what it is that we have on the screen here?

A This is a study of the brain of individuals with autism spectrum disorder by MRI, conductive resonance imaging, and it talks about a particular aspect of imaging which is called the "T-2 phase" of imaging.

Q And do you recall that Dr. Rust characterized your citation of this particular piece as inaccurate because his claim was that this article doesn't talk about directly neuroinflammation leading to the symptoms of autism.

A Could.

Q Now, you didn't cite it for that proposition, did you?

A No. I didn't cite it for that.

MR. POWERS: Let's go ahead and turn to page

4 of the exhibit, and, actually, it starts on page 3. I'm sorry. The very last sentence on page 3, and then going through the first full paragraph on page 4, and it will take a moment to get that on the screen. We'll wait for that to happen so it's easier to work through this.

BY MR. POWERS:

Q It won't all fit there, so what we can do is describe, first off, the beginning of the sentence of interest, is that their findings in children with autism, and these were findings that came after the children were diagnosed, as they say, it may reflect brain mechanisms involving neuroinflammation which have been implicated in this disorder. Correct?

A Right. There are now interpreting their findings, yes.

Q And then, as it goes on to say, such processes are typically accompanied by edema. Do you see that?

A Yes, I do.

Q Now, I'm going to step out of Dr. Rust's critique for just a moment. If you recall, Dr. Kemper specifically said that you are incorrect in describing edema as a consequence of neuroinflammation. Do you remember him making that specific comment?

A Yes, I do.

Q Now, this paper actually says that neuroinflammatory processes are typically accompanied by edema. Correct?

A Could.

Q So that support, in the scientific literature, for your contention that edema is a characteristic of neuroinflammation.

A It does.

MR. MATANOSKI: Your Honor, at this point, I would like to request of the Court, please let the witness answer some questions rather than counsel simply leading him through articles. This is supposed to be Dr. Kinsbourne's rebuttal, not Mr. Powers'.

BY MR. POWERS:

Q So, Dr. Kinsbourne, if you would look at that paragraph, what is the significance of this paragraph and what these articles are saying to your report?

A The significance is that the findings on MRI are consistent with ongoing inflammation, and they also themselves relate their findings to studies to which I refer in which microglial activity and cytokines have been found to be associated with autistic disorders.

Q So let's turn to page 14 of your report, and I just want you to be able to show the Special Masters what statement in your report you cite to this article for support for. Again, it's on page 14, and it's the very first sentence at the top of the page.

A Correct.

Q And, again, on the page previous is a sentence that talks about another Friedman article, but the one we're talking about is the one that's highlighted.

A Yes. I made the point, briefly, that the Petropolous article did find evidence of neuroinflammation in the cerebral gray matter of these individuals.

Q So if that's what you cited, the article that we just discussed, in support of. Correct?

A Yes.

Q So it would be your contention that that's a very fair and accurate citation to the literature that we just described.

A Yes.

Q I want to talk a little bit about Dr. Kemper's testimony with you. Do you recall Dr. Kemper testifying -- I think it was during the second week of this hearing --

A Yes.

Q Do you recall Dr. Kemper having, on his direct examination, specific criticisms of your "expert report" generally but specific components of your theory?

A Yes.

Q Now, one was a reference to page 13 of your expert report. We're going to put page 13 of your report up, and the first portion of the second full paragraph. I would like to highlight the first two sentences there that deal with circulation.

Do you recall listening to Dr. Kemper describe -- he believed that edema was not a characteristic of neuroinflammation.

A He did make that statement.

Q And we just discussed the citation in the scientific literature where you find support. Correct?

A Right.

Q He did not take issue with activated microglia. Correct?

A Correct.

Q Now, he did take issue and say that there is no local invasion of immune cells. Do you remember that criticism?

A Yes, I do.

Q Do you believe that, in the process of neuroinflammation, there can be a local inflammation of immune cells?

A Yes. That's documented in the literature.

Q Let's talk about where it might be documented in the literature.

We're going to be referring to Petitioners' Master Reference List No. 72. This is Dr. Pardo's article that's been much discussed.

So you have the article in front of you, Dr. Kinsbourne. I'm going to draw your attention to page 6, and on page 6 we're going to highlight the last full paragraph on that page, the bottom right-hand corner.

Now, the third sentence in there talks about an increase in MCP-1 expression. First off, what is "MCP-1"?

A It's a cytokine that's released by DL cells.

Q And is this part of the neuroinflammatory process?

A Yes, it is.

Q If you read further in that sentence, what does it describe about the significance of MCP-1 as it relates to the pathogenesis of autism?

A It mentions the relationship of this chemical not only to microglial activation but also specifically to the recruitment of monocytes, macrophages, to areas of neuronal cortical abnormalities, which is, in other words, the same phenomenon that I was referring to in my report that Dr. Kemper took issue with.

Q So monocytes and macrophages; what types of cells are those?

A These are cells that are not inherent in the brain but in the body and in the circulation, but I tracked it into locations around the blood vessels that supply the brain by the MCP-1.

Q Is it your testimony that this description is consistent with the statement in your report that neuroinflammation is associated with the invasion or the infiltration of immune cells?

A Yes. That's what I was referring to.

MR. POWERS: Let's take that down from the screen, and I'm also going to hand you another very well-known exhibit number. This is Petitioners' No. 69. It's Dr. Vargas's article.

I would like to direct your attention, Dr. Kinsbourne, to page 5 of this exhibit. There is a section highlighted there, but we're actually going to

look at something below that. About two-thirds of the way down the right-hand column, there is a phrase that begins, "In addition to the presence of activated macrobriala," and go ahead and highlight down to the bottom.

BY MR. POWERS:

Q Do you see a section in there where the authors describes their observation that there was a marked accumulation of perivascular macrophages and monocytes in the cerebellum of the autistic?

A Four of the autistic individuals. Well, as I pointed out, these cells come from the circulation, and they pass through the walls of the blood vessels into a perivascular location, which means around where the blood vessels flow in the brains of at least four of these 10 autistic people.

Q So, again, do you believe that this statement in the published literature is consistent with your description of the characteristics of neuroinflammation?

A Yes, it is.

MR. POWERS: We can pull that down.

BY MR. POWERS:

Q If you recall, Dr. Kemper took issue with something that you said on page 17 of your expert

report. If you look at the third paragraph, it's the paragraph that begins with a citation to Dr. Vargas, but the sentence I'm interested in is at the very end of that paragraph, and it begins, "The inflammation becomes chronic...."

Now, Dr. Kemper took issue with the idea that cells, particularly astrocytes, are dying. What he said, if I recall the testimony, was that the Vargas folks did not find dead astrocytes, and, therefore, given the lack of dead astrocytes, that your friendly fire description was inaccurate. Do you recall that testimony?

A I do.

Q How would you respond to that criticism and let the Special Masters know exactly what you're describing with astroglial activation here?

A Well, there are two aspects to this. One is that what I have seen saying was that there are circumstances under which the immune attack is so severe that the astrocytes can, in fact, die.

I wasn't arguing that this was generally the case in autism. My point in autism is that there is a functional abnormality of astrocytes, and, specifically, that the astrocytes no longer perform their function of regulating the flow of glutamate,

which, therefore, can spread and activate neurons that otherwise would not have been activated.

Death is not part of the model that I'm proposing, although I have no doubt that this is something that can happen and, on occasion, does happen.

Q In fact, in fairness, let's go ahead and highlight the remainder of the paragraph here.

So, in your report, you actually describe specifically what you think is going on with astrocytes. Is that correct?

A Yes.

Q Anywhere in there do you say that a necessary part of your model is that astrocytes are dying?

A No, and, in fact, it's a necessary part of my model that most of them don't die because if they die, the neurons would die, and we would have a totally different situation in the brain.

Q Now you do say that some will die. Correct?

A Yes.

Q I want to go back to Petitioners' Master Reference No. 72 and page 7. Halfway down the left-hand column, there is a sentence that begins, "Importantly, cells undergoing...."

Now, you say that some astrocytes might die, and Dr. Kemper said no astrocytes are dying. Where can you find any support for the idea that some astrocytes might be dying, even if you didn't find the evidence of the actual dead cells?

A The substance, TGF-beta-1, as is pointed out here, is produced mostly by reactive astrocytes and neurons. That's the sixth line down of the highlighted section. It then says that this chemical, the cytokine, may reflect an attempt to modulate the neuroinflammation or repair injured tissue. In other words, it's, in a sense, considered to be anti-inflammatory as opposed to pro.

It doesn't the same in this paragraph, but the understanding is that that substance is, in fact, produced by astrocytes in the course of dying.

Q So if this is a substance produced by astrocytes in the course of their death, and elevated levels of this substance are present, what do you think the significance of that is, in terms of your description of what goes on with astrocytes in this process?

A Well, some astrocytes, in fact, have succumbed, but there is a mechanism for holding that process in check. It's a self-regulatory, protective

mechanism that's being described here.

MR. POWERS: We can pull the article down.

BY MR. POWERS:

Q You also hit on another point that -- I think it was Dr. Rust specifically said that he thought your model implausible because he did not understand how it could be self-regulating. Do you recall that testimony?

A I do.

Q How would you respond to that accusation by Dr. Rust that your model is undermined because it cannot explain the natural process of neuroinflammation?

A Well, there are two ways of encountering that. One is that a number of articles in peer-reviewed journals have, in fact, found the concept of the overactivated glutamanergic state to be a feasible, reasonable concept.

The second is that, as Dr. Rust himself described in some detail, there are self-regulatory, corrective provisions in the brain for holding neuroinflammation in check so that, up to a point, it is quite biologically plausible that neuroinflammation may occur but not escalate to an overwhelming assault on the brain as a whole.

In fact, this must be the case because both the Vargas group and, subsequently, the Lopez-Hurtado group found evidence of neuroinflammation not only in children but even in adults up to the age in the forties, and nobody argues that this neuroinflammation just began in the forties in those cases. So the evidence is that neuroinflammation can, as it was a similar way at some low level, continue for many, many years, which implies both that the pro-inflammatory factors continue and that anti-inflammatory factors hold it to some level of check.

Q Now, finally, Dr. Rust took issue with your characterization of the neuroinflammatory process, in particular, as being an environmental contribution to autism. Do you recall that critique?

A Yes.

Q I would like to go back to Petitioners' Master Reference List No. 72, and we're going to look at page 9. Again, this is a page that has been oft discussed, but I want you to discuss this in terms of responding to Dr. Rust's critique that he saw no way that neuroinflammation could be an environmental contributor.

Let's go ahead and look at the table at the top left hand of that page. Let's blow that up.

Can you describe for the Special Masters the significance of that table in this published paper to your theory of causation in these cases?

A Yes, sir. It, in fact, talks about interactions between environmental and genetic factors that influence neuroglial activation and the presence of autism. Among the environmental factors, on the top left-hand, he mentions infections and toxins, maternal factors, and others.

So the notion that environmental factors are of significance mechanistically is embodied in this sketch, which then centers on neuroglial activation, and, at the bottom right-hand corner, the flow chart proceeds to the outcome of the autistic phenotype, featuring, particularly, regression as part of the phenotype that's being described here in terms of its mechanistic origins.

Q Let's go ahead and look at the text of this page, under the "Conclusions" section. In that section, about half-way through the section called "Conclusions," there is a sentence that begins, "Our neuroimmunopathological studies...."

Let's go ahead and highlight that, if you would, please.

Now, the authors make a point here that, to

the extent there is an immune response involved, it's innate rather than adaptive. Correct?

A Yes. That's been made very clear throughout.

Q Have you ever, in your testimony or in your report, implied that what's going on in the brain is a response of the adaptive immune system.

A Not at all.

Q What immune response are you describing in your testimony, your report, and your opinion?

A I'm describing the innate immune response, which, in the body, has to do with macrophages and mononucleocells, and, basically, it's a kind of inflammation that one has if one scratches one's arm, and the area gets red and a bit swollen through edema and hot and so on. But that immune response, when it occurs in the brain, is still innate, but it features the macroglia and the astrocytes as we have discussed.

Q Well, move down a little bit further, and the sentence beginning, "The roles of neuroglial activation...." Now, in this sentence, there is talk about some sort of preexisting central nervous system abnormalities, and it says that "neuroinflammation might maintain some of those abnormalities." Do you see that?

A Yes. It might maintain them, but it goes on to say, if not also initiating some of them. That's consistent with the Courchesnean point of view that we have already talked about.

Q Now, Dr. Kemper, the neuropathologist who testified, it was his position, if you recall, that the neuroinflammatory responses seen here were in response to the underlying brain pathology. Do you remember that testimony?

A Yes.

Q And, certainly, that's a possibility that these authors are leaving wide open.

A Right.

Q Does that possibility exclude the possible that the neuroinflammatory process might initiate some of the abnormalities in this disorder?

A No, it doesn't at all. It might be either, or it might be both.

Q It's just uncertain.

A Correct.

Q Let's look at the very last sentence in the paper here. This is the sentence that says, "Neuroglial and neuroinflammatory responses likely have polygenic and environmental bases and may have important clinical and therapeutic implications in

autism."

Can you explain what you think the significance of that concluding statement is to your opinion and to your report and your testimony?

A Yes. I've been arguing that gene environment interaction is an important factor potentially in causing autism, and they are saying that, that "polygenic," the gene component, and the environmental basis interacting may set up the neuroglial neuroinflammatory responses, and they, in turn, may have important implications for autism.

Q Is it your opinion, Dr. Kinsbourne, that the work of Drs. Vargas and Pardo supports your theory and your mechanism of injury in these cases?

A Indeed, I based a lot of it on their work.

MR. POWERS: I have no further questions right now.

SPECIAL MASTER VOWELL: Thank you. Is Respondent's counsel ready to proceed?

MR. MATANOSKI: I believe so, ma'am.

(Pause.)

CROSS-EXAMINATION

BY MR. MATANOSKI:

Q Welcome back, Dr. Kinsbourne.

A Yes.

Q For the record, I'm Vince Matanoski.

Doctor, I'm going to begin where Mr. Powers began, with the settlement that you reached with the University of Toronto. Now, as part of that settlement, you agreed to tender your resignation. Isn't that right?

A No.

Q As part of Petitioners' Trial Exhibit 12, paragraph 4, it says, "The applicant tenders his resignation from the university."

A There were two parts to that. The first part was that the charges were rejected, and they were quashed, and I was offered the opportunity of staying at the University of Toronto. However, I elected, as part of my settlement, to leave.

Q And that is part of the settlement that you attend to your resignation.

A That is part of the ultimate settlement which you have before you.

Q Thank you. Doctor, you were asked a series of questions about criticisms from Dr. Kemper. Did you listen to his testimony?

A Yes.

Q Could you tell me what those criticisms were?

A Do you mean the ones we just went over?
Q Yes.
A He criticized my statements about neuroglia.
Q Can you be any more specific about what his criticism was?
A Yes. He said that were was no edema in neuroinflammation, and he agreed with the microglial activation, and then he disagreed with the third item that I mentioned --
Q What was that item?
A -- which I've forgotten for the moment.
Q Even though you listened to his testimony, and you were just testifying about it, you can't remember the number.
A Even though we just talked about it, yes.
Q Are you sure you listened to his testimony?
A Am I sure I listened? Yes, of course, I'm sure I listened.
Q I was just wondering, if you were not being led through the questions, whether you can even count what the criticisms were.
A Well, I'm sorry you're wondering, but I listened to his testimony.
Q But you can't recall even what the third matter that Dr. Kemper brought up in his testimony.

A It will come back to me, if you would like me to think further.

SPECIAL MASTER VOWELL: Counsel, I'm just going to ask -- I'm reading lips, but I would like to further be assisted by hearing you, as I'm sure everyone else will, if both Dr. Kinsbourne and counsel would speak up just a little.

MR. MATANOSKI: I'm sorry.

BY MR. MATANOSKI:

Q Dr. Rust; you listened to his criticisms, too. Is that right?

A I did.

Q Can you tell me now what those criticisms are?

A Oh, there were an awful a lot of criticisms.

Q How about giving me --

A I'll give you a few, yeah. My theory is unbelievably complex. My theory is well put. My theory is totally novel. These are my discoveries. I have ignored 30 years of neuroscientific research. There are some highlights.

Q Can you be any more specific about what --

A Well, I'm telling you things that he said, and I'm using almost exactly his specific words.

Q You can't be any more specific than that.

A I haven't finished my response to your question.

He criticized my point of view about regression as being striking, although Dr. Richler, in fact, describes regression as being striking.

He criticized my scientific approaches, speculative. He didn't believe that regression could be interpreted as the cause of an ongoing disease because, in Rett syndrome, there is regression, which is attributable to genetic causes.

He found my model of overarousal to be really a misinterpretation of the behavior of children with autism under stress. He pointed out that once they are in familiar, calm situations, that they quiet down, and on the longer -- here are some examples.

Q He was pretty broad and pretty much criticized just about every part of your opinion, didn't he?

A Oh, he did, yes.

Q Doctor, you were given a study to look at. I think this is Trial Exhibit 13 perhaps. Now, that study was for safety, wasn't it, a drug safety test?

A What are you referring to?

Q The one you were just handed, Trial Exhibit

13, a study by -- they were recruiting participants for a drug study.

A Oh, the riluzole study?

Q Yes.

A Yes.

Q That was a drug safety study, wasn't it?

A Well, it says, on the front sheet, "This research study will examine the effectiveness of riluzole for treating such a composite result."

Q And on page 3 of that study proposal?

A Are you going to direct my attention to it?

Q I don't have it in front of me. Actually, I do. Doesn't it say, "This proposal is for a 12-week, single-arm, open-label study that will evaluate safety and estimate dose of children," the second paragraph, first full paragraph, of that page?

A It does say that, yes.

Q And is that study limited to children with regressive autism?

A Did you say, is it limited?

Q Is that study limited to children with regressive autism?

A As I pointed out, this is an agent which was initially shown to be of some effectiveness for OCD, and now it's being extended to the autistic children

as well.

Q It is not limited to children with regressive autism.

A No, it's not limited.

Q Your opinion is limited to children with regressive autism, is it not?

A I'm talking about children with regressive autism.

Q You limit your mechanism, for purposes of this proceeding, to children with regressive autism. Correct?

A No, I don't limit it. I am discussing it in the context of regressive autism. Whether the mechanism is applicable in other conditions, I haven't considered.

Q So your mechanism is not applicable solely to regressive autism.

A I don't know. I haven't considered that. I haven't considered it in the context of regressive autism, and I have not considered it in other contexts.

Q Then consider it now. Would it be applicable equally to other kinds of autism, not just regressive?

A I don't know. I would need to consider

that, based on the medical literature. I can't give you --

Q Well, why did you consider it only with respect to regressive autism?

A Because the issues before this Court have to do with possible and environmental postnatal effects of certain agents, in one case, the measles vaccine virus and, in other case, the mercury. When postnatal effects are being considered, the disorders that appear to be postnatal, such as regressive autism, which seem to be the relevant disorders to consider in the first instance.

Q But if your mechanism applies equally to all of the kinds of autism, then it certainly doesn't just explain away regressive as postnatal. It could be anything. Correct? It could be any kind of autism that your mechanism applies to.

A I am not giving an opinion about whether or not my mechanism applies to other kinds of autism.

Q So, at this point, you can't say that it is limited only to regressive autism, your mechanism.

A I have not considered the universe of other possibilities for this mechanism.

Q Yet you would use it as part of a differential diagnosis to determine whether or not

autism occurred as a result of vaccination exposure.

A I don't use a mechanism for a differential diagnosis.

Q That's how you came to your conclusion. Your mechanism is how you came to the conclusion, at the end of your report, that you would consider vaccine exposure in the differential diagnosis of autism.

A I did, indeed. I offered a medical reason or mechanism, and then I said that, given that, among the potential triggers for neuroinflammation, are viruses and heavy metals, viruses and heavy metals should be considered a differential diagnosis, which would intuit, of course, any source of virus, such as the measles vaccine virus, and any source of heavy metal, such as thimerosal.

Q And so you concede that your postulate that you have would apply equally to other exposures, even if we were just to consider potential postnatal causes.

MR. POWERS: Excuse me, Special Masters. I'm going to object to the extent that we're now beyond surrebuttal. These are questions that go to Dr. Kinsbourne's earlier direct testimony and could have been raised, and may even have been raised, on

cross, at this point. These are way outside of the scope of the rebuttal testimony of Dr. Kinsbourne this morning.

SPECIAL MASTER VOWELL: Mr. Matanoski?

MR. MATANOSKI: I'll withdraw the question. I think he has answered this before, actually. I think it's in his report. I imagine it's clear to the Court now that his mechanism is not specific to the mercury vaccine.

MR. POWERS: Again, I object to counsel, on an examination of a witness, making arguments on the record to the Court here. I just raise the objection that when counsel is directing questions to the witness, that they be questions to the witness and not argument to the Masters.

SPECIAL MASTER VOWELL: So noted.

BY MR. MATANOSKI:

Q Doctor, you talked a lot about glutamate excess. How do we get to that process of glutamate excess from vaccines? Is it the inorganic mercury in your causal mechanism?

A Neuroinflammation involves a process that I have already explained in detail in my report and in my direct testimony, which raises the discontrol of glutamate by its normal regulatory mechanisms.

Therefore, whatever might cause neuroinflammation is also -- cause glutamate excess. I pointed out the three categories, known categories, of agents that could cause neuroinflammation.

One category would be viruses persisting in the body, the second would be heavy metals, and the third would be neurodegenerative disorders.

Among that range of causations, vaccines could play a role in two respects: one, insofar as delivering a virus which stays in the body of particular children, and the measles vaccine virus has been shown to do so in some autistic children; and the other, a vaccine that contains, or, at least, contained, mercury as part of its chemical constitution and, therefore, would be one of the available vehicles for delivering mercury to the body and, therefore, to the brain.

Q And that would be in the form of inorganic mercury, in your opinion.

A Well, it wouldn't enter the brain in that form, but once in the brain, it would become decomposed to that.

Q And this glutamate excess is built up because of inorganic mercury in the brain.

A One of the many possible causes of glutamate

excess in the brain would be a triggering by the effect of low levels of inorganic mercury.

Q And this glutamate excess is going to exacerbate, or continue to increase, as the inorganic mercury continues to increase. Correct?

A Not necessarily.

Q Why not?

A Why should it?

Q So you don't know why it should or shouldn't.

A No. You don't know why it should or shouldn't. I never made the claim that the glutamate excess would necessarily become worse and worse, and I pointed out today, in testimony that I did give as opposed to this topic, which we didn't address today, that regulatory mechanisms, which can also keep the glutamate excess in check.

Q So what causes those regulatory mechanisms to fail?

A I didn't testify that the regulatory mechanisms failed.

Q If they are in check, there isn't excess glutamate.

A No. That's not true. You have a certain amount of excess glutamate, but it's capped. It is

precluded from becoming out of control by anti-inflammatory cytokines and regulatory cells.

Q And after this initial impact on that glutamate regulatory system by inorganic mercury, subsequent amounts of inorganic mercury had no impact on that regulatory system.

A I don't know whether it has no impact. It might have some impact. It might have no impact in some people than others. It might have less impact over time and yet others. This is a level of specificity which I can testify to and don't need to establish my mechanism.

Q So you're willing to say that inorganic mercury will induce glutamate excess, but then, after it induces it, you have no idea what inorganic mercury might do after that.

A As long as it stays there, it will maintain the neuroinflammation. That is something I have an idea about, and I've just stated that idea. Whether that neuroinflammation will become worse, stay the same, or get better, I'm sure, varies from person to person.

Q And you have no way of determining that.

A You would have to show me the persons.

Q Well, what would you look for in a person to

determine why there would be more glutamate excess in one person or another as a result of inorganic mercury?

A First of all, we have to show that there is more. Secondly, I would then have to consider the particular case where there are no conceivable reasons. This goes way beyond my report and will be in my testimony.

Q So you just got us to some will do it, and you don't know what's going to happen after that. Some inorganic mercury will do it, create this excess, but you have no idea what's going to happen after that.

MR. POWERS: Again, I object. You were talking about a dose issue, and Dr. Kinsbourne, on rebuttal testimony, wasn't talking about dose at all. This was an issue that he raised on direct testimony. He was crossed and re-crossed on that issue, and now, rather than rebuttal cross-examination, re-re-re-cross, and, again, I object because we're going way outside his rebuttal testimony and his cross-examination.

SPECIAL MASTER VOWELL: Mr. Matanoski?

MR. MATANOSKI: Ma'am, I don't know why Dr. Kinsbourne is telling us about neuroinflammation, if

he can't tie it to the vaccine or the inorganic mercury, and tell us what's going to happen with respect to the inorganic mercury. He is only telling us that neuroinflammation, which, he admits, can be caused all kinds of possible factors.

If he can't tie it to inorganic mercury and explain how he is tying the neuroinflammation, the inorganic mercury, to reach a conclusion, at the end of his report, that you should consider thimerosal-containing vaccine, it is impossible --

SPECIAL MASTER HASTINGS: This is not argument.

SPECIAL MASTER VOWELL: No.

MR. MATANOSKI: Well, I was trying to explain why he thought --

SPECIAL MASTER VOWELL: -- the questioning. I think he has limited his answer. He has delimited his answer with he hasn't considered, or he is uncertain, and needed to examine the individual. So perhaps we can move to other lines of questioning.

MR. MATANOSKI: Yes, ma'am.

BY MR. MATANOSKI:

Q How much glutamate excess needs to be built up before you get the excitatory effect that you are postulating?

A No one that I know of has quantitated that.

Q So that's not capable of being tested.

A No. I think it is capable, ultimately. In fact, I think that magnetic-resonance-spectroscopy methods are either currently available or will be very soon available to actually see whether, in the brain, there is microbial activation; whether, in the brain, there is inorganic mercury. This is really a good range, and, within a short time, we'll know whether it's right or wrong.

Q My question was the amount of glutamate, not neuroglial activation.

A No. I understand your question, sir. This is a question that I can't answer, and I don't believe Respondent witnesses could either.

Q So is there a way of measuring how much glutamate will be needed, excess glutamate, to create the excitatory effect that you're postulating and trying to defend here?

A To my knowledge, that cannot be measured in humans, in living humans. There are in vitro models in which it can potentially be measured.

Q Do you have any idea what the measurement of excess glutamate would be before it becomes excitotoxic?

A I offer no quantitative opinions, no.
Q Can the glutamate excess that you're postulating manifest in the overexcitation in the period of a day?
A I based my testimony on medical literature, and I'm unaware of any medical literature that addresses that question.
Q Could it remain latent for years?
A Could it do what?
Q Could this process of glutamate excess remain latent for years without it manifesting itself in clinical symptoms?
A I know of no literature which puts a timeframe on this.
Q You cited the Purcell paper, which was PML 567, I believe -- maybe that was "67" -- that paper didn't deal with regressive autism, did it? Not exclusively with regressive autism, did it?
A That's correct. It didn't.
Q It was 567. In that paper, the authors -- this is a portion that you did not cite or discuss -- didn't the authors state, and this would be on page 9 of 567, "As we are examining postmortem samples long after one set of the disorder, it is more likely that we are identifying secondary consequences of the

disorder." Isn't that right?

A It probably is, but could you refer me to where it says that?

Q Under "Discussion."

A Yes.

Q It's up on your screen now, too.

A Okay.

Q So those authors are saying these are secondary effects, not causative ones. Correct?

A In this particular sentence, they are saying that, yes.

Q They are discussing their article.

A Correct.

Q Now, you mentioned the article by Dr. Casanova. You called it an "important article" in your testimony just this morning.

A Yes.

Q Now, he proposes a deficit of inhibition, not an excitation.

A Correct.

Q That's not what you're postulating. You're postulating an overexcitation, not an inhibition. Correct?

A I am postulating a change in the excitation-inhibition balance in favor of excitation.

Q Actually, sir, you were saying it's glutamate excess.

A Yes.

Q That's only one side of the balance.

A Correct. In other words, the balance is skewed in the direction of excitation.

Q Because of glutamate excess.

A What's that?

Q Because of glutamate excess in your postulate.

A That's correct.

Q How does Dr. Casanova propose that the deficit of inhibition occurs in his article?

A He is arguing that there is a problem with inhibitory interneurons.

Q So this inhibition, this deficit of inhibition, is actually a function of brain development. Isn't that right?

A Not necessarily.

Q Isn't that what he postulates in his article?

A As we have discussed, the question of brain development is an issue which is postnatal as well as prenatal.

Q In his article, doesn't Dr. Casanova

postulate or say that he believes that it occurs in the prenatal period?

A You may be right, but I don't want to rely upon that. Can I refer to the article?

Q Certainly. Well, would you accept that he does and that, in fact, he says that it's in the first trimester?

A I think that's perfectly possible. However --

Q Aren't minicolumns formed in the first --

A Let me explain the relevance of Dr. Casanova's statement to my theory. I was not referring to his article necessarily as corroborating, or even being pertinent, to my proposals as to the origin of the new information and the autism.

I was pointing to his article in response to the criticism that the overactivation-overarousal theory is outdated and not to be considered. He was considering it very seriously. That was the point about his article that I was presenting to the Court.

Q But his mechanism is one that's prenatal in origin.

A His and some other people's, too. Dr. Zimmerman has also taken that position, absolutely.

Q Now, your attention was drawn to the

Courchesne article. You cited that in your report. That would be Petitioners' Master Reference No. 104.

In your report, and today, you cite this article for the propositions where support for your postulate, neuroinflammation, as part of your causative mechanism. In your report, you cited that part of the article that dealt with neuroinflammation. However, you omitted the other factors that the Courchesne authors were looking at as possible causes, didn't you?

A You have to show me the report and the other factors. I don't have my report before me. Perhaps you can refer me to the statement.

Q Here is the article. I guess we've already highlighted the sections that are involved.

You cited the last part of this, "Compensatory neurogenesis during a prenatal or postnatal life that is triggered by adverse events such as those that ignite the neuroinflammatory reactions reported by Vargas, et al."

SPECIAL MASTER HASTINGS: Can we identify that number for the record?

MR. MATANOSKI: It's page 8, going onto page 9, sir.

SPECIAL MASTER HASTINGS: Thank you.

BY MR. MATANOSKI:

Q Prior to that, they listed two other possible mechanisms here to explain their findings. Didn't they say, prior to that, that the possibilities also included a failure to correctly regulate the number of neurons produced during the neurogenesis stage of prenatal development in autism, and, as another possibility, a deficit or delay in apoptosis so that too many survive into postnatal life?

A I would like to make it clear, again, that I'm not presenting a discovery as to what impact is the true and scientific cause of autism. I'm presenting one of a number of medically reasonable possibilities.

I'll make it clear again that there are other reasonable medical possibilities, and the responsible articles mention those. I'm not arguing that my proposal is better or worse, and certainly not that my proposal excludes other interpretations. Of course, it does not.

Q Your attention was drawn to Petitioner's Master List No. 247. You described that as an article of some interest. Is that article and the discussion therein limited to regressive autism?

A I'm sorry. What are you referring to here?

Q You had just discussed, in your direct testimony this morning, Petitioner's Master List No. 274, which you described as an article of some interest, and I was just asking you if that article was limited to a discussion of regressive autism.

A I don't have the -- Casanova did this.

SPECIAL MASTER VOWELL: Yes.

THE WITNESS: No, not specifically.

BY MR. MATANOSKI:

Q In defending your reliance on an overarousal model, you did mention, this morning, your list article, which you actually cite in your report.

A Right.

Q Your list article came out in 2006, and you describe overfocusing in that article. Is that overarousal?

A I think overfocusing is caused by overarousal, yes, but that article was not a neurobiological article; it was a behavioral article.

Q And you didn't mention, in that article, that glutamate is a model of overflow --

A No, because it was not a neurobiological article; it was a behavioral article.

Q Now, you seemed to, in your testimony this morning, be making it clear that you're not

necessarily saying that it's astrocyte death that's occurring. Is that right? Would that be a fair representation of what you were telling us this morning?

A I would like to reword it. It's not that I'm not necessarily saying it; I'm not saying it. My model does not postulate astrocytic death as being an essential component, no.

Q In your testimony in Cedillo, you postulated the same mechanism and described it as one of astrocyte death. Correct?

A You would have to show me that. I cannot remember that at all.

Q You can't remember. And, in Snyder, the case that you testified last fall with the same mechanism, you described astrocyte death occurring. Is that right?

A I don't know because you would have to show me what I said. Obviously, I don't remember the words I used.

Q And in support for your proposition, in both your report and in your discussion this morning, you referred to the Aschner article. 570, I think, was one that you put up, and there is also 568-P for this Petitioners' Master List References 568 and 570 as

support for your model of glutamate excess.

Let me just turn to that quickly. In Dr. Aschner's discussion of this, as he describes it, an "excitotoxic model," doesn't he describe this process in Petitioners' Master List No. 568 as a "vicious, amplifying cycle of neurotoxic cascade"?

SPECIAL MASTER VOWELL: And counsel is referring specifically to --

MR. MATANOSKI: -- page 5 of --

SPECIAL MASTER VOWELL: -- PML 568.

MR. MATANOSKI: Yes, ma'am.

SPECIAL MASTER VOWELL: Thank you.

THE WITNESS: Where on page 5 should I look?

MR. MATANOSKI: It's actually up on your screen, sir. Doctor, if you would like to, it's right up on the screen, so it might be easier for you.

THE WITNESS: Right. I can see the words.

BY MR. MATANOSKI:

Q And, in 570, that you were discussing this morning, page 2, the same page you were on, if you went down the paragraph a little bit further from where your attention was directed, to the very end of that same paragraph, second column -- if we can bring that up -- perhaps we can't.

Do you still have 570 from where you were

discussing it this morning?

A 570.

Q Is that in front of you, Doctor?

A Yes, it is.

Q Page 2. Right above the paragraph that begins with the bold, "Role of --" could I draw you attention to that?

A The paragraph that begins with what?

Q The paragraph that immediately precedes the bolded part that says, "The Role of Reactive --"

A Yes, okay.

Q Your attention was drawn, this morning, to some discussion in the text a little bit before that that talked about astrocytic glutamate uptake being inhibited, and you were using that as support for a proposition of not necessarily astrocyte death but just an inhibition in the function of the astrocytes could result in this glutamate imbalance.

A That's correct.

Q If you could carry that discussion down from Dr. Aschner to the end, doesn't he conclude that it sets in motion an unimpeded cytotoxic cycle?

THE WITNESS: The exact phrasing, if we can go back to it -- can we go back to it?

MR. MATANOSKI: It's right there in the

document that you were looking at.

THE WITNESS: My screen is blank, unfortunately.

MR. MATANOSKI: It was page 2 of the document that you had in front of you.

THE WITNESS: Okay.

MR. MATANOSKI: The same paragraph you were reading from, Doctor. It's now up on your screen.

BY MR. MATANOSKI:

Q My question to you was, if you carried the discussion on past where you were relying on this as a proposition that inhibition, without necessarily astrocytic death, can lead to glutamate excess, don't the authors here, Dr. Aschner, in particular, say that it sets in motion an unimpeded cytotoxic cycle?

A Yes. There was a statement about if it became synchronous, and I'm trying to find that statement again. You showed it to me earlier. I don't see it now, but the point is that, indeed, the end point is potentially a cytotoxic death, indeed, but, as I pointed out, in the living brain, there are regulatory mechanisms that could preclude that cycle from coming out of control in this fashion.

Q And in your report, in further discussing the role of astrocytes and trying to tie it into

mercury, you discussed the Charleston article, and, in that article -- that's PML 116 -- and on page 10 of your report, you state that the astrocyte population -- you describe that article as standing for the proposition that the astrocyte population in the brain decreased significantly.

A Yes, it did.

Q But, in Vargas, which you described this morning and talked about, PML 69, the authors did not find any astrocyte loss. Is that right?

A That's correct.

Q And that was true in all of the autopsy samples of all of the autism patients they looked at. Isn't that right?

A That is correct.

Q Both regressive and nonregressive.

A Right.

Q And, in Lopez-Hurtado, PML 446, another autopsy study in autistic individuals, they reported no astrocyte loss. Isn't that correct?

A That's correct. And the Charleston people also didn't report any at 12 months and at 18 months, only at six months.

Q So then, in those articles, they actually recovered, and it was not a lasting impact.

A Either it recovered, or there was a compensatory proliferation of astrocytes, and, in fact, in Charleston, people point out that toxic insults often do cause a reactive proliferation of astrocytes.

Q In compensation.

A Yeah.

Q So the astrocytes are available, then --

A Right.

Q -- to mop up the excess glutamate.

A I think that may or may not be an outcome of that. They don't talk about that.

Q But the astrocytes would be available.

A Would be available?

Q Yes. You discussed Dr. Pardo's article, which is PML 72. You would agree that Dr. Pardo is in the best position to interpret the significance of his own work, don't you?

A I think that's true of Dr. Pardo, I'm sure, yes.

Q I'm sorry?

A Yes, of course, yeah.

Q And your opinion that mercury from a vaccine is a potential cause of autism was only formed in the last few months. Correct?

A It's true that I've only studied this seriously in the last few months, yes.

Q And you only came to that opinion in the last few months.

A I have been aware since I first began to study for this cycle of cases that one of the causes of neuroinflammation is heavy metals, and I believe I mentioned that in previous reports, but I haven't paid serious consideration to the issue specifically of mercury until recently.

Q When I asked you that question in November in Snyder, you indicated to me that you had not formed a conclusion at that point.

A That's true.

Q And this postulate that you've laid out before the Court; you've never presented that for publication or peer review. Correct?

A I only came to this conclusion quite recently.

MR. MATANOSKI: Thank you. I have no further questions.

SPECIAL MASTER VOWELL: Thank you. Anything further from Petitioners' counsel?

MR. POWERS: No, Special Master. Nothing further.

SPECIAL MASTER VOWELL: Any questions from my colleagues?

(No response.)

SPECIAL MASTER VOWELL: Okay. It looks like it's about ten-forty. I do see that Dr. Mumper has arrived, but I understood, from our earlier off-the-record discussions that -- apparently, it's ten-forty-seven. My computer is now connected up to the chronometer I've just been handed.

But my question is, did counsel want to prepare for a brief break to address the item that counsel had indicated that they wanted to take up off the record?

MR. MATANOSKI: I'm sorry, ma'am. Are you proposing that we take that up right now or take the break and then take it up, or during the break?

SPECIAL MASTER VOWELL: We take a break so that we can take up the item before we get to Dr. Mumper's testimony.

MR. MATANOSKI: That sounds fine, Your Honor.

SPECIAL MASTER VOWELL: I suggest we take it up so that we have some opportunity to think about it, have a little bit of a break, and resolve, if there is anything that needs to be resolved, and then proceed

into Dr. Mumper's testimony.

MR. POWERS: Thank you.

SPECIAL MASTER VOWELL: Okay. Let's see, if we're here, my thought would be just about a 15-minute break for the mid-morning break, which would put us roughly
at -- I'm shortchanging you a couple of minutes, but roughly at 11, or we'll say five after so we can have our brief conversation here.

MR. MATANOSKI: Thank you, ma'am.

SPECIAL MASTER VOWELL: Okay. Thanks. We are in a brief recess.

(Whereupon, a short recess was taken.)

SPECIAL MASTER VOWELL: Please be seated. We are back on the record, and I understand that, based on our off-the-record discussion, whatever concerns Respondent had pertaining to the videotaped testimony that will accompany Dr. Mumper's testimony, there is no objection but a reservation by Respondent, as I understand, to counter with video as necessary. Does that accurately reflect your position?

MR. MATANOSKI: That's correct, ma'am.

SPECIAL MASTER VOWELL: Thank you. To proceed, Petitioners' counsel, just let me draw to your attention, Dr. Mumper, that you will continue

under the same oath that was administered and you took earlier in the proceeding. Thank you.

Whereupon,

ELIZABETH MUMPER, M.D.

having been previously sworn, was recalled as a witness herein and was examined and testified further as follows:

DIRECT EXAMINATION

BY MR. POWERS:

Q Good morning, Dr. Mumper.

A Good morning.

Q We, obviously, have been in this position before earlier when you gave direct testimony, but, to make it clear on the record here, my name is Tom Powers, along with Mr. Williams.

We represent the King and Mead families, as well as the Petitioners' Steering Committee, and we have you on the witness stand today to respond to specific testimony that was offered on direct testimony by the Respondent's experts. Is that your understanding of why you're on the stand today?

A Yes, sir, I understand.

Q Did you have opportunity to listen to the direct testimony and cross-examination of Dr. Rust?

A Yes, I did. I listened to the audio and

took 40 pages of notes.

Q And when you say you listened to the audio, did you listen to the live version, the audio download, or some of both?

A Some of both.

Q Did you listen to the entirety of his testimony?

A Yes, I believe I did.

Q I want to go through some of the issues that Dr. Rust specifically raised as they apply to William Mead and Jordan King. Obviously, Dr. Rust covered a lot of ground, but we're going to focus on the case-specific testimony of Dr. Rust. Again, is that your understanding of what your testimony today is directed to?

A Yes, sir.

Q Now, do you recall some of his testimony about Rett's syndrome?

A Yes. I recall quite a bit of testimony on Rett's.

Q And as it applies to these cases, that testimony about Rett's syndrome, do you have a response to that for the Special Masters to explain how you think that testimony fit or didn't fit with his analysis of the two cases?

A Well, I had thought that he was on elaborating on Rett's syndrome a lot in order to lay some groundwork and then make some type of extrapolation or determination as specific to these two cases, and, as time went on, I had the same question in my mind that Special Master Hastings did, in terms of where it was going.

Rett's syndrome is a very well-described syndrome that, the vast majority of the time, occurs in girls, and the genetics of it have been identified, in that we know actually the MECP-2 gene is involved, and, at some point, Dr. Rust seemed to be making the extrapolation that Rett's syndrome has a lot of autistic-type features, and we know the genetics of that, and, therefore, we can extrapolate that other versions of autism may well be genetic, and, you know, we still need to determine the genetics.

No doubt that that is true, to some extent, but to spend so much time on a disorder that is so fundamentally different from the way these two boys presented was very puzzling to me. He did make the point that Rett's is now being described in some boys, which I actually find intriguing from the standpoint of it opening the door to certain environmental causes because if boys typically do not get Rett's, one

wonders what it is about those boys that they are now being identified, even though they are in the vast, vast, vast majority.

We do know, from work that Jill James has done and other people who work in oxidative stress literature that there are more challenges for boys in terms of handling environmental toxins, specifically with regard to the role of glutathione because, in general, females tend to have better preserved glutathione, and boys are at higher risk because of their relatively lower levels of glutathione.

So the Rett's issue, to me, was a lot of time spent on a disorder that is not really relevant to these two particular boys, and I understood that what I was supposed to do when I reviewed the records was to look at case-specific analyses, given the information from the medical records and the videos about these two particular boys, and try to generate some hypothesis about factors in their case that might be more specific to them as individuals.

Q Was there anything about Rett's syndrome that was informative to your opinions on individual causation in either of these cases?

A No.

Q There was also discussion by Dr. Rust about

the possible that William Mead had a trajectory of head size or head circumference that reflected a pathological and congenital cause of autism. Do you recall that testimony?

A I do.

Q What is your response to the testimony that Dr. Rust offered?

A Well, I think the opinion that he was trying to make was that William initially had a relatively low- sized head circumference, and then he showed an increase in his head trajectory with a subsequent decline.

The thing that seems inconsistent to me is the fact that his newborn's head circumference was well in proportion to his body length and weight and was in around the 80 to 85th percentile at the time of birth.

Now, on -- I believe it was cross-examination, that Dr. Rusk said that, Well, perhaps that measurement was not very accurate because, you know, the child had just been through birth drama, and maybe he had bruising on his head.

So I went back to the medical records to see if, in William Mead's specific case, I could find any evidence of that, and I found three different

references.

One is Exhibit 1, page 00031, which is an intake form with a physical exam in which it says, "Healthy male newborn and head and neck normal."

The other was a nursery record from Providence St. Vincent titled "Newborn Nursery Admission Assessment," and, Scott, I'm sorry, but my copy does not have an exhibit number, but I can turn it over to the Court where it says, "Head and face symmetrical, normal," and the skin says "normal," and there are opportunities there to check off a box for either bruising or petechiae, and that is not checked.

So whereas I can accept, in concept, Dr. Rust's observation that, in certain cases, the newborn head circumference might not be reliable, if there is significant trauma. Again, I don't think that we can just speculate about cases that he has known of. I think we have to look specifically at the child he was talking about, and I do not find any evidence in the medical record that substantiates that claim.

Q And is it your testimony that if that claim was, in fact, true, there would have been ample opportunity in the medical record to reflect that?

A I believe that is true.

Q And a reasonable physician would have made

note of something that was abnormal as Dr. Rust described.

A Typically, you will see physicians documenting things like cephalhematoma if there is bleeding that's causing a large bruise on the brain that might interfere with the head circumference measurements. I know that it's certainly my practice to do that.

There is another thing called a "caput succedaneum" that is another term that physicians could document on their initial newborn physical examination. Neither one of those notations appears in the records, to the best of my observations of the records.

Q Do you also recall testimony by Dr. Rust that he believes that both Jordan and William were not normal in their development prior to regression? Do you recall that testimony?

A Yes.

Q Do you recall Dr. Rust being able to cite to any specific piece of evidence in the medical record in support of that contention?

A No. I did not see him point to anything specifically. He talked in terms of generalities, and I was actually struck by the fact that he seemed

somewhat confused about the cases as he was testifying.

For example, one striking thing for me, when I reviewed William Mead's videos, is that his sister, Eleanor, appears in virtually all of the videos, and Dr. Rust was not able to remember that William had a sister.

So I would submit for the Court that I had paid some close observation to that fact and that it concerned me about the level of Dr. Rust's scrutiny, that he was unable to recall that, for example.

Q So it's your understanding, from listening to his testimony, that he was not able to identify anything in the videos with particularity, but also nothing in the medical records with particularity. Correct?

A I do not recall him saying anything specific. It's been a week since I listened, and I am open to a point where he may have said something, but I honestly do not recall it right now.

Q Now, Dr. Rust did describe the importance of talking to the parents and getting a good parent history as part of making any assessment of autism and the onset of autism. Do you recall that testimony?

A Yes. He was describing his practice in his

own clinic at the University of Virginia in Charlottesville, and he went so far as to describe setting aside extra time at the end of the day so that he would have time to get a careful history.

What was not clear to me was how much of that history was actually performed by him versus taken by his residents, which is a very typical practice at most universities, including that university where I had some many years of experience.

Q In your clinical practice -- let me back up a little bit.

Do you agree, in principle, that a thorough parental history and thorough information from the parents; is that important information you have when diagnosing and treating autism?

A Yes. I think the history from the parents is probably the most crucial piece of information in putting together a picture of the entire child, not just with respect to his autistic symptoms but also with respect to his other medical problems. So I think it's absolutely very important.

Q In your practice, are you the physician that actually conducts that interview and collects that information?

A That is correct.

Q And that's your standard practice.

A That's correct.

Q In listening to Dr. Rust's description of the development of Jordan King and William Mead, do you recall whether he ever heard the parents' history at any point?

A I believe that he testified that he had not been here when they testified, that he had not listened to the audio transcripts of their testimony, and that he had not read the written transcripts of their testimony.

Q And it's your testimony, is it, that having that information is, again, critical to assessing both the diagnosis but also the timing of onset of an autistic disorder?

A I believe that to be very important, yes.

Q There was a significant part of Dr. Rust's testimony that critiqued the care and treatment that Jordan King and William Mead got. Do you recall that testimony?

A I do.

Q And this was testimony that specifically took issue with some of the treating pediatricians', Dr. John Green's, medical intervention, as well as a general critique of the type of interventions that you

do at ARI. Is that correct?

A That is correct.

Q Could you describe your response, just in general, to that critique, including the critique that, in large part, these interventions are not science based?

A I was disappointed with the way Dr. Rust handled that line of questioning because these are issues that I have studied in some detail in an effort to try to figure out how to help these children, and it seemed to me that he dismissed various interventions almost out of hand, saying things like, "There is no evidence that IVIG helps children with autism," and stating that as if it were a fact.

In reality, there is published science about that very fact, and so I think that if you want to state something like that, you should be more specific and say, "IVIG only helps certain children with autism," for example. So that's one objection I had.

The second objection I had is that he tended to go down this laundry list as if Dr. Green was trying to cure autism with these different interventions and almost as if he would try one thing and then move to something else if the first thing didn't work.

It's a crucial distinction here to realize that John Green was taking care of his whole patient, and he was addressing the specific medical problems of the child. So it wasn't that he was moving from one supplement to another to another, hoping that eventually he would hit on something that would cure his autism.

He was following, I think, a very rational approach, given what he knew about the child and the interventions he had available to him, and looking at the risk/benefit ratios of those interventions with respect to the biochemical and the underlying medical problems that the child had.

For example, the most egregious example from Dr. Rust was when he was asked about valtrex, and he said something along the lines, and I'm paraphrasing here, I don't have any idea why that would be helpful in autism. That's used for genital herpes.

Well, I would like to demonstrate later that there is a very well-established biochemical reason that John Green would have considered that and that it has nothing to do with treating genital herpes in, you know, a two- or three-year-old little boy.

Then the third thing I would just like to say is that if Dr. Rust, you know, didn't know why we

would use some of these things -- for example, he said that he has never heard of eskimo oil, so he doesn't understand why that would be helpful.

We live in the Internet age, and he can Google it and, within just a few moments, find out that that's a type of omega-3 essential fatty acids, and then, if you look at the literature on omega-3 essential fatty acids, there is a broad amount of information in the literature that documents the value for that for immune regulation and for being able to help cell-to-cell communication and to help heal the lining of the intestine.

So, in general, that describes some of the issues I had with the way he handled that line of questioning.

Q You mentioned specifically that Dr. Rust characterized some of Dr. Green's interventions as attempts to cure autism. You described, generally, it was to address the whole patient.

What do you believe were some of the underlying medical conditions that William Mead and Jordan King had that were being addressed by the therapies that Dr. Green recommended and that you used in your own practice, again, from the perspective of the ones that are being used to cure autism but to

treat the whole patient?

A Right. They both had evidence of chronic diarrhea and, I think, subtle signs of abdominal pain, and when we get a history from the parent that they have ongoing chronic diarrhea for as much as a year, I think we need to take that seriously and not just write it off to toddler's diarrhea in a child who is losing function and deteriorating before our very eyes.

Q So whether it's curing autism or not, it's to treat a significant medical condition, which is the chronic diarrhea.

A Right. And another thing that John Green was trying to address were abnormalities in methylation and transsulfuration biochemistry, and that was the underlying reason that he would choose things like certain B vitamins or methylcobalamin injections or folinic acid.

By examining the record, one can, at least, get reports back from the parents that the child seemed to improve when those interventions were undertaken.

When I had the opportunity to listen to Mylinda King's testimony here, and then also further interview her, she says that, even now, if she takes

away his methylcobalamin injections or misses a day, she sees deterioration in his performance.

So I think that for the Special Masters to understand that it was Dr. Green's perspective in trying to treat those methylation abnormalities that would make his choices seem more reasoned and more rational.

SPECIAL MASTER VOWELL: Pardon me. Can we just take a moment and everyone check your electronic devices? I was handed a note that there is a little feedback coming through the system.

THE WITNESS: Special Master, I'm wondering -- I have two mikes in front of me. Do I need both of them, or is this the live one?

SPECIAL MASTER VOWELL: Yes. You need both. You need to keep a little bit of a distance. Okay. To proceed. Thank you.

BY MR. POWERS:

Q So, Dr. Mumper, you just mentioned this idea of the methylation cycle. Do you recall Dr. Rust, again, describing some of these interventions as having no basis in science?

A Yes.

MR. POWERS: I would like to put up on the screen, and, unfortunately, we don't have copies right

now, but we'll have copies over the break, three slides that you prepared and brought with you today.

SPECIAL MASTER VOWELL: Tom, I have a set of copies, if that would be helpful.

MR. POWERS: If Respondent would like to take a look at -- it's not marked up, is it?

SPECIAL MASTER VOWELL: No.

MR. POWERS: Okay.

SPECIAL MASTER VOWELL: Well, if it's on the screen, I guess it's --

MR. POWERS: If it's on the screen, I think we can look at the screen, and, Counsel, we'll have copies for you on the break.

I should stop for a second. This would be Petitioners' Trial Exhibit 13? -- 14, I'm sorry.

SPECIAL MASTER VOWELL: It's going to be the three-slide component from Dr. Mumper.

MR. POWERS: Yes. That's correct. So it will be page 1, page 2, and page 3 of Exhibit 14.

(The document referred to was marked for identification as Petitioners' Exhibit No. 14.)

BY MR. POWERS:

Q So, Dr. Mumper, can you describe for the Special Masters what you have there as page 1 of

Exhibit 14 on the slide?

A Yes. This is the methylation and transsulfurations biochemistry that Dr. Deth talked so much about, and this is the way that we teach it to doctors who are learning how to take care of children with autism.

Q Let me interrupt you for just a second. Now, did Dr. Deth actually prepare this chart, or is this something that somebody else prepared, or is it adapted from Dr. Deth?

A This is Dr. Jill Janes' slide, and then, several place on the third of these, I have made some notations about treatments that she did not put in but that are my notations, and I'll be sure to clarify those.

Q Okay. I just wanted to make it clear that this is not something taken from Dr. Deth's testimony so that the record here is clear that this is something that was prepared for you in your clinical work. Correct?

A That's correct.

Q Okay. I'm sorry for interrupting, but go ahead and explain again what this slide is.

A Basically, this is just showing, number one, is the folate cycle, and the five

methyltetrahydrofolate at the bottom is converted up to tetrahydrofolate at the top, which is the active form of folate that's utilized in the body to support methylation reactions.

Q And that's the part of the diagram with a box that has the number one in it.

A That's correct.

Q Okay.

A I was just going to say that the "MS" in the little green box there is methionine synthase, which is the enzyme that Dr. Deth discussed that has that crucial role for helping make that conversion.

Q Okay. Now, let's move on to the portion of this slide that has a box with the number two in it. What is that?

A That is the methylation cycle where homocysteine is remethylated back up to make methionine. Methionine is a very important, essential amino acid, and it is converted to sand, which is S-odenosylmethionine.

That is the major methyl donor in the body, and so that allows you to assess methylation potential, and one of the values that's been very important for us to assess, as a result of Dr. James' work, is the SAM/SAH ratio and the fact that the

proper balance of that needs to happen in order for methylation to continue properly. So this slide is simply setting the stage for a normal cycle.

Q And then the portion of the slide that has number three in a box next to it --

A -- is the transsulfuration cycle, and this process by which homocysteine is converted to reduced glutathione, which is the important kind, as opposed to oxidized glutathione, is what is labeled here as "anti-oxidant potential," and a lot of our interventions are designed to try to help the child make more reduced glutathione. So this is normal methylation and transsulfuration biochemistry with the folate cycle.

I might mention that this process is so important to nature that it's built in a couple of redundant mechanisms, the remethylation mechanism as well as the folate cycle, in order to supply methyl groups to make methylation happen.

Q So let's go to page 2 of Exhibit 14.

A This is also from Dr. Jill James, "The Effect of Oxidative Stress on Methionine Transsulfuration," and, basically, what this shows is the same cycle that I've shown you but with an idea of what happens to this very crucial cycle when children

are under oxidative stress.

For example, they, therefore, are not able to remethylate their homocysteine, and they end up with lower levels of methionine to start. That leaves them with lower S-odenosylmethionine, and as these methyl transferase enzymes are trying to enable the child to methylate their DNA, their RNA, make proteins, make membrane phospholipids, make creatine, which is the power currency of the cell, and make neurotransmitter. If all of those reactions are inhibited, it's going to be very difficult for children to turn their genes on and off.

One of the things that I did find intriguing about Dr. Rust's testimony is that he talked about how methylation is such an important process and how being able to methylate genes is gene regulation in action.

We have a lot of concerns about that because we are concerned about the epigenetic effects of any toxin or environmental factor that would impact on the cellular biochemistry.

Q Okay.

A And then, ultimately, at the end, I just wanted to point out that the glutathione in the reduced form, which is the good guy, is down, and the glutathione in the oxidized version is up and that

cysteine is depleted in this model.

Q And, again, to make it clear, your discussion here is not based on your personal expertise as a biochemist, is it?

A No.

Q It's not based on any expertise or original research you've done as a molecular biologist.

A No. This is based on my initial reading of the Jill James work, my sheer honor to get to work with her on some research projects, my having heard her explain the cycle in lectures that we mutually attended probably 10 to 20 times, and the way that I use it to impact on my clinical practice and the teaching of the doctors that we teach.

Q So let's talk about that final point, I guess, on Slide 3. Can you describe for the Special Masters what this chart represents?

A In this chart, and I have added some notations of my own here, I have tried to look at the interventions that physicians like John Green and I use to try to help these children, and to put it into context into this crucial pathway so that it becomes clear that we are trying to fit the intervention to the scientific profile, the metabolic profile, of the child.

Q I want to direct your attention to a particular portion of this slide, then.

A Okay.

Q To the left, there is a note that you added that says, "M-B12 methylcobalamin."

A Right.

Q Can you describe for the Special Masters the significance of that notation that you made?

A Yes. One of the theoretic interventions that one could do to make the methylation cycle work better would be to give methylcobalamin, which is also called "M-B12," to help generate methyl donors. A methyl group is a carbon and three hydrogens and four methionines so that it can take it through the cycle.

Jill James' work actually looked at children with autism, compared them to controls, documented that the children with autism had low methionines, low cysteines, and low reduced glutathione. So she designed an intervention trial in which she would give substrates and nutritional interventions that would help that methylation cycle work better.

She used methylcobalamin, she used betaine, which is the same as TMG, and she used folinic acid. So you can see that all of those interventions are working on helping that remethylation cycle take

place.

So in a university lab, using well-demonstrated scientific techniques, and, ultimately, published in peer-reviewed literature, she was able to demonstrate the normalization of those methylation metabolites in the children that she treated, to quite a dramatic extent, and that's why we cited her paper in my expert report.

So that is why Dr. Green, when he got laboratory evidence implying impairments in this methylation cycle, chose to use things like methylcobalamin and folinic acid, and sometimes we use TMG, and sometimes we use DNG.

Q Can you direct the Special Masters' attention to any other notations that you made on this slide indicating the type of treatments and therapies that you would use as a clinician and that you would teach to other doctors that you work with?

A Well, another thing that I think that's very interesting is, if you look at B-6 in magnesium, which is to the left of a circle that says "CBS," which stands for cystathione beta synthase, there are about 22 studies in the medical literature that have shown efficacy of B-6 or B-6 plus magnesium, and these go back several decades.

Dr. Rimland, at ARI, was noticing this many years ago, a couple of decades before Jill James' work was published. Now, I think, in retrospect, we can postulate that one mechanism by which those vitamins and minerals make a difference is in helping the body generate cysteine, which is this rate-limiting amino acid for glutathione production.

You'll recall from Dr. Deth's testimony a fair amount of information about how important it is for kids, when they are trying to detoxify substances, to be able to have adequate cysteine and make adequate glutathione in order to feed their detoxification pathways and how poorly their cellular biochemistry works when they have a decrease and reduced glutathione and an increase in oxidated glutathione, which is what the big pink box with the "GSSG" is showing, high oxidized glutathione.

So that's another nutritional intervention that ties specifically to this cycle.

Q Can you identify any other nutritional interventions that you believe provide scientific support for the clinical practices of yourself and Dr. Green?

A The other thing that I think that's very interesting is, on the sort of right-hand part of the

slide where I've labeled "DPP-4, casein-free, and gluten free." This relates to some biochemistry related to adenosine, and if you'll bear with me for a few moments, I will ultimately take you back to the valtrex issue that Dr. Rust was asked about.

Adenosine, in the pink box there, when it is elevated, as we have documented, per Dr. James' work, seems to be the case in about 20 percent of children with autism, there is a feedback loop that makes it have an adverse effect on S-odenosylhomocysteines such that that builds up. That leads the children to be in a situation where they have an abnormal SAN/SAH ratio, where the SAH part is too high, and the SAM part is too low.

By negative feedback, the effect of that is, once again, that they are not able to methylate their DNA. Remember the concerns we have about effects on gene regulation and gene expression when that's the case. They are not able to make proteins adequately. They are not able to make their phospholipid membranes nor their creatine, which is the power currency of the cell.

So another potential target for adenosine intervention, for interventions to work on helping methylation function well, is to try to get the

adenosine down when it's too high.

So, in our group at Defeat Autism Now, one clinician noticed that a mother who was on valtrex had given her child valtrex three different times -- given it, taken away, given it, taken away, given it, taken away -- and there was always a challenge-rechallenge effect, where the child started speaking when he was on the valtrex and regressed when he was off of that.

So we took that anecdotal experience as a reason to look into the biochemistry, and Dr. Baker and Dr. James ultimately did a study in which they looked at adenosine levels and found that, in the kids who had high adenosine levels and were given a acyclovir, which valtrex is broken down to acyclovir, that the adenosine levels normalized, and as the levels normalized, the children improved, in terms of their speech, language, communication, and social reciprocity.

So this is a situation in which we are looking at valtrex not as treating genital herpes in a two-year-old but as in trying to, in a very fundamental way, correct this very important, cellular biochemistry.

Now, if you'll bear with me for a minute, there is something called "adenosine deaminase binding

protein" that is important for the adenosine deaminase enzyme to work appropriately on adenosine. That binding protein, we know, is impaired with heavy metals, including mercury, and that was shown in 1982 by a scientist called Pershell. I believe he was from Germany, but I'm not positive about that.

The binding protein for ADA, DPP-4, which I told you last time was dipeptitalphosphodase 4, which is that enzyme that works on gluten and casein, and a lymphocyte called CD-26 are all essentially the same thing, and this is very confusing initially. But the point is --

MR. MATANOSKI: Your Honor, I'm going to object at this point. At the outset of this, I thought there was going to be some rebuttal. I thought it was in the form of criticism about treatment.

At this point, we're way beyond any qualified testimony on these matters, these charts, everything that's going on now about Dr. Deth's pathways. I would just say, can we move on to something that's actually rebuttal to this case specific instead of something that the witness is not qualified to know.

SPECIAL MASTER VOWELL: Mr. Powers?

MR. POWERS: We are getting very close to the conclusion of this line of questioning, but it's appropriate on rebuttal because a fundamental topic of Dr. Rust was that Dr. Green, the treating physician, as well as Dr. Mumper in her approach to these cases generally, are not relying on science for the treatments and the interventions. Dr. Mumper is detailing her reliance on the science explanation.

MR. MATANOSKI: Which we would submit she is not qualified, or has not been qualified, to explain how this could happen, how she could rely on this. She is a pediatrician.

SPECIAL MASTER VOWELL: Dr. Mumper has stated that she is not testifying as a biochemist and has no expertise in that area, and your comment, Mr. Powers, to the last one, do you have any further comment?

MR. POWERS: No further comment.

SPECIAL MASTER VOWELL: We are at the end of the casein-free, gluten-free matter.

MR. POWERS: Yes. We're about to move off of this slide.

THE WITNESS: I will move off the slide just to say that the reason for trying to show the chemistry here was Dr. Rust said that he was never

aware of any children that had benefitted from a gluten-free, casein-free diet.

I think this is one of the scientific bases, that there is a subset of children that improved, and I am very surprised that, in his population of many hundreds of children, he has not seen improvements in at least a subset.

BY MR. POWERS:

Q Now, we'll take that slide down, and, Dr. Mumper, you just expressed surprise that Dr. Rust hasn't seen improvements related to the gluten-free, casein-free diet. What is your experience, as a clinician with your own practice, as well as somebody who is working with a network of doctors, what is your opinion on the efficacy of the diet?

A We tend to recommend the diet based on a clinical picture in which we have some history of the child either craving dairy or craving gluten or otherwise deteriorating when they eat these foods.

Our best clinical estimates, when we ask people to try the diet, is that about 30 percent of the children will improve dramatically, another 30 percent will have some significant improvements, and there is probably about 30 percent or so who do not seem to improve where that is not part of their

pathology.

But, in this situation where the parents were reporting chronic diarrhea, I think it is an entirely reasonable thing to do, and when we use those diets, we're careful to supplement calcium. So I think that, in given situations, there is rational reason to use those diets in children with autism.

Q Now, you were describing your reliance on peer-reviewed, published literature, as well as materials prepared by people like Dr. James, a little while ago. Are you relying on any other review or compilation of scientific literature beyond what you just described in the slides?

A Well, we are constantly upgrading our bibliographies of scientific articles. I've got one now that I'm tasked to review that is looking at five or six different categories. So, yes, we try to look at the whole literature. We're specifically interested in autism in the gut, autism in the metabolic pathways, autism and immune disregulation, and autism as relates to detoxification.

Q And when you say "we," who are you referring to?

A The scientists, researchers, and clinicians associated with the Autism Research Institute.

Q Now, Dr. Rust described a concern that, in a lot of these care and treatment interventions, there seems to be an absence of controlled clinical trials and an absence of placebo controlled clinical trials, in particular, you know, the double-blind, crossover placebo studies. Do you recall that testimony?

A Yes, I do.

Q And that that was a criticism of your work and that because of the lack of that evidence, he found that the care and treatments that you recommended as being ineffective and not based in science. Do you recall that?

A I do.

Q How would you respond to that point that Dr. Rust made?

A I will acknowledge that we need many, many more placebo-controlled, double-blind studies, but we're very concerned about only using that model. Our paradigm is that these children have multiple medical problems and that if you are not careful when you pick your placebo-controlled trial, if you have a very heterogeneous constellation of children with multiple medical problems, you may stumble upon something that does not look as if it will be helpful, even though it's helpful for a subset.

I think the best example of that is a secretin study, which Dr. Rust referred to, expressing surprise that William Mead had gotten secretin, saying that the gold standard study had shown it was not efficacious, but I have two points to make about that.

One is, if you actually look at the Herlihy study, there were clear responders who did dramatically well, and then there were a lot of other patients who did not do well with secretin. We discussed this at length in the think tank, and the scientists from the ARI that were involved in that study were concerned from the beginning that the population was too heterogenous.

So in kids who had certain kinds of gut symptoms, there were several of the children that got dramatic responses, and if you'll recall from William Mead's laboratory data, he had pretty significant laboratory findings in which, at Harvard Hospital, his pancreatic enzymes were shown to be dramatically low and then shown to improve dramatically after a secretin infusion. That's Exhibit 15, pages 51 and 52.

So, again, for Dr. Rust to just paint a broad brush that secretin is not useful in a placebo-controlled study and, therefore, can't be useful in

this particular patient, who clearly shows a need for it, I think, reflects a very superficial understanding of the importance that we place on taking care of the individual patient based on their individual problems.

Q Now, in response to the criticism that there are no clinical trials and no placebo trials, you, in your practice, or you, in your role with ARI, are you endeavoring to conduct such trials?

A Yes, we are.

Q Can you describe, very briefly, for the Special Masters what type of trials you are planning, either that are underway or that are planned to start soon?

A Well, we've submitted grants for a placebo-controlled, double-blind crossover on diflucan. We've submitted, for looking at trying to work with the NIH on a chelation study, looking at DMSA probably initially.

We're trying to do what are called "single-subject, multiple-baseline studies," where we can take a single subject and do lots of initial measurements and then do interventions and measure their response so that we can deal with the issue of the fact that different biochemistry and different medical problems in a single child may need a certain constellation of

interventions.

That's used very widely in behavioral psychology, and we are working on adapting that to the medical model, working with a guy named Ted Carr, who is a behavioral psychologist, well published, who wants to do some initial studies in that model with gut disease in my clinic at the Rimland Center.

Q Now, the last issue that Dr. Rust raised that I wanted to discuss with you, you sort of touched on a second ago, and that is chelation. Do you recall his testimony that chelation is harmful, or potentially harmful, potentially fatal, that it's painful, and that he didn't understand how it could possibly have any efficacy in treating a disorder that one would postulate is caused by inorganic mercury and inflammation?

A Right.

Q Do you recall that testimony?

A Yes.

Q How would you respond, for the Special Masters, to that particular critique on the chelation issue that Dr. Rust raised?

A I have a couple of thoughts. One is to point out that chelation is a well-recognized and widely used pediatric modality in children that have

blood poisoning and lead toxicity, and, in many of the children we treat who show mercury in their chelation urines, they also show evidence of lead.

So we think that it's important to go after the lead, and we've had many discussions at ARI about how we're just as concerned, if not more so, about lead than mercury in many of these children because, even though we took lead out of paint and gasoline, we just found out, a year or so ago, that we put it in a bunch of toys we got from China, and so they are still being exposed to lead.

With regard to the dangers and the fatalities, I would like to comment that when both Dr. Green and I use chelation in our offices, it's primarily oral chelation, and we tend to use blood count monitoring for complete blood counts and chemistry screens very four to eight weeks, and so that's why you saw some white counts in chemistry screens in those boys' charts.

When IV is used, John Green is one of the ones that has a vast amount of experience with that.

The death that Dr. Rust was referring to was actually a pharmaceutical error in which sodium EDTA, not calcium EDTA, was given to the boy, who died. We would expect that if the child was given sodium EDTA,

it would have horrible consequences on his calcium and probably lead to asystole, which is probably how that child died. But that does not paint all of chelation as being dangerous or potentially fatal. That was a pharmaceutical error.

Q Now, Dr. Rust also just raised the question, or made the statement, that he couldn't understand how chelation could possibly have any efficacy, particularly since the theory in these cases is that there is inorganic mercury in the brain that, obviously, chelation is not going to bring back out of the rain across the blood breaker. Do you recall his comments on that issue?

A I do.

Q How do you think it is that chelation could possibly assist in the treatment of the symptoms of children that you see?

A A lot of work remains to be done in this area, but we are able to mobilize mercury, lead, and other toxins from where they are hiding. Typically, mercury hides in the brain and in the kidneys and in the liver and in the fat, and we know that we're not typically removing anything from the brain, but, by working on the rest of the body burden and taking off the chronic stress that mercury provides, we're

enabling cysteine to be regenerated, and we're enabling glutathione to function more productively, and we are eliminating some heavy metal burden by doing the chelation.

It's also entirely possible that some of the chelating agents are working by an antioxidant mechanism. For example, DMSA is a good anti-oxidant, and so sometimes we wonder if we are actually achieving an anti-oxidant rather than a chelating effect.

I will say that our preference is to try to mobilize the body's own mechanisms to do a natural form of chelation, so that's why we promote working on the methylation biochemistry and the nutritional support as a crucial component and not relying just on chelation.

Q Now, finally, Dr. Mumper, I want to move away from the specific-treatment discussion that Dr. Rust engaged in and that you've now replied to.

Do you recall Dr. Rust saying that he reviewed videotape of both Jordan King and William Mead?

A Yes, I do.

Q And do you recall Dr. Rust saying that, upon his review of the video that he watched, he thought

that both boys were abnormal before they actually regressed?

A Yes.

Q Do you recall him citing to any specific portions of video in his testimony in support of his conclusion?

A I do not recall that he did.

Q Okay. Have you identified specific portions of video that you think are responsive to Dr. Rusks's characterization of the preregressive symptoms of both Jordan and William?

A Yes. I tried to do that after taking notes on his testimony.

Q Now, you had an opportunity to review the video -- I think you described this on your direct testimony -- but you reviewed the video before Dr. Rust testified. Correct?

A Right.

Q Are you saying now that you reviewed the video again after you heard Dr. Rust testify?

A Yes. When I reviewed the videos the first time, I took extensive notes about the ages of the child and things that they were doing that either appeared age appropriate to me or not.

The second time when I went through, I was

trying to look at specific criticisms or suggestions that had been made that the boys had deficits and address specific criticisms about they must not be talking, they must not have gestural language, they must not have social reciprocity, those kinds of things, and I tried to find very short clips that would demonstrate it. I think the whole total of each child is less than 10 minutes or so.

MR. POWERS: So I'll interrupt asking questions of you and just address the Special Masters. We do have video that we're going to show. We have done what is essentially an index of the video. Jordan King would be the next exhibit, I guess, 15?

SPECIAL MASTER VOWELL: Yes.

MR. POWERS: And William Mead's would be 16.

(The documents referred to were marked for identification as Petitioners' Exhibit Nos. 15 and 16.)

MR. POWERS: What we will do, and propose doing, is that we will take the video clips that are going to be shown here today, put those onto one compact disk, and have an electronic index in that disk that allows one to match up what you're about to

see on this piece of paper with the contents of the CD, and we'll file that as soon as we can get that produced.

If that sounds sufficient to the Court, that's how we propose proceeding, and, obviously, providing copies to counsel.

SPECIAL MASTER VOWELL: That's fine.

MR. POWERS: So before showing the video, I'm just going to take a moment and pass out to the masters and to Respondent's counsel Exhibits 15 and 16.

SPECIAL MASTER CAMPBELL-SMITH: Thank you. Also, counsel, without disturbing your plan for how you plan to proceed, but to the extent that Dr. Mumper could lay some groundwork before we look at the video as to why she picked this particular clip, what we should be paying attention to.

THE WITNESS: Right.

SPECIAL MASTER CAMPBELL-SMITH: Because without your sort of guidance even beforehand, we might get it after, but subtleties are certainly lost if we don't have a sort of a preview before we get into it.

MR. POWERS: And that's what we anticipated doing here, both a little setting some context and

then any description of what is actually seen.

SPECIAL MASTER CAMPBELL-SMITH: Thank you.

MR. MATANOSKI: Your Honor, just for the record, as you know from your prior orders that this designation was exactly what the Court had asked for prior to trial. The Respondent gave you the designation of the particular points of the videos that the Respondent will be looking at or relying on. Petitioners declined to do that, instead saying that they would have to wait, they were just going to essentially rely on the entire video and then designate later what they were going to rely on.

And with respect to replying to this, we will rebut what we can today, if necessary, however we reserve the right to designate or counterdesignate other parts of the video later for your review in a similar fashion to see -- what you saw from us before where we designated certain portions that we could be potentially relying on.

MR. POWERS: And Petitioners, as you also know, made it clear that we didn't designate anything early on because we would not anticipate relying on that in our case-in-chief. The designations now we're in rebuttal it's impossible to designate ahead of time what one might use in rebuttal because you haven't

heard the testimony of the witness that you might be rebutting. So these are offered in rebuttal. And if Respondent is saying they would want to reserve the right to designate more video, then if the record is open in these cases and more designations are needed and you want to see more information from video we are happy to do that and designate whatever the Special Masters think they need to see to get the full picture of the video.

SPECIAL MASTER CAMPBELL-SMITH: I would ask that, Dr. Mumper, as you go forward with this that you make clear in your preliminary comments what portion of Dr. Rust's comment to which you are specifically addressing.

THE WITNESS: Okay.

SPECIAL MASTER CAMPBELL-SMITH: You indicated you had taken very careful notes.

THE WITNESS: Right.

SPECIAL MASTER CAMPBELL-SMITH: And you were trying to respond to concerns about that.

THE WITNESS: Okay.

SPECIAL MASTER CAMPBELL-SMITH: So if you could make that clear as to what portion of Dr. Rust's testimony to which you are responding that would be very helpful.

THE WITNESS: Okay.

MR. MATANOSKI: And then if I may, just to clarify our position in this, we designated, our experts designated certain parts of the record, the video record that they would be relying on, provided that to the Court and to opposing counsel. During their testimony they did not refer to any other parts of the record, the video record, so these designations that Respondent has were well available to the Petitioners in advance. The notion that they are rebutting something other than that is a bit strange at this point since neither witness that referred to videotapes actually referred to any specific part other than the ones that have been designated. Indeed, they didn't even refer to those. But those had been designated already.

So the notion that rebuttal would come in now without prior designation is again a bit strange. And that is the reason why we'd ask that some relief, if necessary be given.

SPECIAL MASTER CAMPBELL-SMITH: I think that request has been granted Respondent.

MR. MATANOSKI: Thank you.

SPECIAL MASTER CAMPBELL-SMITH: That to the extent that you need or want to counter with

additional video testimony that we are certainly willing to entertain that.

MR. MATANOSKI: Thank you, Ma'am.

SPECIAL MASTER CAMPBELL-SMITH: To proceed.

MR. POWERS: Thank you.

So and, Dr. Mumper, before I ask about the first thing I want to make sure we are technologically ready to go. Okay.

BY MR. POWERS:

Q Excuse me. Now, we are going to talk about Jordan King first. You designated segment number one, which you have entitled "cooing"?

A Right.

Q Can you explain to the Special Masters why the little segment about 30 seconds long that they are going to see is significant in responding particularly to Dr. Rust's testimony?

A There was discussion in Dr. Rust's testimony about non-verbal language and other measures to communicate that did not involve actual words. And it was related to the, later to the topic of word count. And so this is an early language marker. The child in this video is about 3 months of age. And by showing it I show normal language development at that time plus a to and fro reciprocal relationship with the

mother who is cooing with the child.

Q Okay.

SPECIAL MASTER HASTINGS: Now wait a minute. I'm not sure I understand this exhibit. Part one you taped 12-98. What does taped 12-98 mean?

THE WITNESS: That's a date, December '98.

SPECIAL MASTER HASTINGS: So this is, it is, means December '98.

Now you just said age 3 months. And I have it Jordan King, born September 29, 1997. Is that not?

THE WITNESS: Is that a typo?

MR. POWERS: Yeah, no, it's not the date it's just the title of the tape.

SPECIAL MASTER HASTINGS: All right, the title of the tape.

MR. POWERS: It's just it is a number that is the title of the tape but it's not a reference to a date.

SPECIAL MASTER HASTINGS: It's not a reference to the date of the tape.

MR. POWERS: Right.

SPECIAL MASTER HASTINGS: All right.

THE WITNESS: Okay, Tom, in that tape we had --

SPECIAL MASTER HASTINGS: Let me also ask,

again what did Dr. Rust particularly say about the word development that you are trying to rebut here? If you can before we go into this on Jordan King, tell me what in general he said about Jordan King that you are taking issue with?

THE WITNESS: The concern was that he talked about how he thought it was a artificial distinction between regressive and classic autism and that he thought if you really look carefully and ask careful questions you'd find out that the child were not initially normal but that they had subtle signs of abnormality. And when I looked at these tapes as a pediatrician I thought that the things that we picked out to show showed some very normal developmental milestones both for non-verbal language, gesturing, as well as social reciprocity, as well as appropriate toy play initially. And --

SPECIAL MASTER HASTINGS: All right, let me stop you there.

THE WITNESS: Yes.

SPECIAL MASTER HASTINGS: Certainly lots of experts in this proceeding have said when you look at people who are said to have regressive autism and you look back, study videos, you'll find evidence of abnormality. That in general has been said.

Help me with my memory, to what extent did Dr. Rust say that about Jordan? Did he point to specific evidence of abnormality in Jordan?

THE WITNESS: Yeah, in --

SPECIAL MASTER HASTINGS: To the best you remember.

THE WITNESS: Yeah. On the basis of the notes that I took which I -- it's on page 25 of my notes, so that's about a little over halfway through his testimony, but I don't have the clarity to know if that was specific for Jordan King or not. So maybe if I can't do that, and we're not allowed to show the video, just tell me what the rules are.

SPECIAL MASTER HASTINGS: I'm not going to stop you from --

THE WITNESS: Yeah.

SPECIAL MASTER HASTINGS: -- showing any videos, I just want to understand what point you are trying to refute here because I don't, I'm not sure I recall.

Mr. Powers, do you understand what point you are trying to refute here?

MR. POWERS: Yes. Certainly as Dr. Mumper described it was general testimony that Dr. Rust offered that in his opinion relying on video that he

reviewed, and certainly without any reference to specific frames, that Jordan King and also William Mead were not normal prior to their regression.

SPECIAL MASTER HASTINGS: Okay.

MR. POWERS: And again, he did that without reference to specific frames but definitely was placing the onset of symptoms, or conversely the absence of normalcy, further and further back in time. So these are simply offered to show in that time continuum that describes the onset what Dr. Mumper has identified from her skill and experience and training as indications that Dr. Rust was either mistaken or was not looking at the appropriate signs. And that's her approach here.

SPECIAL MASTER HASTINGS: And I do think he said some general comments to that effect. I couldn't remember any specific comments. And okay, so very good.

THE WITNESS: I actually have found my notes now that are specific to Jordan King. I have that he said he had looked at the record regarding the timing of loss of speech. And then he had a discussion about the fact that it's not so much the number of words but it's important that he was communicating and then stopped talking.

And then he also said in the record it said something like he was never a "I want to be held" baby. And he always takes that very seriously.

And in the cooing video even though he is not being held there is a social reciprocity that speaks to social interactions that I thought would be valuable.

SPECIAL MASTER HASTINGS: Very good. Please go ahead.

MR. POWERS: Thank you.

BY MR. POWERS:

Q So let's go ahead and show what is designated on Jordan King's video clip index as Video Segment Number 1.

(Jordan King Video Clip No. 1 played.)

A So the good eye contact, the social reciprocity with the mother, and the fact that he is doing the appropriate language for a 3-month-old baby.

Q Let's move to Clip Number 2 please, Dr. Mumper. Can you give the Special Master some context for Clip Number 2 briefly?

A One of the frustrations in looking at these clips is that the timing wasn't clear, the actual dates did not show up on Jordan King. So the videos that I am going to show next I can tell you are

between the ages of 13 and 16 months but I can't tell you specifically how old the child was. We can get some clues perhaps from the progress of his development.

But that seemed to be a critical time in which Dr. Rust was saying that already, you know, the child was showing signs of autism, impaired showing language improvement or failure to progress, loss of social reciprocity. And so I wanted to address some areas in which he seems to be demonstrating age-appropriate normal behavior in that time period that was questioned.

SPECIAL MASTER HASTINGS: Now, when you got the tape, you just referred to a time frame of sometime between 13 and 19 months of age. Is that what you --

THE WITNESS: Yes.

SPECIAL MASTER HASTINGS: -- just said?

THE WITNESS: To the best of my ability to interpret the tape, the next one, two, the next series of tapes are in that time frame.

MR. POWERS: But was it 13 to -- I think Dr. Mumper said 13 to 16 months.

SPECIAL MASTER HASTINGS: Okay. Well, I wanted to inquire where you got that? Because now in

Exhibit, Trial Exhibit 15 here it's been identified as this is the tape from 1999, January to June. Now, on my calculations that would be 15, 15 to 21 months. So I want to know where you got the idea of 13 to 16?

THE WITNESS: Okay. In my original dating of the one that's marked "Playing Marimba" the date is October '98 to January '99.

SPECIAL MASTER HASTINGS: Right. Right, I see that.

THE WITNESS: Which is 13 to 16.

SPECIAL MASTER HASTINGS: So that's the 13 to 16. All right.

THE WITNESS: I'm sorry. The "Drop the Objects, Smile at the Camera" would be --

SPECIAL MASTER HASTINGS: Anyway, I think you've answered my question.

THE WITNESS: Yeah.

SPECIAL MASTER HASTINGS: You're getting the date just from the dates of the tape. So the tape was marked January through June of 1999.

THE WITNESS: Right.

SPECIAL MASTER HASTINGS: And you're just getting the dates from that?

THE WITNESS: Right.

SPECIAL MASTER HASTINGS: All right.

MR. POWERS: And not to delay actually seeing the video, but just as a technical matter the way that the parents maintained these on 4-hour VCR tapes. And so 4 hours of tape would have -- this is the date range they wrote on there. In many cases there's not a stamp on the film itself.

SPECIAL MASTER HASTINGS: I understand.

MR. POWERS: So that explains some of the --

SPECIAL MASTER HASTINGS: My videotapes at home are marked exactly the same way.

MR. POWERS: Okay.

BY MR. POWERS:

Q So, Dr. Mumper, let's go ahead and show Tape Number 2, please.

A So I think we've established the child's actually older here per Special Master Hastings.

(Jordan King Video Clip No. 2 played.)

So what I wanted to demonstrate there was the child dropping the toy and then looking to see where it went has to do with the establishment of a concept called object permanency and making the connection in his brain that when you do something with an object and it goes out of site that it continues to exist beyond what you see.

It also can be interpreted as processing

cause and effect.

And then I also wanted to show that in that age range above 16 months he was still smiling and having social reciprocity with whoever was running the video camera.

Q Now Clip Number 3 please. This is one that is called "Playing the Marimba."

A And now, Tom, I believe we are back to the somewhere in the 13 to 16 month age range now. And this is looking at reciprocity in terms of play with another person and being able to socially interact in a musical game.

(Jordan King Video Clip No. 3 played.)

Q Okay.

A And he was also looking around at the videographer again in that.

Q Clip Number 4, "Playing with the Cat." Let's go ahead and cue that up, please. And can you describe what the Special Masters ought to have an eye out for here?

A Yes. In this situation it seemed like very appropriate interactive play with an animal and with the grandmother.

Q Okay.

(Jordan King Video Clip No. 4 played.)

A And again he looked at the camera.

Q Clip Number 5, quick context? And I think we've got our process down for going through these.

A Yes, right.

Q So if you could provide some context here for the Special Masters and then we'll show the clip?

A One of the discussions in testimony was about not being able to use gestures, that it wasn't just language but that children also had gestures that were postulated to be absent or of poor quality in these children. And this is demonstrating gesture to be picked up, which is typically around, emerges around 9 months of age as a skill.

(Jordan King Video Clip No. 5 played.)

And again still making eye contact with the people in the scene.

Q Okay. What's been designated as Clip Number 6 called "Dancing" I'm guessing is Jordan dancing. But if you could provide again some context for the Special Masters?

A Showing ability to enjoy play, ability to interact and look at the person who is filming him. You will see when you see the tape that he is very engaged.

(Jordan King Video Clip No. 6 played.)

Q Okay. Now, the next one it's called "Toolbench," and this is Clip Number 7.

A In this it demonstrates his ability to use tools in a functional way and an appropriate way to play as opposed to lining up toys or playing with them in an inappropriate way.

(Jordan King Video Clip No. 7 played.)

Q And is that Maya, his sister?

A That's Maya, his sister. So we know that he is at least 15 months old in this video.

(Jordan King Video Clip No. 7 playing.)

Q This is from the -- that was on the original tape.

Now, Clip Number 8 is called "Harmonica." Again quick little context for the Special Masters and we'll play that clip?

A Showing the social reciprocity between him as he plays a harmonica and the other people in the room, showing interactive play.

(Jordan King Video Clip No. 8 played.)

Q And actually if we could stop it there for just a quick second. Jordan was shown being held. Do you recall Dr. Rust making comments that one of the things that he thought might have been going on with Jordan early on was an aversion to touch and an

aversion to being held?

A Yes, I do recall that. And, in fact, there are many, many, many examples in the video I reviewed where he was being held by various people, grandmother, mother and father.

Q Okay. Let's go ahead and complete rolling this clip please.

(Jordan King Video Clip No. 8 played.)

A So he perked up when he was told he had a good job. And so he was responding to the mother there. He clearly was smiling brightly and interacting. And so at that point he was also showing gestural language.

Q Now, you also, tell me if you did, recalled Dr. Rust saying that Jordan had splinter skills?

A Right.

Q You have to stay back from the microphone.

What was his description of splinter skills relative to Jordan King?

A Well, I believe he was postulating that he had musical abilities. And so between the fact that he came from a musical family and had demonstrated his work with the harmonica and marimba he may have been referring to that. Whether it's a true savant skill, you know, time would tell.

Q But at this point there's nothing savant-like -- I mean not to denigrate Jordan's harmonica playing -- but there is nothing savant-like that you would identify in any of the musical sequences? And I say it jokingly, but since Dr. Rust did mention this, there is nothing savant-like that you've identified in any of the musical scenes here involving Jordan, is there?

A Yeah, I would say that was very rudimentary, age-appropriate for a toddler harmonica playing.

Q Okay.

A Yes.

Q We're going to go to Video Clip 9 then, please. And this is "Building a Marimba."

A And the thing to look for here is his ability to use a nail in a functional way and to imitate his father trying to put a nail into a hole and repeatedly getting it out of the bag, the nail bag.

(Jordan King Video Clip No. 9 played.)

Q And so demonstrating the nail but did you see anything else in that video that would be significant, any interactions with his dad or anything of particular mention?

A Yeah, he was looking back and forth for

approval from and interaction with his father.

Q And then we're going to show Clip Number 10.

A And the reason I chose this is that there was some speculation about Jordan withdrawing around the time of the birth of his sister and being withdrawn and not socially interactive with her.

(Jordan King Video Clip No. 10 played.)

Q Okay.

A And --

SPECIAL MASTER HASTINGS: Before we leave this tape, in that segment his sister looked like a very, very young newborn.

THE WITNESS: Right.

SPECIAL MASTER HASTINGS: Would that be your interpretation?

THE WITNESS: Yes. I think she was a very new newborn. So my best guess on his age would be that he was around 15 months at that age.

SPECIAL MASTER HASTINGS: All right.

THE WITNESS: And that's all we have to show looking at normal characteristics. We have two brief clips post-regression that show a clear, I think, contrast to what we've been looking at.

BY MR. POWERS:

Q And before we move to those I just want to

note in watching the videos here there were a couple of videos where he was vocalizing and babbling but honestly I didn't hear a lot of fully-formed words. What's your assessment of his language skills based on the video clips that we've seen here?

A I agree that we don't hear a lot of clearly articulated words in these video tapes. I did hear Mrs. King testify, and I found here to be a very reliable historian, and she gave word counts which would suggest that he did have normal language development. But what's striking in these videos is that he almost always either has a pacifier in his mouth or he's eating something or he's playing the harmonica and so I don't see a lot of language. So I think we have to be clear that for that aspect of those three domains of his development I don't have good examples on video and I am relying on parental history.

Q So you mentioned that the last two clips that we'll see here for Jordan King, 11 and 12, these are two that represent a presentation of post-regression symptoms?

A Right. And I mainly want to have the Special Masters look for a qualitative change on his facial expression, how much more detached he is now,

how he doesn't show the same kinds of social reciprocity, and how he is oversensitive to auditory stimuli and exhibiting hand flapping.

Q Okay. So we will go ahead first and show Clip Number 11. And this is, the short title of this is he has "hands on his ears."

(Jordan King Video Clip No. 11 played.)

Is that a behavior that you noted in multiple videos after regression?

A Oh, after regression, yes. Did not see it before.

Q And finally for Jordan we're going to show Clip Number 12.

(Jordan King Video Clip No. 12 played.)

So what's significant about this videotape, particularly as you would compare it to the clips that we viewed and that you've reviewed before he regressed? What are the significant things to take from that clip?

A So it shows to me a significant qualitative change in the interactions with his father. Whereas before he was so engaged and now he seemed to be withdrawing. And he also is demonstrating a lot of hand flapping. Again the vacant expression in his face. And whereas before he seemed to enjoy

manipulating tools in an appropriate way, now he seems to have lost that higher level of toy usability.

Q And particularly with the toys you are talking about the way that he just kept flipping the puzzle piece back and forth?

A Right; as opposed to putting it into the form board.

Q Okay. So now we're going to talk about some of the videos from William Mead?

A Yes.

Q And this is the list that is Petitioners' Trial Exhibit Number 16. We will use the same process here, Dr. Mumper, in introducing the context for the Special Masters and then showing the clips in sequence.

A Okay.

Q So Clip Number 1, can you explain what they are going to see and what they should be looking for?

A Actually, if I could just get a minute to get organized here? Because I was trying to find the specific things in Rust's testimony, which I have done. So now I just need to get oriented to his videos.

Q Okay.

SPECIAL MASTER CAMPBELL-SMITH: You

anticipated my question, Dr. Mumper.

THE WITNESS: Say it again?

SPECIAL MASTER CAMPBELL-SMITH: You anticipated my question.

THE WITNESS: So on my page 5 of Dr. Rust's testimony he talks about kids with autism being head shy, not wanting to have their head touched or hair washed, that this is a very striking finding that comes on very early.

He also talked about aversive eye contact and how that was a systems problem that was worthy of careful scientific investigation.

And he also talked about parents in the family history tending to be rigid and aloof and hypersensitive to criticism. Through multiple video clips I did not find that to apply to either set of these parents.

And so with that as a background, the first tape that's called --

SPECIAL MASTER CAMPBELL-SMITH: Just a moment.

MR. MATANOSKI: I would just observe that I believe those comments by Dr. Rust were general comments. As I think the Court has observed before about some of the other comments that he had made they

were to apply more generally to descriptions of autism.

MR. POWERS: And, Special Masters, he was describing why those general comments informed his opinion that these two boys demonstrated what he described as abnormal courses of development before their regression and that they had early onset. So again his comments were general but he was applying them in a way to support his opinions on the case-specific determination that both of these boys were abnormal at particular stages of their development.

SPECIAL MASTER CAMPBELL-SMITH: Okay.

MR. MATANOSKI: I recognize the Special Master can go back at the testimony of Dr. Rust. And we'd submit that our recollection of that is that it was general in nature and that I think it's pretty clear in his report and through his testimony that he did not dispute that either the King or Mead child had regressive autism.

SPECIAL MASTER CAMPBELL-SMITH: That is what I recollect. But Petitioners' counsel, if you would like to proceed with this demonstration in the absence of any objection from Respondent.

MR. POWERS: Yes. We would like to proceed and just with the note that while Dr. Rust did not

dispute the what ultimately was regressive autism, he did make reference to both boys having -- he was very non-specific about it so we can't be more specific, but he did make reference to both boys being not normal before the regression. And if he had been more specific we could point to a particular page of his testimony, but he did make a general observation about the lack of normalcy before the regression that we all concede.

SPECIAL MASTER CAMPBELL-SMITH: I will observe that it was my recollection of Dr. Rust's testimony that at the time that it was documented one could assume that it had appeared earlier. But it was, there was an inability to determine, and he acknowledged he had not met the children and had not examined them personally. But based on what the reflections were in the medical record that the time that you are documenting something there is an understanding that the activity was a loss of the activity or function occurred before the notation.

But with that in mind we will -- and again, Dr. Mumper, if you would just describe, as you have.

THE WITNESS: Okay. And I will try to be brief.

The "Johnny Jump Up" tape is showing

reciprocal social interactions with his, one of his parents.

SPECIAL MASTER CAMPBELL-SMITH: Do you have an estimated age for this? These are pretty well dated but I don't know what this is.

THE WITNESS: Hang on one second. On my -- Scott, if you can help me, what I am looking for is not the recounted notations that you did this morning and last night but the ones that I set you by e-mail that had better ages?

BY MR. POWERS:

Q For "Johnny Jump Up" does it sound accurate to believe that this was something from November of 1998 when he was about 5 months old?

A Yes. Yes, that is correct.

(William Mead Video Clip No. 1 played.)

The next one is marked "Pushing Up" and --

SPECIAL MASTER CAMPBELL-SMITH: What is the purpose of "Johnny Jump Up"?

THE WITNESS: To show the reciprocal interaction, the smiling, the fact that he's bright-eyed and alert, that he looks like a normal 5-month-old.

SPECIAL MASTER CAMPBELL-SMITH: Thank you.

BY MR. POWERS:

Q So the next clip is Clip Number 2 on Exhibit 16, it's called "Pushing Up"?

A Right. And that's demonstrating great eye contact.

(William Mead Video Clip No. 2 played.)

Reciprocal smile, bright-eyes, laughter with the father.

Q Clip Number 3, "Bath Time." And I will note that it is with his sister, to Eleanor's everlasting embarrassment perhaps, but this is actually a significant clip, as Dr. Mumper will explain?

A And this clip speaks to the issue of Dr. Rust's testimony that not wanting to have their heads touched or their hair washed is a very early sign of children with autism. And in this video you will see that he tolerates that from his sister and he also does a fair amount of babbling.

(William Mead Video Clip No. 3 played.)

Q And again what was significant about that clip?

A Well, he seemed to tolerate or perhaps even enjoy the head touching. But he's showing a lot of reciprocal smiling and giggling and laughing and normal appearing bathtime play.

Q Tape Number 4, this one is called "Hi, Dad."

What is the context and the significance of this clip? What should the Special Masters be looking for here?

A This is a tape that was done around the time of his first birthday when he was around a year old. And he demonstrates the words "Hi, Dad." Two-word phrases typically come in around 18 months. It's demonstrating that at a year he at least had several words which is very much in keeping with the history given by the parents.

This tape also shows some reciprocal play with the sister again.

(William Mead Video Clip No. 4 played.)

Q And then we will just keep going, sort of an extension of this is Clip Number 5 which is called "Play Nice."

(William Mead Video Clip No. 5 played.)

Q And what was significant about that clip again having seen it again?

A He says "Hi, Dad" again and he's having reciprocal interactions with both the parent and the sibling.

Q Everything about that video was developmentally and age appropriate?

A It seemed very age appropriate to me, yes.

Q Okay. Now, the last two videos can you

describe to the Special Masters what we'll be looking at?

A The last two are after his regression. The first one is showing him covering his ears and hand flapping as a stark contrast to his initial prior normal behaviors that we've attempted to demonstrate here.

And the second one I believe to be demonstrating that he has abdominal issues.

(William Mead Video Clip No. 6 played.)

Q Okay, now that, the date on that was July 2000, so he would have been about 27 months old?

A That's correct. And I think you can appreciate the deterioration in the quality of his language. Whereas at a year he was able to say "Hi, Dad," he is pretty much reduced at this point to these guttural utterances. I think that there is a qualitative change to his facial expression, he has more of a vacant look. And he wasn't able to imitate saying cheese. It just is a way of demonstrating the regression.

Q And several times he was holding his hands to his ears?

A Yes. As if he had hyperacusis or was trying to modulate the incoming sensory stimuli.

Q And was he also flapping his hands?
A And he also was flapping his hands, yes.
Q Had you seen any behavior like that prior to the, say, 16 months of age?
A I did not.
Q The final clip we're going to show is Clip Number 7. This is William at the computer?
A Yes.
Q Okay.
A And I would like to set up the Special Masters to look for his abdomen in this picture. One of the things that John Green did for which he was criticized by Dr. Rust was to work on aspects related to the child's diarrhea and bowel movements. And I believe that this tape shows inferential evidence that he was having abdominal pain. You will notice that his abdomen seems quite distended, quite bloated, that he pushes on the lower part of his abdomen. That at one point he is pulling on the skin. And this, these are behaviors we frequently see in children with autism. And I believe that we at least need to be open to the possibility that they are trying to communicate with us that their stomachs hurt in ways that they have to use since they no longer have language.

(William Mead Video Clip No. 7 played.)

Q So, Dr. Mumper, in addition to the stomach issues was there anything else in that video clip that merits description or mention to the Special Masters?

A That he seemed nonresponsive to multiple efforts by his dad to engage him, that he was sort of staring fixed on the computer screen but not attempting interactive play.

Q So based on your listening to the parents' testimony, your review of the medical records, and now the videos that you've identified here, do you agree or disagree with Dr. Rust's testimony that each of these boys was likely not normal prior to their regression?

A I don't find evidence, so I disagree with him.

MR. POWERS: I have no further questions.

SPECIAL MASTER CAMPBELL-SMITH: Thank you.

CROSS-EXAMINATION

BY MR. JOHNSON:

Q Good to see you again, Dr. Mumper.

A Hi.

Q As you know, my name is Vo Johnson. I am representing the United States.

Doctor, you covered a lot of different

issues in the early part of your direct, and so I just want to make sure that in the last two weeks since you've testified that you have not become an expert in biochemistry; is that correct?

A That is absolutely correct.

Q And you've not become an expert in neurology?

A That's true.

Q You've not become an expert in psychiatry?

A That's true.

Q And you have not become a clinical psychologist?

A That's true.

Q Okay. And you have not become an expert in toxicology?

A That's true.

Q And you've not become an expert in neurotoxicology?

A That's true.

Q And you've not become an expert in genetics?

A That's true.

Q Would it be fair to say that your knowledge of those areas is based on what you have learned from your colleagues at the Autism Research Institute?

A And through my reading of other literature,

yes.

Q What other literature are you specifically referring to?

A We maintain bibliographies not just of the papers written by people officially associated with us but other articles in the autism literature. So the works of, you know, Pardo, Zimmerman, Vargas, Martha Herbert, people that are in Italy working on the environmental components of autism, people at the Mind Institute that are working on immune disregulation and autism, Federico Balzoa in Italy that's working on gut abnormalities in autism. So the list could go on but we don't limit ourselves to what is just within our institute's publications.

Q Would it be fair to say that you give more weight to those articles that your colleagues at the Autism Institute are feel are helpful?

A That would be a fair statement. And I also give more weight to articles where I've had the opportunity to discuss them with the authors.

Q Doctor, you were asked a number of questions about the different treatment therapies that Dr. Green provided to both William Mead and Jordan King, and that I think you also use to some extent in your own practice?

A That's true.

Q One issue that was asked about was chelation, the use of chelation therapy. And I believe that you said that, you testified that even though or that the justification for the use of chelation in your practice was really targeted towards the lead that was present; is that what you testified to?

A That's not exactly the way I meant to say it. I was saying that we look at various types of toxicity, and lead is very, very common. So when we do porphyrin analyses the two main things that we're looking for in those porphyrins are lead and mercury. And we have come to very much appreciate how much they co-exist. And so treating lead toxicity is well within something that pediatricians have had experience with in terms of treating that with DMSA, which was also used in these boys.

Q What symptoms of lead toxicity are you relying on for the justification to do chelation therapy?

A Well, the classic symptoms of lead toxicity include irritability, hyperactivity, or declines in cognitive performance. But as you may know, the American Academy of Pediatrics and the CDC have

recommended ongoing lead screening for children because it is not felt to be prudent to rely on development of symptoms as opposed to trying to address lead toxicity if it exists in a child somewhat unsymptomatically at the time.

Q So you would require some testing showing an abnormal lead level in the blood before you would do chelation therapy in that child?

A No. Because the lead levels in the blood only persist for a relatively short time. The blood turns over very quickly within two to three months. So unless you are getting the child at the age of the acute lead exposure, you may miss the exposure in the blood. And so you are left with indirect measurements.

Q So it's your testimony that blood testing is not a reliable measure of lead body burden?

A Right. It can be used to look for acute exposure.

Q Doctor, you would at least agree that people have died from chelation therapy; correct?

A Yes.

Q And I believe you mentioned one case that Dr. Rust raised in his testimony but that's not the only case in which someone has died from chelation

therapy; is that right?

A He mentioned four. And I consulted with several of my colleagues and we could not find four cases. We were only aware -- I'm mostly aware of the one that I mentioned. And I think that there was one other one of which I'm not familiar. But I do not know the third or fourth case.

Q Are you aware of one case that actually involved there was a lawsuit that was brought and one of the defendants that was named in that lawsuit was Metametrix which is one of the labs that's done testing in these two cases?

A I was not aware that Metametrix was named in that lawsuit, no.

Q You talked a little bit about some of the therapies that Dr. Rust criticized. And I wanted to ask you a couple of questions about those. And let's start out with IVIG since that was the first one that you discussed.

A Uh-huh.

Q How does IVIG treat persistent inorganic mercury in the brain?

A I am not saying that it does.

Q So whether IVIG treatment is effective in any given case really doesn't speak to the issue of

whether thimerosal from vaccines contributed to autism; is that correct?

A It speaks to the issue that he was treating documented low IgG levels in those children.

Q And that's not specific to persistent inorganic mercury in the brain; is that right?

A Not to my knowledge.

Q How does Eskimo oil treat persistent inorganic mercury in the brain?

A I am not aware of any studies that have assessed that specifically.

Q So the ineffectiveness or effectiveness of Eskimo oil in treating symptoms of autism really doesn't speak to whether thimerosal from vaccines contributes to autism; is that right?

A That's correct. It's being used for intestinal reasons and the other reasons that I articulated.

Q How does valtrex treat persistent inorganic mercury in the brain?

A Actually I think that if you use valtrex to decrease adenosine which would then allow methylation biochemistry to proceed, the ultimate result of that would be an increase in glutathione as demonstrated in Dr. James' work. Cysteine and glutathione are part of

the integral mechanisms for handling mercury. And so whereas John was not doing it specifically with the target of working on inorganic mercury in the brain, that is actually quite a biologically plausible way to improve detoxification capacities through the body's own natural mechanism since glutathione is the primary thing that we rely on to try to handle mercury toxicity.

Q And remind me again, what is valtrex, what's the primary clinical use for valtrex?

A It's an antiviral agent but it's also a purine analog and so that's where its utility in dealing with adenosine comes in.

Q And when you say "antiviral" I believe you said Dr. Rust testified that it was used for use in genital herpes; is that correct?

A Right. And it's also been looked at for other types of viral infections, HHV6, Epstein-Barr virus, cytomegalovirus. I'm not sure from John's notes if he was primarily using the viral mechanism or the adenosine mechanism, or both.

Q Are you aware that valtrex has never been tested in a pediatric population?

A I would not be surprised because many drugs that we use are not tested under the age of 12.

However, acyclovir is the drug of indication for newborn herpes encephalitis. And valtrex breaks down to acyclovir. So we have clear precedent in standard medical practice for using it in even newborns.

Q Would you be more comfortable using that, using valtrex if it had been tested in the pediatric population?

A We have become used to not always having that luxury, but it's always great when the studies are done on the children. So, yes, I would be more comfortable.

Q And I think you alluded to earlier that there aren't case-controlled studies on the use of many of these therapies; is that right?

A That is true.

Q Would you feel more comfortable as a pediatrician treating children if these various treatments had been tested in a case-controlled study?

A As long as the case-controlled study took into account the medical problems of the child and was not very heterogeneous, yes, I would.

Q And are you testifying here today that you believe that your clinical judgment about the effectiveness of these treatment therapies is more reliable than a case-controlled study would be?

A I'm testifying that when we are trying to take care of a generation of children and being overwhelmed by their medical problems that we are in a position where we are trying to take care of the individual patient and we feel some urgency that we can't wait for 10 or 20 years. These children seem to have a window of opportunity where if you treat their medical problems they get better. And with the timeline of applying for grants, getting the studies completed and analyzing the results and then the meta-analyses, we are proceeding in good faith, using our best clinical judgment, realizing that we don't have good case control studies for all that we do.

Q And I've heard you use the phrase in the past, refer to the concept the child is your laboratory. Is the approach you just described what you are referring to when you say the child is your laboratory?

A That's a shortcut way of saying that when you're doing intervention your biggest outcome is how it affects a particular child. We certainly use a lot of laboratory values in helping us assess the child. But if we are able, for example, to give valtrex and document that for a particular child their adenosine level went from high to the normal range, as it did in

Jill James' work, that is more important to me than what acyclovir did in 20 kids that are not my patient, because for that patient it demonstrated an improvement.

Q So in other words, you're willing at least at this point to rely on your clinical judgment, even in the absence of case-controlled studies showing that these treatments are effective?

A There are case controlled studies looking at a number of these treatments showing their efficacy. That has been demonstrated, for example, for B6. There are about 22 studies demonstrating efficacy. There have been studies looking at omega-3 and demonstrating efficacy. We have looked at multiple vitamins and we demonstrated efficacy.

But much more work remains to be done.

Q And those treatments that you just talked about are those the ones that are targeted at the oxidative stress issue?

A Many of them are, yes.

Q And oxidative stress is not specific to mercury toxicity; is that right?

A That's correct.

Q Those, other things can cause oxidative stress?

A That's correct.
Q Doctor, did you listen to the testimony of Dr. Rutter or Dr. Lord or Dr. Fombonne?
A No. I was not able to hear Dr. Rutter or Dr. Lord. And I only heard part of Dr. Fombonne's testimony when I was driving up yesterday.
Q I believe you testified when you were here a couple of weeks ago that you don't diagnose autism; is that right?
A Yes. I do rely on other psychologists, psychiatrists to be the one who makes the diagnosis. I'm concerned that if I were to diagnose them and then take care of them and they get better that the criticism would be levied that I must have misdiagnosed them in the first place.
Q Do you know what the ADIR is?
A Yes.
Q Can you tell us?
A Autism Diagnostic Interview Revised.
Q Do you use that tool in your practice?
A I do not. I get reports on it from other people but we do not do those intakes ourselves.
Q Do you know what the ADOS is?
A The Autism Diagnostic Observation Scale.
Q Do you use that in your practice?

A I typically do not. We did use the ADOS in one of our clinical trials in which we hired a psychologist to administer it to our patients. But I do not have any experience administering it myself. Again I rely on reports from other doctors.

Q Do you know whether the ADIR or ADOS have any questions that are targeted to the issue of determining whether a regression has occurred?

MR. POWERS: I'm going to object. This is a re-do of the cross-examination of this witness and is not addressed to any of the issues that she discussed in her rebuttal testimony today. I believe that opportunity to raise these issues would have been during cross or during re-cross following her direct testimony. This is not surrebuttal.

MR. JOHNSON: Special Masters, we have heard a great deal of testimony from Dr. Mumper today based on the videos in which she is purporting to identify abnormal development as opposed to normal development. I think this goes directly to her qualifications for being able to offer that testimony.

SPECIAL MASTER CAMPBELL-SMITH: Proceed.

MR. JOHNSON: Thank you.

THE WITNESS: My memory is that the ADIR does have some targeted questions that work on

identifying regression.

BY MR. JOHNSON:

Q Do you know what those questions are?

A No, I do not.

Q In your own practice do you use any standardized questionnaire when you are taking a parent history or a patient history from the parent?

A We use an intake form. It is not standardized.

Q What questions do you ask to determine if there's been a regression?

A We look for -- we ask questions about age-appropriate language, social and reciprocal behavior. We look for a time at which the child seems to be meeting milestones. Then we look for a period where they clearly lose those milestones.

The classic example is to expect that the skills are obtained and then they're clearly lost and that there's a period of time, some people use three months, between the time that they clearly demonstrated that and then have clearly lost it.

Q Can you give some examples of specific questions that you ask?

A How many words did your child have at one year? Momma, Dadda, hi, bye and Nonna.

How many questions did your child have at 18 months? He was no longer speaking any words but sometimes he's just "ummm" or "mmmm."

Q Were you giving examples of both the question and an answer to the question?

A Right. Right. The question initially is assessing language at a certain point and then assessing language at another certain point. And I was trying to give an example of regression.

Q You determined in this case that there was totally normal development based solely on the review of -- your review of the medical records; is that right?

A I made the judgment that up to some point that the child appeared to me to be normally developing based the notations in the well-baby checkups which I went through month by month, and on the basis of the videos that I was able to review in which the normal development seemed to correlate with what had been annotated in the pediatrician's records. And then at some other point there was loss of language, loss of social reciprocity, loss of reciprocal behavior and appropriate play versus ritualistic play.

Q Now, you didn't review the videos until the

Thursday before you testified; is that correct?

A That is correct. I did not get them until then. So at the time that I wrote the report I was very much dependent on the pediatric records which seemed to be doing a state of the art kind of assessment at the well-baby visits and then clearly documenting a regression.

Q And you also at the time of your report had not interviewed the parents; is that correct?

A That is correct, yes.

Q Did you hear Drs. Rutter, Lord and Fombonne all testify that parents often don't recognize early subtle signs of abnormal development?

A I did not hear that testimony but I do know that Rutter and Lord and Fombonne have written about that and talked about the subtle signs.

Q Do you disagree with their testimony on that issue?

A I think there are certainly cases in which parents overlook subtle signs. And if there are subtle signs that I missed on these videos I will be open to learning from those colleagues.

I think the fundamental issue though is do these kids look like they're abnormal from birth or do they look like they're on a normal developmental

trajectory and then something happens that interferes with that. So that for me is the crucial kind of issue.

Q I think you testified that you did not see evidence on the videos of Jordan King not wanting to be held; am I characterizing your testimony correctly?

A I think I said that I saw a number of cases where he was being held. Now, there were a couple of examples on the videotape where he did try to get out of the parent's arms. And so I just was trying to point out that the sort of all or nothing situation doesn't exist. And I think that he was able to tolerate being held many times.

Q You would agree that there are notations in the medical record that indicate his mother reporting that Jordan didn't like to be held as an infant, wouldn't you?

A Yes.

Q In fact, at Jordan King Exhibit 8, page 109, notes "Mother noted that Jordan was more content not to be held as an infant." Would that be one of the notations that you saw when you reviewed the record?

A I think so. I'd just like to look and see where it is.

(Witness reviews document.)

Yes.

Q And also at Jordan King Exhibit 8, page 87 -- no, sorry. Yes, page 87, does it say "at 3 months he was never an I-want-to-be-held child but did allow it then grew out of that"?

A Uh-huh.

Q Doctor, I think you testified a couple of weeks ago that you don't typically use videos in your own practice; is that right?

A That is correct.

Q That you normally just don't have time to view the videos?

A Right.

Q Were you ever asked -- let me ask this. When were you first asked by counsel to go through the videos and identify clips that you thought or that in your opinion showed normal development?

A Gosh. I can't, I can't really remember the timing. I think it was sometime about two weeks after the DAN conference, which would have put it maybe in the third week of April. But I'm not at all sure about that.

Q And you obviously didn't view the videos at that time, is that right, because you only saw them for the first time the Thursday before you testified?

A The -- I'm trying to remember now. I remember there was a Saturday morning that I spent a great deal of time looking at them. I guess what I really need to determine is when I actually received them. And, I'm sorry, I can't remember the timing on it.

Q So as you sit here you just can't recall when you first viewed the videos?

A All I can say with certainty is that it was sometime after our big Defeat Autism Now conference which was sometime in early April.

Q And did you prepare any notes at that time regarding the videos?

A I have a bunch of notes. One set the first time I reviewed them, another set trying to hone in on what was testified on by Dr. Rust. So the honing in happened this past weekend. The first review I think I only, I think I only got the notes the Thursday before I was due to testify the following Friday, so I had looked at it the weekend before my testimony. That's my best recollection. So I have two sets of notes from the first review the weekend before I testified and from the second review the weekend before this testimony.

Q Was it communicated to you when you first

received the videos approximately two weeks after the Defeat Autism Now conference that you're referring to, was it communicated to you at that time that the Petitioners were asked to designate specific portions of the videos that they contended showed normal development?

A I may have misunderstood the timing on that because I didn't realize I was supposed to submit that way ahead. I'm sorry. I guess I may have misunderstood that.

Q And have you ever been provided a copy of Respondent's video designations?

A No.

MR. JOHNSON: Thank you. I have nothing further.

SPECIAL MASTER CAMPBELL-SMITH: Any further questions from Petitioners' counsel?

MR. POWERS: Not at this time, no.

SPECIAL MASTER CAMPBELL-SMITH: Any questions from my colleagues?

SPECIAL MASTER HASTINGS: Yes. I have just a couple I think, Dr. Mumper.

According to your report and my view of the record as well, Jordan received the thimerosal in question at birth and at age 2, 4 and 6 months. So

according to your report your summary is that by the time he was 7 months old he had received a total of 187.5 micrograms of ethyl mercury?

THE WITNESS: Yes.

SPECIAL MASTER HASTINGS: Is that right?

THE WITNESS: I think that sounds correct.

SPECIAL MASTER HASTINGS: So I want to ask you then is the timing of the onset of Jordan's symptoms is it crucial to your ultimate opinion, you've indicated the opinion that in Jordan's case you think it's probable that the thimerosal and that series of vaccines contributed to his autism?

THE WITNESS: Yes.

SPECIAL MASTER HASTINGS: Would it matter in that opinion whether the first symptoms occurred at 18 months or 13 months or 9 months? Does it matter? Would you opinion be the same?

THE WITNESS: No, sir, it really doesn't matter to me because I think the crucial thing here is that mercury can be latent for a period of months before it manifests. The classic example of that is a lab researcher who got two drops of mercury on her gloved hand and seemed fine for about three or four months, then go dramatically ill and ultimately died. So the concept of it being there and not causing overt

symptoms for a while as yet to be determined until we study this better is entirely consistent with what I believe to be the case here.

So for me the crucial thing is more than at least initially he seemed to be developing normally and then he had the development of autistic symptoms. And whether they started at 15 months, 18 months, 20 months or 22 months doesn't really change my mind about the plausibility that thimerosal was a contributing factor.

SPECIAL MASTER HASTINGS: All right. And that wouldn't change if they occurred even earlier than that, say 13 months?

THE WITNESS: Right. Because in this case his exposure, his first exposure was a hepatitis B vaccine at birth which he got when his mother had been given antibiotics for a fever and he had just been born. So the initial exposure was quite early on. So it's very difficult for me to tie an exact timeline to overt symptoms.

SPECIAL MASTER HASTINGS: All right. That's all I have.

SPECIAL MASTER CAMPBELL-SMITH: I have a couple.

Would that same observation apply in the

Mead case?

THE WITNESS: Yes.

SPECIAL MASTER CAMPBELL-SMITH: The other matter I wanted to get from you, you had indicated there were three particular record citations regarding the normal head size at birth --

THE WITNESS: That's correct.

SPECIAL MASTER CAMPBELL-SMITH: -- for William. I only noted one. Perhaps you didn't say all three of them but I'd like to get those.

THE WITNESS: Yeah. Let me see if I can find that page. The problem is is that the second one I cited did not have an exhibit number on my copy. So I will turn my paper copy over and one page has two different citations, one about head size and one about skin. And so it's titled Providence St. Vincent Medical Center nursery admission record.

SPECIAL MASTER CAMPBELL-SMITH: Right.

And the third one?

THE WITNESS: The third one is on the same page as the second one.

SPECIAL MASTER CAMPBELL-SMITH: Okay.

THE WITNESS: It was just three different places that addressed the issue of maybe the head size was off because of trauma.

SPECIAL MASTER CAMPBELL-SMITH: Let me inquire, I recall that your testimony on -- during your initial time, and I can't remember whether it was direct or cross, but you look for deviations from the standard that would cause you to be concerned about head circumference. Dr. Rust gave some testimony that really it didn't matter what the head, the birth size or birth time measurement for the head circumference was, he looks for trends.

THE WITNESS: True.

SPECIAL MASTER CAMPBELL-SMITH: Do you disagree with the looking for trends in your personal practice or what I'm trying to get at is do you think that is an invalid way or are you challenging the validity of what he said?

THE WITNESS: No. I agree completely with him that trends are important. And I also am open to the possibility that any isolated point could be an error. That's why when he postulated an error in this case I went back to see if maybe the head was noted to be misshapen or have a cephalhematoma or caput succedaneum because he was postulating that the higher head circumference at birth might have been artifactual.

The trend he's looking for is a normal or

low head size that then goes up and then comes back down. And that has been classically described in many different cases of researchers that are looking at head circumference as one way of understanding autism. And that model fits well with a lot of the published literature. I was just pointing out that we didn't seem to have that model in William Mead and that if you were going to throw away that first measurement because it was high and therefore the trend wouldn't have been as dramatic, it would be nice to have more than just speculation that it might have been wrong or that the child might have had head trauma.

And it just seems like from the medical records that potentially limited as they are that we do not have reason to think that his head really wasn't that size at birth, that it really wasn't 80th to 85th percentile at birth.

But I agree, trends are important, much more so than individual numbers; correct.

SPECIAL MASTER CAMPBELL-SMITH: And just to be clear about your position in this particular case, you don't think that that trend exists, it is your interpretation of William Mead's records that that trend does not exist for William Mead, the trend to which Dr. Rust referred?

THE WITNESS: I think for me it's going to be an unanswered question. It seems to me that we have evidence that he started out on a growth percentile for his head that was very much in keeping with the rest of his body. He did show some elevations in his head circumference at the 4, 6 and 9 month checkup. And then he comes down a little bit above the 50th percentile. So it is a little bit of a trend that shows the decrease in head circumference after an initial higher point. I just don't want to leave out the possibility that initially he was already at a high point.

SPECIAL MASTER CAMPBELL-SMITH: Thank you. Have my questions of Special Master Hastings' questions provoked further questions from counsel?

MR. POWERS: They have not, Special Master. Just to note for you that the exhibit number that Dr. Mumper was referring to, and this is in William Mead's individual file, it's Exhibit 3, page 13.

SPECIAL MASTER CAMPBELL-SMITH: Thank you very much.

Does that conclude Petitioners' presentation of your rebuttal witnesses?

MR. WILLIAMS: We have one more matter. Special Master Vowell had asked me to lay a foundation

for the limitations on the data that Dr. Young and Geiers had to deal with when they produced their study. And I have a letter from Dr. Young explaining that and also responding to some of the criticisms that Dr. Fombonne made two days ago. And we've marked this as Petitioners' Exhibit 17.

We will file it.

(The document referred to was marked for identification as Petitioners' Exhibit No. 17.)

SPECIAL MASTER CAMPBELL-SMITH: Thank you. Are you planning to address these?

MR. WILLIAMS: No. Although I will state I checked with her and she is available that week in July if the Special Masters would want to ask her questions or if Respondent wants to ask her questions, she'll be here. I think she could come any one of those five days. And I doubt if her testimony would be very lengthy in any way, so.

SPECIAL MASTER CAMPBELL-SMITH: Thank you.

MR. MATANOSKI: Your Honor, I will consider this new trial exhibit and determine whether we have any objection to the extent it may constitute a rebuttal evidence to prior testimony that was previously unexplained, unanticipated as it were.

SPECIAL MASTER CAMPBELL-SMITH: So noted. Should you like to lodge a formal objection you will draw it to our attention?

MR. MATANOSKI: Yes, that's correct, ma'am.

SPECIAL MASTER CAMPBELL-SMITH: Let me take a look here. We are at about 1:20. And my question to Respondent's counsel, do you have witnesses that you intend to introduce or put on this afternoon?

MR. MATANOSKI: Yes, ma'am, we do.

SPECIAL MASTER CAMPBELL-SMITH: Do you have an idea about does it make sense for us to press on a little bit longer or is this an appropriate time for I will call it a lunch break?

MR. MATANOSKI: I think it would be the appropriate time for a lunch break, ma'am.

SPECIAL MASTER CAMPBELL-SMITH: With that said, how much time would counsel require to eat and for your working lunch?

MR. MATANOSKI: If I may have a moment, Your Honor?

SPECIAL MASTER CAMPBELL-SMITH: Please. We won't charge this minute.

(Pause.)

MR. MATANOSKI: Forty-five minutes should be fine for us, ma'am.

SPECIAL MASTER CAMPBELL-SMITH: Okay. That puts us roughly at 2:05 that we will return. And we will take a lunch recess and return then.

MR. MATANOSKI: Thank you, ma'am.

SPECIAL MASTER CAMPBELL-SMITH: Thank you.

(Whereupon, at 1:20 p.m., the hearing in the above-entitled matter was recessed, to reconvene at 2:05 p.m. this same day, Friday, May 30, 2008.)

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A F T E R N O O N S E S S I O N

(2:12 p.m.)

SPECIAL MASTER CAMPBELL-SMITH: Please be seated.

Respondent's counsel, I understand you have some witnesses to introduce to rebut some testimony that you've heard. It appears that Dr. Fombonne has retaken the stand.

Dr. Fombonne, you will continue under the oath that was administered to which you swore earlier.

Whereupon,

ERIC FOMBONNE

having been previously duly sworn, was recalled as a rebuttal witness herein and was examined and testified further as follows:

MR. MATANOSKI: Thank you.

DIRECT EXAMINATION

BY MS. RICCIARDELLA:

Q Good afternoon, Dr. Fombonne, welcome back.

A Good afternoon.

Q Would you please state your name again for the record?

A Eric Fombonne.

Q Dr. Fombonne, there was some discussion today by Dr. Mumper about the various treatments that

Jordan King and William Mead had been receiving for their treatments for autism and other related, allegedly related conditions. Are the majority of those treatments recommended by the majority of autism experts?

A No. Actually none of them is recommended by autism experts. And there are actually published guidelines about the evaluation and the management of treatment of autism by the American Academy of Pediatrics or neurologists, and none of them recommends these practices.

Q Is there any evidence as to the efficacy of those treatments?

A No. That's one of the reasons that there is no evidence for their efficacy, no evidence for the reason for them to work, but there is no published studies which would suggest that it would change the course of autism.

Q Are any of those treatments dangerous?

A Yes. Often these treatments are thought to be innocuous by parents who are trying to do everything they can. And we understand that. But some of these treatments might actually be detrimental to the health of the children. So chelation therapy could be, as we know, dangerous if it is not well

controlled. The use of megavitamins, B-12, B-6 and magnesium treatment has been associated with cases of neurotoxicity at times. And the diet with greater frequency in fruit, for instance, has been studied two years ago where it has been shown that the children who were strictly on this diet actually had lower levels of plasma amino acids which are essential for growth and brain growth in particular.

So the belief that these treatments can be tried and would be harmless anyway is actually not supported by the data.

Q Are there standards that are used by the medical and scientific community before a treatment is recommended?

A Yes. There are different kinds of standards the efficacy of interventions. The evidence which is the most conversed which stems from randomized clinical trials which are obviously double blind placebo controlled and for this method there is no study which has been relying on this method for the practices of the treatment which has been discussed this morning.

Q Do you have experience with randomized clinical trials?

A Yes, actually I did. I started working on a

randomized clinical trial, did a thesis on that, my first two publications I think had to do with randomized clinical trials. And I am currently we are testing the efficacy in a randomized clinical trial of a treatment which is not biomedical which a language-based intervention to improve communication skills in young children with autism. And we did a randomized clinical trial. It's a 12-weeks treatment. And I looked at it at random parents and attached them to a group where they were immediately treated with this intervention. And there was a waiting list control group of 36 families or children in each group, so it's quite powerful in terms of the statistical power.

I just want to share with you our findings that it's an intervention that everybody likes. When we did the trial we had all the impression that it was actually achieving some of the positive results. Parents were happier, were convinced that the methods were showing efficacy. And we did too. But as we did the study well we didn't analyze the data before the data were finally collected. And when we broke the blind and looked at the results and there is no evidence for a big difference between the two treatment groups which is breaking my heart in some ways. But that also shows that our experience as

clinicians and as parents can be misleading.

And I think the field of autism has been replete over the last 30, 40 years of treatments and interventions that practitioners engage into and their parents apply to that treatment. And the story has been that when you take these practices and put them to redraw some clinical tests, that of the randomized clinical trial usually the story is much more disappointing. And a case in point is this secretin study.

Q Is it the secretin study that you're referring to?

A Yes, yes. And again that was a usual progression after acute case reported by the researcher, by practitioners. It is changing with autism, and it was to the extent that parents worldwide were wanting to have their children using secretin. And I think the NIH at that time founded three separate randomized clinical trials which were converted, it took about five years to do that. And when the results were released all these three randomized clinical trials were negative, there was no, absolutely no advantage for secretin over placebo. So that had to result in question. But still you had like five or six years of practices where people

believed in it, both practitioners and parents.

And the point is that the clinical experience is in no way a measure of the efficacy of a treatment, including mine.

Q Dr. Mumper also discussed IVIG treatment and she took issue with Dr. Rust's criticism of IVIG treatment. Do you have any experience with IVIG?

A Yes. Actually we did publish, we see the first offer in my C.V. is, last term, is a study which I supervised. It's a small study of a group of about 20 children. We were assessed in the Immunology Department of the Montreal Children's Hospital at the time when this treatment became very fashionable, should I say, so many parents wanted to have access to this treatment. And rather than to do nothing with that our immunologists reluctantly initially they said, well, let's explore the immune system and see if there is really a deficiency in, immune deficiency genes in the children.

And we published this study in an immunological journal. And in fact we didn't, we failed to find evidence that there was a deficiency in leukocidins and there was just one child who had an unusual pathology. We see that as a sort of attempt to repeat that, there was no documented evidence for

efficacy.

So the story is that as a routine treatment it has no place in the management of autism unless you have a documented deficit, immunological deficit which has to have some certain characteristics.

Q Now, Dr. Mumper also discussed single-study baseline studies. You take one child and you look a the efficacy of various treatments applied to that one child. Do you have any experience yourself with single study baseline studies?

A Yes. We want to have randomized clinical trials but often we don't have this level of evidence, so there are lower levels of evidence to ascertain the efficacy of interventions, particularly in the behavioral domain but also in the use of medication or biomedical intervention. So the single subject designed with multiple baseline evaluation is a way to test.

You measure a child without doing anything with him at several points in time so you assess his baseline of behavior. And then you administer the treatment that you think might make a difference and then you follow by several assessments and then you remove the intervention and you expect that the child would respond to the treatment. And you would go back

to baseline to remove the interventions. So that's a way to observe over time the child before, during and after treatment in a way which is more rigorous and allows to draw some meaningful inferences. The causality inference might sometimes be subject to coaching, but it's a progress compared to the simple clinical acumen that people have when they say that's what I like to do, that's what I do, it seems to work; that is not enough.

And I was told that this design has been available for years and the people who support the chelation therapies and all this sort of treatment have failed completely to publish data which is rigorous and can be analyzed in this sort of preliminary way.

Q Doctor, I'd like to discuss the videos. We were shown some videos this morning by Dr. Mumper that allegedly show Jordan King and William Mead's normal development before their regression. Do you have any comments, before we look at some specific videos that we saw this morning do you have any comments with regard to Dr. Mumper's methodology, the way she assessed the videotapes?

A Yes. I think there are some videos in which her comments were not actually supported by what's on

the video. And I will give some examples of that.

As I said the other day, what is very important when we assess them and we look at them is to look at the quality of the behavior. It's not only it's there or not, we need to evaluate the quality. So when we talk about social reciprocity we need to assess if the child, for instance, initiated interaction or responded to an initiation of interaction by someone. Then you look at the quality of the interactions and how it goes on back and forth. That's the quality that we want to evaluate.

So that the child initiated at one point behavior is not evidence that there is good quality or good reciprocity in social interaction. That's one aspect.

And the same for babbles. For instance, there are some utterances, babbles or even words which are used you need to assess how spontaneously they are used by the child, do they have a communicating function, is there communicating intent, and what happens in the event they're responded to and is there really a conversation or interchange when the child babbles or a child who has a few words. So you need to assess these qualities otherwise it can be misleading.

So I think that we would represent a few clips again and look at them in a different way.

I also wanted to correct some comments that Dr. Mumper made about object permanency. Object permanency has to do with cognitive development.

Q I'm sorry; what?

A Object permanency. When she was looking at Jordan King dropping the toys and he was looking at his toys, that has nothing to do with object permanency. This is a concept that has to do with cognitive development in children which is assessed when you present an object to a child and then you remove it from his visual field and then you see if he is looking for this object once it has disappeared. In that particular case comments are not appropriate to what we saw.

And that -- yes?

Q Any other general comments before we look at the clips?

A The other comments is that I think the debate was that their evidence of abnormal development before the regression, okay, we determined that the child was developing absolutely normally up to the point of regression. We can re-discuss this issue about the timing of regression later. But I think

it's, again, Dr. Mumper should know that we in the field do not consider that we can actually detect abnormalities in most children with autism before the age of 12 months. So her showing clips at 3 months or 5 months of age are not informative at all because it's not a period of the development where you would expect to pick up the specific abnormalities seen in autistic children.

We have ongoing, it's documented in so many studies that I don't want to overwhelm you with the literature, but we have ongoing prospective studies where we follow children who are siblings of already diagnosed children. And this is an ongoing project in which there are several teams worldwide. And so the siblings, a proportion of which is as high as 15 percent, would later develop autism, is followed from birth. And later we have an opportunity to observe prospectively the development in order to identify the first signs of what will become autism in some of them. And up to the age of 10 months, 11 months we usually when we compare them to those who will not develop autism or to typically developing children we don't find much even with standardized assessment procedure.

It is mostly around the age of 12 months

that we start to see subtle abnormalities in social communication which indicates autism but not before that age. So I think using clips up to the age is not evidence of anything.

Q Would you like to play some of the clips that we saw?

A Yes. So maybe we should go with maybe, I don't know, we should go to Jordan King's?

Q King's first. How about Number 4, "Plays with Cat"?

A Number 4, yes. And let me before seeing the tape, what is important because this is an example of an observation that would fool many people who don't look at the right things. And it's natural. I just want to draw the attention of the Masters of the amounts of vocalization that the child is producing during that clip, and also to look at how he interacts with others who are around him and does he pay -- for instance does he orient to them, does he respond, does he give eye contact to any of them, does he produce any vocalization or any gesture? That is the kind of thing that we would like to see that a normal child in that circumstance should have showed.

So let's have it.

Q And just Dr. Mumper identified this segment

as Jordan's age approximately 13 to 16 months old?

A Yes.

Q Would it be possible to use Number 4.

(Jordan King Video Clip No. 4 played.)

A So he's interested in the cat, absolutely. But he doesn't really look at his parents or look at the grandmother. He will go and follow the cat, which is very interesting.

You see, she approaches, she touches him, he doesn't really give eye contact at any time. And there is no babble, no vocalizations at all.

I want to say that it's a small thing but I want to remind here that the father wrote he was never a babbler. These video are highly consistent with what the parents reported at the time. And just as a point, I reviewed all the videos of Jordan King, I have never heard one word. There is no word that he used, very few vocalizations. When there are a few vocalizations they are usually not socially directed and their communicative intent is dubious.

Q The next clip I would like to play Number 5.

A On the next clip this clip was used as evidence of his gesturing by Dr. Mumper. And you will see a partial gesture. But what matters is the quality and the spontaneity of gesture. And here you

will see that indeed he's responding to another, trying to engage the other, opens his arms. And it's to that initiation by the other of this movement that Jordan starts to respond. And we will see the response is actually partial, he doesn't really get -- doesn't complete the gesture.

But what is important for us when we assess these tapes is to look at the spontaneous initiation of communicative acts by the child. This is not spontaneous, he is responding partially to the initiation of an adult.

(Jordan King Video Clip No. 5 played.)

A You see, she engages him and then, then he responds. But it's not, it's not initiated by him. And this is a quality that you need to assess.

Do we have some clip 9?

Q Yes, Number 9, "Building the Marimba."

A Yes.

(Jordan King Video Clip No. 9 played.)

This is the sequence where he is building up something with his father. And, yes, he is interested in toys. And again, children with autism usually are very interested in manipulating toys, doing physical activities, so this type of physical functional play is often present. And what is lacking is imaginative

play or creative play at this stage. So the fact that he is interested in toys or musical objects is absolutely fine and doesn't rule out autism at all.

But I think on that tape, on that clip again let's look at the amount of vocalization that the child used. Does he direct the attention of his father to something that he does? Does he respond? Is there interchange between the two? You will see there is not much, it's more the father is here, he's there observing it what he does, and then following sort of an agenda in playing with his toys, but there is no really social interaction which I think that's quality which is not there.

(Jordan King Clip No. 9 played.)

You see, he's remarkably quiet. I mean there are a few, a few moments where his father imitates the drill and he copies that, but he doesn't progress. There is no more vocalization and then he doesn't initiate any attempt to an interaction with his dad. Just he follows passively. And there is no words here heard at all.

Q Now, Dr. Mumper described this clip as showing that Jordan was seeking approval from his father. Do you see that in this clip?

A Approval for?

Q She just said it was evidence of normal behavior seeking approval from his father.

A No, I don't think it is. That's an inference which cannot be held. I think this is subtle. I appreciate that for most people it would subtle deficits. But again it's the pattern which is consistent across all videos which I have seen. And again I have not heard any word to the fullblown autism. And he's quiet, doesn't vocalize. When he vocalizes it's very limited, it's not used really to communicate socially, and he usually doesn't reciprocate with vocalization.

Q All right. I believe there's another clip that we wanted to show that we had previously designated of Jordan King.

A Yes.

Q And I'm referring to Number 2 on our designation, disk one, file one. The time period is 1999, January through June.

A This is just on that clip, if I recall, he is playing, he has a pacifier which indeed comes into the way of babbling. But the thing to look at is that his mother is filming him. She made comments several times. She calls him. And he doesn't, he never orients to her at all. So he doesn't look at her, he

doesn't orient to her despite her calling him several times. And in terms of his social behavior he's manipulating toys in an appropriate way but you have a sense that he's following his own agenda and he's really on his own world in some way.

SPECIAL MASTER HASTINGS: What age is Jordan in this video you are about to show?

THE WITNESS: This would be before the 18 month mark. I don't --

MS. RICCIARDELLA: The video just indicates we have sometime between January and June of 1999.

SPECIAL MASTER HASTINGS: All right. Oh, this is the one from January to June. Okay.

MS. RICCIARDELLA: Number 2 on our file one.

SPECIAL MASTER HASTINGS: Right, right. Thank you.

MS. RICCIARDELLA: Disk one.

(Pause.)

SPECIAL MASTER CAMPBELL-SMITH: The silence is the anticipation of getting this technically done.

MS. RICCIARDELLA: I should make that clear, yes. We're having some technical issues.

(Pause.)

MS. RICCIARDELLA: It appears to be working on our computer but not on the Court's computers.

MR. MATANOSKI: It appears we're going to need a minute.

SPECIAL MASTER HASTINGS: All right.

MR. MATANOSKI: Apologize.

SPECIAL MASTER HASTINGS: Let's go off the record for a minute.

(Discussion off the record.)

SPECIAL MASTER HASTINGS: Let's go back on the record.

MS. RICCIARDELLA: It plays on our computer but it's not playing for the Court's computers.

BY MS. RICCIARDELLA:

Q Would you just please describe, and we'd just ask that the Court pay particular attention to this particular designation in the King case, would you please describe why you selected this to show to them?

A As I said before it's a sequence where he's playing alone, manipulating objects of different kinds appropriately. But his mother is filming and trying to engage him socially by calling him, making comments. And at no point in time does he orient towards his mother as you would expect. So is lack of social response which is a good characteristic and which in the case of Jordan really emerged at the

beginning of the second year of life.

It is true that there has been, when I reviewed the tapes, as a child when he was like 9 months, 10 months he was really much more socially engaged, eye contact was much better. But as you move on in time you see that the eye contact is slowly disappearing, that he's less responsive, much more following his own agenda in what he does, and there is therefore gradual onset of autistic symptoms. But it doesn't occur like overnight by a loss of skills.

And I think the other thing I want to reemphasize is that both by parental descriptions and the father's descriptions and by my own observations of the video he's a remarkably quiet, not using vocalizations as a normal baby would do, and has no words at all. So I do not doubt that he had maybe a few words at one point that he might have used once or twice in very highly -- in highly contextualized fashion, but it's not a child who had developed language properly and for me it's very clear.

SPECIAL MASTER HASTINGS: Dr. Fombonne, let me ask again about the particular segment that you were just describing and you weren't able to play for us. But did you say that what time frame you were assuming this video was taken, what age?

THE WITNESS: I think it's about like 15 months of age, about that. I've been trying to look at clips which will be occurring before the 18 month mark.

SPECIAL MASTER HASTINGS: Before the 18 month.

THE WITNESS: Yes. Because it seems to be.

SPECIAL MASTER HASTINGS: But and the reason you're concluding this was about 15 months is it because it came off a particular tape?

MS. RICCIARDELLA: Yes.

THE WITNESS: Oh, yes.

SPECIAL MASTER HASTINGS: I mean how do you know this is at 15 months?

THE WITNESS: Let me see. Yeah, it's a tape, it's a tape which is in 1999 from January to June.

SPECIAL MASTER HASTINGS: Okay.

THE WITNESS: And in that case it's in the early part of the tape.

SPECIAL MASTER HASTINGS: Okay.

THE WITNESS: So that's, I don't think I could come up with a precise date otherwise I would have noted that. But it's probably around that time.

SPECIAL MASTER HASTINGS: So you're

surmising from where it is on the tape, it's at the beginning of that tape?

THE WITNESS: Yes. Yes, it's at 20 minutes after the beginning of the tape.

SPECIAL MASTER HASTINGS: And how long is that tape, is that 4 hours? Did anyone say how long that tape was?

THE WITNESS: It's at least going up to 48 minutes. But probably more than that. It's probably one hour long, yes.

SPECIAL MASTER HASTINGS: All right.

MS. RICCIARDELLA: And it's disk one, file one.

SPECIAL MASTER HASTINGS: Right.

MS. RICCIARDELLA: Is the designation of the cue.

THE WITNESS: But if I may explain on that, it's again it's the consistency of observations across different clips at different ages before that age or before the 18 month mark which is what I rely upon for my opinion.

BY MS. RICCIARDELLA:

Q Doctor, I'd like to turn to the videos of William Mead. If we could go back to them.

SPECIAL MASTER HASTINGS: Before you go on

to William Mead let me ask one more question about Jordan King. Do you recall how much video of Jordan King you witnessed, how many hours' worth?

THE WITNESS: Probably 10, 12 hours, 15 hours.

SPECIAL MASTER HASTINGS: All right.

THE WITNESS: Because I did that very long I sat to review. It's a long, long, long, long time.

SPECIAL MASTER HASTINGS: And how much of that was the pre-18 month period, roughly?

THE WITNESS: I couldn't say. I couldn't say between that, I don't know.

SPECIAL MASTER HASTINGS: Half of it, do you think it was half or at least a substantial portion or?

THE WITNESS: Yes. Oh yes, I would say. I would say probably, let's say half or it or more or less. There are long sequences which are also not informative. You know, there are longer musical scenes where actually Jordan is not present. But I had to watch it to be sure he was not there.

So anyway, I would say about half of it.

SPECIAL MASTER HASTINGS: All right.

THE WITNESS: But it's --

SPECIAL MASTER HASTINGS: Go ahead.

THE WITNESS: -- half is still lengthy.

BY MS. RICCIARDELLA:

Q I'd like to turn to the William Mead videos. Do you have any general comments about the videos that we saw today with regard to William Mead before we look at a specific clip?

A Yes. Again, all the clips which have been presented are from birth to 12 months of age. So as for the reasons I indicated before I don't think this is very informative for our debate. We will return on the one taking his bath, for instance, where I could have a different spin, interpretative spin on what is presented. But more or less I would think that the first, this first year of life is not particularly informative. We will show a clip for which we have a date, which is 15 months I think exactly, which will be more informative in terms of showing signs before the alleged regression at 18 months of age.

But before we see it I just want to again talk about the 18 month time. It's highly inconsistent in the medical record when the regression occurred. I know Mr. Mead during his testimony dated back to 18 months of age the onset of regression or loss of skills. But it is fair to give some weight to the medical record evidence because these records are

based on parental reports at the time as well. So it's parental reports forward. And again the regression is said to occur in the summer of 2000 several times. And at 18 months of age. And at other times it's a bit uncertain, again, at what time exactly the loss of skills occurred. And we will discuss it by which skills might have been lost in a minute.

So can we just look at --

Q The "Bath Time" tape?

A Yes.

Q It's Number 9, or excuse me, Number 3.

A So just to maybe alert you on the types of behaviors, I think Dr. Mumper used that example to indicate that William was not hypersensitive to his head being touched. And, you know, we can discuss that if we listen to his somewhat negative reaction with his sister is pulling his hair. But it's not the point. He does look at the camera with a smile forward but there is not much of a variation otherwise.

And I want to draw your attention on, again, the amount of spontaneous vocalization and babble that William produced during this long scene. And also to which extent he does or does not relate to his sister.

But relating to him considering his position in the bath would be to look at his sister and you will see he doesn't make eye contact really to her at all.

(William Mead Video Clip No. 3 played.)

You see there is a slight emotion.

(Video continues playing.)

So he has a, again, there is not much interaction with his sister using eye contact. He seems to be responding to his father or engaging him, and that's fine. But in terms of his spontaneous vocalization there is not much. I mean there aren't basically any spontaneous babble coming out of him. The noise is from his sister and the father but he doesn't really spontaneous babble.

It's, again, it's a kind of observation which is very technical. Nobody would put too much weight in the clinical assessment when you observe that. But it's of note. Also, he had done some unusual movements in the headline that are generally brief but they're noticeable.

Q We've also selected another clip of William Mead.

A Yes.

Q Do you have that ready to go, Brandon? Okay.

A So this is -- sorry, can you hold onto that?

I think Dr. Mumper presented a clip this morning where she spoke about social reciprocity and said that William was playing with his sister. And if you look again at that clip you will see that William does not play with his sister. He's there, his sister is there, and then at one point he goes into the shade spot alone. She follows him in the shade. He gets out of the shade but there is no reciprocal play between the two. It's misconstrued to say that because there are the two together in the shade at one point in time that there is reciprocal play between the two of them.

I will not review that clip but the clip that you will be presented now is also a clip which involves him and his sister. As you will see, there is no reciprocal interactions between the two. When there are interactions they are initiated by the sister and William responds but he's not initiating it.

And secondly, I would like to review it is 18th of July, 1999, so we are there he's 14 months and a half, sort of, yeah. And again evaluate how much language he has. Evaluate how much vocalization he produces, their quality, their communicative function,

and evaluate how he can gesture as well to communicate. And you will see his father at the very beginning is asking him to raise his hand. A child will normally do that, and he just cannot do it. He doesn't understand then already what is being asked from him. His sister does it, he doesn't copy her.

Q Unfortunately, Dr. Fombonne, I'm getting the high sign that we do not have that ability to show that to the Court. However, what we will do is we will let the Court know what clip and what the time frame if the Court would like to review what Dr. Fombonne is talking about. Sorry.

Dr. Fombonne --

A So --

Q Go ahead, if you would like to further explicate what is on that clip?

A So again, it's 14 1/2 months of age. William has no words. In reviewing all the tapes of William I heard two 2-word sentences, "Hi, Dad." which has been shown this morning which is not presented as a 2-word sentence, "Hi, Dad" is like one word. And then "mac cheese." "Mac cheese" he says in a sort of meal that he takes with his sister. This is the only word utterances which are present on the tapes.

Other than that, and this tape at 14 months

and a half of age is clear in showing that at that age he is not babbling, he is not communicating, he is not gesturing really, he cannot copy a gesture, he cannot respond to his dad, he doesn't play reciprocally with his sister. It would be obvious to every person who knows a child of 15 months.

Q Doctor, there's been a lot of discussion this morning about the age when Jordan King and William Mead allegedly went into a regression. Do you have any further comments about the age of the onset of the regression in both little boys?

A No, as I said, you know, I was hoping we would not go into the video exercise, but the video just as clearly shows to me that both boys were abnormal and that they were abnormal before the regression or the loss of skills which occurred maybe at 18 months of age. I think there is an inconsistency of reports in the case of William Mead in particular that when exactly he lost his skills. I don't dispute that he lost skills. That's fair.

I want also to say that those children who do have regression of language usually have reached the language developmental stage which is not very advanced. They have usually five words, 20 words maximum, or 30 words sometimes. It's very rare that

they will have 60 words or that they'll have phrase speech including a verb and like "I want" something or "I see the horse." So the kind of language that William has been presenting as having before the loss I have some doubts that he had that level of language.

So to me the tape of 15 months of age shows that he had no language of that type at that age. And for those who are parents, like me, if you have a child with 60 words and who is speaking 3-word sentences and you lose that skill you go to the emergency room and you see a pediatrician right away. So this kind of loss would be dramatic, observable and would precipitate an immediate consultation with a neurologist.

Q Did you see anything in the medical records or the videos that William suffered such a dramatic observable loss?

A No, no. Because as we said previously, William's pediatricians note a delay, delay lack of speech at age 2 I think, as I recall. I mean had he lost 60 words at age 18 months and 3-word sentences that would have been followed by some kind of medical consultation.

So I think it's not to -- I don't want to dispute any further what is the true reality; it's

difficult. I think recall by parents is tainted by too many expanse, it's hard retrospectively to time with accuracy this phenomenon. It's true in autism, it's true for regression, it's true for neural disorders. So we know that. So I think that there is an area of difficulty in terms of assessing retrospectively the timing of loss of skills or emergence of skills as well. It's very hard.

But it's very clear for me that William, I see no evidence that he had normal language development by 15 months of age and he had no gesturing and no vocalization of the kind that you would expect to be for a 15-month old. So I think we can safely conclude that in his case there was a progressive, gradual onset of autistic symptoms which emerged more saliently over a period of time. That's the experience of parents. That's why it's very hard to point at a particular date. It doesn't happen overnight, it's a progressive change in the child.

Q And what about Jordan King, would you say the same for Jordan King?

A Yes. Yes, very much so.

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

SPECIAL MASTER CAMPBELL-SMITH: Any

questions from Petitioners' counsel?

MR. POWERS: Yes. Thank you, Special Masters.

CROSS-EXAMINATION

BY MR. POWERS:

Q Good afternoon, Dr. Fombonne.

A Good afternoon.

Q I think I will be brief here, just a few questions. You mentioned in your earlier testimony today some questions about the types of treatment, the medical care and treatment and Jordan King and William Mead got. There's no evidence in the medical records and no testimony that you're aware of indicating that the medical care that these boys received caused them any harm, is there?

A No. No.

Q And it's fair to say that the parents and the treating physician Dr. Green both report improvements. Now, I understand that I'm not asking you to attribute it to anything, but the record is that the parents and the treating doctor both noted improvements; correct?

A Yes. But can I comment on the meaning of these improvements?

Q No, that wasn't my question. My question

was what the parents reported and what the doctor reported.

A Yes.

Q I think you've already given your opinion on the nature of improvement.

A Okay.

Q Is it your testimony that both boys actually did regress?

A I think they lost skills probably, yes, absolutely.

Q And they lost skills in all three developmental domains that are relevant to an autism diagnosis?

A I cannot assess that based on the records or the videos. It's not clear.

Q Now, we heard representations this morning when Dr. Mumper was being cross-examined that Dr. Rust agreed that both of these boys have been diagnosed with regressive autism and that he agreed with that diagnosis. Do you agree or disagree with Dr. Rust that these boys have regressive autism?

A I disagree with the fact that regressive autism is not a diagnosis.

Q Do you agree with Dr. Rust's characterization of both of these boys having

experienced autistic regression?

A That's yes.

Q In describing some of your descriptions of William Mead, and particularly William Mead's video, you used the term "this is my interpretative spin." Is that a correct characterization of your analysis as you testified here today that it's, as I wrote down, your interpretative spin?

A I think for the reasons I mentioned before the clips in a very young child are very difficult to interpret because some children, for instance, have several type movements of the body which are brief, so it's hard to interpret what we see with some stronger conclusions particularly. That's why we do not pick up abnormalities in the siblings of autistic children before age 12 months. So I'm just presenting that tape to show where this boy even at that very early age he's not vocalizing much, he's not directing babble to anyone, he's not looking at his sister. These are observations but I'm cautious about what kind of inferences I would draw from them because of the narrow behavioral repertoire which exists at a very young age.

Q And would it also be fair to say that any particular analysis opinion in looking at these tapes

is going to be somewhat subjective in that one particular reviewer might look at a particular video and there could be different conclusions that are reached based on one's interpretative spin; correct?

A No. No. It would not be true for video clips which are when the child is older. When the child is older and you don't see any communicative attempt, no gesturing, no response to the name being called, no vocalizations, no pointing, no copying of gestures, this is quite robust.j

Q At what point in a child's life can video analysis move from the realm of interpretative spin into objective analysis in your opinion?

A Well, the results show actually that the analysis of home videos show good prediction of later diagnosis starting at the age of 10 or 12 months. In some studies it's earlier but most studies it's about 10, 12 months of age.

Q When you say that these boys are abnormal are you describing that they were in the bottom 2.5 percent of their age cohort at any particular point in time?

A On which domain?

Q In any of the domains.

A I cannot, I cannot make a comment on that

based on what evidence I have.

Q I ask that because in my understanding of looking at a distribution of development over time there's a bell curve; is that correct?

A Uh-huh. Yes. Sorry.

Q Yeah, I knew that you were saying "yes" but we have to have it out loud.

A Yes.

Q And there's a median; correct?

A Yes.

Q And the normalcy or abnormalcy or the closeness of a child to the median is often measured in standard deviations; correct?

A Yes, correct.

Q And two standard deviations is typically what is used to evaluate abnormal, that is the 2.5 percent at the tail end of both sides of the bell curve those would be the abnormal numbers; correct?

A Correct.

Q So that's why I'm asking, can you tell the Special Masters whether Jordan King or William Mead in their overall development were in the bottom 2.5 percent of their age cohort?

A I would say probably in terms of language. You would have to refer to a standardized test. You

need to establish that to have standardized tests of language development. One of them which is used is called the Communicative Development Inventory, the CDI, from MacArthur which has norms for language development which are separate for boys and girls. At the age of 15 or 18 months these boys should have had more language than they have in terms of words.

Q How about in the other domains, are they in the bottom 2.5 percent of their age group at any point in their first year of life in, say, social reciprocity?

A There is no good instrument to evaluate social reciprocity. We don't have norms for that. So that's the only instrument which can assess that is the environment, the scale which have scores which give you a communications score, social interaction score. But at that it's apt to be unreliable. And in order to get a score like that you will have to be present at the time and to have administered the instrument at that time. So I cannot --

Q And so the answer would be you don't know whether they were in the bottom 2.5 percent.

A Yes, I don't know for the other domains, no.

Q Okay.

A But for, again for language, yes, and for

gestures as well.

Q And then again you do not disagree that both of these boys experienced an autistic regression; correct?

A No, I don't. No.

MR. POWERS: Thank you. No further questions.

SPECIAL MASTER CAMPBELL-SMITH: Any questions from my colleagues? Nothing?

MS. RICCIARDELLA: I just have a couple more.

REDIRECT EXAMINATION

BY MS. RICCIARDELLA:

Q Dr. Fombonne, Mr. Powers was using the phrase "interpretative spin" because you used that in yours, and he kept throwing it back at you. When you review a videotape, Doctor, what skills do you apply when you are looking at a videotape?

A My observations and my vast clinical experience and being trained to measure the ADOS, which is an observational measure. We develop I think particular accuracy to look at situations there you have a pressure on the child to communicate or to gesture or to request something, and we develop this kind of experience based on our training and number of

ordinary children which we have seen or untypical children as well.

Q Now, Doctor, Mr. Powers also asked you whether an analysis of a videotape can be somewhat subjective. Now, Dr. Mumper is using the videotapes today as saying that she can rely on the videotapes to show normalcy or typicality during the first 12 to 15 months of these two little boys' lives. Are videotapes a reliable source to show typical behavior?

A Typical? What do you mean typical?

Q Do clinicians use videotapes to actually diagnose autism or as evidence to show that a child is developing typically?

A No. Because they -- first, when we code, when we use video for research purposes we have coding schemes which are extremely precise. So we look at sequences, we rate particular behaviors according to rules. We take into account the amount of time of the tape because obviously if you have a tape which is very long we need to take that into account because it gives you more opportunity to observe abnormal or normal behavior. So there are a lot of rules which are followed in the research that of course we cannot follow here.

I would say my clinical practice I often see

parents come in with films or videos or children. And, you know, when you see a child who is young and who is normal it's often not always informative because there are some clinical deficits which can occur but in particular situations which have not been filmed by the parents. So I think if you have on the contrary a situation which is consistent where you don't see skills that you would expect to find in the child, then we can give some credence to these observations. But you don't diagnose a child based on retrospective video assessment for clinical reasons. For research it has been used, not for clinical reasons.

MS. RICCIARDELLA: Thank you.

SPECIAL MASTER CAMPBELL-SMITH: Anything further?

MR. POWERS: No, not from us.

SPECIAL MASTER CAMPBELL-SMITH: Thank you, Dr. Fombonne.

THE WITNESS: Thank you.

(Witness excused.)

SPECIAL MASTER CAMPBELL-SMITH: Does Respondent's counsel have any additional witnesses to call?

MR. MATANOSKI: Yes, ma'am, we do. At this

time we call Dr. Jeffrey Johnson.

MR. WILLIAMS: While they're setting up I want to pose just a fairness objection. Last Friday we discussed that we were going to deal with Dr. Deth issues on Thursday. And we arranged for Dr. Deth to be here all day yesterday. And they had no one to call yesterday in response to Dr. Deth. And now I guess, I assume that this is what we are going to hear now.

And I just put that on the record as a fairness objection. And we may want to seek relief for it depending on what happens.

SPECIAL MASTER CAMPBELL-SMITH: Mr. Matanoski?

MR. MATANOSKI: Thank you. Actually, ma'am, Dr. Johnson is going to be responding to the rebuttal testimony of Dr. Kinsbourne this morning.

SPECIAL MASTER CAMPBELL-SMITH: Thank you.

Dr. Johnson, as a preliminary matter, you are still under the oath that you took earlier in this proceeding.

DR. JOHNSON: Absolutely.

SPECIAL MASTER CAMPBELL-SMITH: Thank you.

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Whereupon,

JEFF JOHNSON

having been previously duly sworn, was recalled as a rebuttal witness herein and was examined and testified further as follows:

SPECIAL MASTER CAMPBELL-SMITH: We're having a technical adjustment again.

MS. BABCOCK: Seems to be an afternoon of technical difficulties.

SPECIAL MASTER HASTINGS: While we're waiting for the technical difficulties, a technical issue I wanted to address. Last year during the Sabile hearing we also heard video reviews. We decided as direction for the court reporting service that we didn't want them to -- there was no need for them to transcribe all the words that were said during the video by the parents or just today the parents of both children, and we had also William Mead and his sister say a few words. I think I hope we are all in agreement, they don't need to transcribe that part.

MR. POWERS: Yes, sir.

SPECIAL MASTER HASTINGS: Okay. I just wanted to clarify that for the court reporter especially.

SPECIAL MASTER CAMPBELL-SMITH: Technical

matter is resolved. Respondent's counsel to proceed.

MS. BABCOCK: We'll discover as we go along, I suppose.

DIRECT EXAMINATION

BY MS. BABCOCK:

Q Could you please state your name for the record?

A Dr. Jeff Johnson.

Q And since there may be some confusion, Dr. Johnson, are you a neurotoxicologist?

A Yes.

Q Now, Dr. Kinsbourne spent some time this morning emphasizing that he was putting forth a hypothesis or model that could explain how TCVs cause autism. What is the scientific community's understanding of the terms "hypothesis" or "model"?

A Well, in the context that I would put that a hypothesis is something where you put together certain aspects and certain ideas that you see in the literature, put it together and formulate a hypothesis that you think might be relevant. And, you know, 99 percent of the time it could be completely wrong. And if you're lucky, I mean very lucky usually in science you might actually think of something that might be correct.

Q And does the same apply to a model?

A Oh yeah. The model, developing a model, I mean I could go back to my office and develop ten models tomorrow, you know, and none of them could be, you know, right or wrong, depending on the science. But I mean it's something that you can, anybody can do that.

Q And both a hypothesis and model would certainly require testing before any real credence could be given to them; correct?

A Oh, absolutely. I mean if all my hypotheses worked I would have cured Alzheimer's, Parkinson's, ALS and every other disease I study.

Q Now, do you agree that what Dr. Kinsbourne has put forth would be considered a hypothesis?

A Yes.

Q And just as a clarification, do you think this would rise to a level of, say, more than likely than not true, to be true?

A Oh, absolutely not. It's at the lowest level.

Q Now, is neuroinflammation involved in other neurological diseases?

A Yes. It's involved in almost every neurodegenerative disease that's been looked at at

least to some extent, including Alzheimer's, Parkinson's, Huntington's, ALS.

Q And you study these diseases; correct?

A Yes. Yes, I do. Yes.

Q Including both you have a laboratory and an academic practice and research?

A Yes, absolutely.

Q Does current research indicate that neuroinflammation is involved as playing a causal role in these neurodegenerative diseases?

A In general the concept in these other neurodegenerative diseases is that the neuroinflammatory response in astroglialosis and microglial activation are part, a progressive part of the disease, the progression part of the disease as a result of the pathologic process. I don't think that anybody at least in the field would argue that they're a causative factor at this point, it's more an outcome.

Q Now, does treatment of symptoms via drugs or clinical trials necessarily implicate a cause of the disease?

A Absolutely not. And I think one of the key examples of that is in Alzheimer's disease. In Alzheimer's disease the patient manifests a lot of the

symptoms that, if you're familiar with, and a lot of people have seen Alzheimer's patients, so you see these symptoms. And a lot of the symptoms in Alzheimer's disease are due to a loss of a specific neurotransmitter called a acetylcholine. And so a lot of the drugs, most of the FDA-approved drugs for treating Alzheimer's disease actually increase those, the levels of acetylcholine in the brain. So the patient cognitively appears to get better. But in the background the pathologic process and the mechanism that's killing the cells is continuing on unabated.

So treating symptoms is a way to, is a thing that you can do. Such as if neuroinformation is part of the progression if you can treat that then you may alleviate some of the symptoms. But none, there's really no causal, direct causal association with treating symptoms and what's causing the disease.

Q Now, Dr. Kinsbourne also discussed a paper on his rebuttal today by Dr. Lopez-Hurtado which I believe is PML-446. You were also asked about this paper during cross-examination. So obviously I assume you've got some familiarity with it. In your review did you identify a fairly significant methodological flaw used by those authors?

A Yeah. When I asked about this I said I

hadn't had time to evaluate the data. Now, I have. And so there is a significant issue that I have with the paper. And that is simply this, and I want to try to be very clear on this. They do a lot of statistical analysis in this paper comparing one sample to another sample and things like that. But that cannot be done because really what they've done in this paper is they've actually counted the density of neurons in one brain. So just to give you an idea, so you take pieces, different layers of the brain and you count, you know, five different parts let's say, and you get a number from each of those five parts. And you average that and you get one number.

Now, the standard deviation that you generate from averaging those five numbers is basically a standard deviation generated by your error in counting. It has nothing to do with standard deviation between samples. And so when you finish this analysis what you end up with is you end up with a variety of numbers that you pool together to get the density of cells in the cortex or in a specific region for one person.

So with the one person you cannot generate a standard deviation or an inter-individual standard deviation to run statistics on. So this whole paper

basically uses N's of one to run statistics and the standard deviations are based exclusively on the reproducability of their techniques for counting but nothing to do with, say, the average of four autistic brains, four different brains. They don't do that.

And so the statistical analysis is really invalid.

Q So let me see if I can boil this down. They use standard deviation with their graphs but they shouldn't have?

A No, no they shouldn't have because there really is no standard deviation for an N of one.

Q And what's the effect if you take out the standard deviation?

A Well, they can't run any of the statistic inferences that they did. And if you take out, I mean if you really look at the data, the way that you can look at the data is to actually look at the rate of change with age with regard to glial cell number and neural cell number and micro -- or the lipofuscin containing cell number. And if you do look at that you actually see that the rate of change in the control patients and the rate of change in the autistic patients is almost exactly the same.

So as the autistic patients age the number

of glial cells go up. As the normal patients age the number of glial cells go up and those lines are basically exactly parallel. So to me what that says as an interpretation of that data which wasn't done in the paper is that the main difference between an autistic patient and a normal patient is not the change the differential during the time or the age, it's actually the baseline where they start.

So if the autistic patients starts with a higher number of glial cells initially then their rate of change as they age is going to be, it's just going to be parallel to what you see in the normal patient. So I don't want to make this complicated. What I am saying is as you really look at the data as an age-dependent process there doesn't seem to be any difference. And it appears to be the baseline, probably from the developmental standpoint and what was laid down during development that's giving you this differential effect as you look across these patients of aging.

Q Now, Dr. Kinsbourne also discussed astrocytic function this morning. Do you study astrocytic function in your laboratory?

A Yes. A lot.

Q And have you published on this topic?

A Yes.

Q In the last, about how many papers in the last two years?

A Probably more than ten. I can count them but I don't want to take the time.

Q We certainly understand.

If astrocytes are unable to mop up glutamate, what happens?

A Well, the glutamate will interact with the neurons and cause excitotoxicity.

Q So neurons die?

A Eventually, yes.

Q And Dr. Kinsbourne also discussed the Purcell article I believe in his rebuttal, which is PML-567. I'll let you find it.

A I got it. Yes, I have it.

Q In autistic brains is there evidence for increased glutamate transporters?

A Yes, absolutely. This article, one of the things that's interesting about this article is it does microarray analysis. So what it does is it actually does gene shift and microarray -- are you familiar with microarray analysis?

SPECIAL MASTER HASTINGS: Can you start that sentence again?

BY MS. BABCOCK:

Q Slowly.

A This paper does a microarray analysis and they look at -- what that is is a fancy way of PCR. So we go back. What they did is they looked at microarray analysis, they identified genes that were different.

SPECIAL MASTER VOWELL: Doctor, you're going to have to slow down.

THE WITNESS: Right.

SPECIAL MASTER VOWELL: It sounds like you're saying "micro ray" when really you're saying "microarray."

THE WITNESS: Array; right.

SPECIAL MASTER VOWELL: Okay.

THE WITNESS: And so the gene chip basically.

And so they identified some candidate genes that were different between autistic brains and normal brains or control brains. And some of those genes were these, we've talked about these EAAT1 and EAAT2 transporters, correct, that transport glutamate into astrocytes. If you look at the paper, not only did they identify some of these as being changed but in fact when they did the RT-PCR and --

SPECIAL MASTER VOWELL: By RT-PCR you're referring to?

THE WITNESS: Looking at messengers. Messengers on A levels in the brains of autistic patients.

SPECIAL MASTER VOWELL: So reverse transcript.

THE WITNESS: The RT-PCR.

SPECIAL MASTER VOWELL: Because we have heard RT-PCR used in a different context as well, real time.

THE WITNESS: Right.

SPECIAL MASTER VOWELL: So what are you referring to?

THE WITNESS: Yeah, I think this -- I don't know what they did on this. What they might have done, I don't know if they did real time or they just did RT-PCR. I think this was just regular RT-PCR, not real time, not quantitative RT-PCR.

But what they, and then what they did is in addition to the RT-PCR they also did Western Blot analysis. So they looked at the protein levels in autistic brains. And in both situations the EAAT1 and the EAAT2, which are the glutamate transporters on the astrocytes were significantly increased in autistic

patients. Which to me suggests that the autistic patient actually has a greater capability to handle glutamate than the normal patient based on these studies.

BY MS. BABCOCK:

Q And are you referring to specific charts or graphs in that paper?

A Yes.

Q And if so, could you specifically identify where they are?

A Yes.

Q I'm not sure if we have it in trial directory but at least if you could identify the page number?

A Figure 2. Figure 2 on page 1623 and Figure 3 on page 1624.

Q Dr. Johnson, if you have continued chronic glutamate access would you expect the process to become neurodegenerative?

A Yes.

Q Now, Dr. Kinsbourne also discussed Dr. Aschner's papers this morning, which I believe are PML-568 and 570. Are you familiar with Dr. Aschner's work?

A Yes. I have known Mickey for a long time.

Q And these papers in particular?

A These papers I've looked at, yes. I tend to not like to look at reviews because I like to under -- I mean I will look at the reviews but then I also like to find the interesting points of the reviews and go and look at the real manuscripts and the real data that actually where they're referring to in their review. So I've seen a lot of Mickey's original work.

Q Now, first, what was the dose necessary to get astrocytic dysfunction?

A It's in the micromolar range in almost all of his work.

Q So that's very high?

A Yes, very high.

Q Certainly much higher than would be administered via thimerosal-containing vaccines? And again I should explain, a different type of mercury also?

A Yes.

Q Which is methyl mercury?

A Yeah. And I'm qualifying, I mean I'm not a mercury distribution expert, but from what I've heard from the testimony and listened to this week I would say, yes, that seems to be. Because we always talk nanomolar versus micromolar. Here it's micromolar.

Q Yes. Just limiting you to the dose and I'll leave the rest to the toxicologists.

Now, do you agree that once triggered, as Dr. Aschner says, a vicious cytotoxic cycle ensues?

A I completely agree with that. And we saw the conclusions I think in cross this morning. Those are valid and solid conclusions based on the data.

Q And is the concept that once you trigger astrocytic dysfunction you do get that vicious cytotoxic cycle, is this well accepted in the scientific community?

A Yeah, I would say it's very well accepted in the scientific community that deals with this kind of process.

MS. BABCOCK: I have nothing further.

SPECIAL MASTER CAMPBELL-SMITH: Thank you. Questions from Petitioners' counsel?

MR. POWERS: Yes, thank you.

CROSS-EXAMINATION

BY MR. POWERS:

Q So, Dr. Johnson, you were talking about the Purcell paper. Ultimately the Purcell paper did conclude that the involvement of glutamate levels in the brain is something that ought to be investigated in autism, and this is what they said in 2001;

correct?

A Yeah. No, I'm not saying that glutamate shouldn't be investigated in autism, glutamate should be investigated in all of these diseases because it's clearly been implied to be part of the pathogenic process.

Q And that the blockage of glutamate receptors might actually improve autistic symptoms, that's one of the conclusions that the Purcell investigators made in their paper; correct?

A you can conclude whatever you want in their discussions but I don't know that there's been any evidence showing that in autistic patients. And again I'm not a clinician but I know there is evidence in some of the other diseases that glutamate inhibitors might have some effect, slight.

Q Right. And in the discussion of the Pardo and Vargas work, the Pardo and Vargas papers do report chronic ongoing neural inflammation in the brains of autistic patients; correct?

A They show inflammation or they show astroglial activation and microglial activation in postmortem brains of autistic patients. That doesn't mean it's ongoing, that means that it's there at the time that the patient died.

Q And that was a cross a wide range of subjects; correct?

A Yeah, across a wide range of ages. I don't remember specifically.

Q Roughly 7 to 44; does that sound about right?

A Okay, yeah, maybe something like that, yes.

Q And in those frames this endpoint of massive neuronal death had certainly not been reached; correct?

A I don't -- I'd have to go back and look. There was something with the Purkinje cells I think. But outside of that I don't think there was massive neuronal death in the brain, no, at that point.

MR. POWERS: No further questions.

SPECIAL MASTER CAMPBELL-SMITH: Thank you. Any further questions from Respondent's counsel?

MS. BABCOCK: Nothing, thanks.

SPECIAL MASTER CAMPBELL-SMITH: Any questions from my colleagues?

SPECIAL MASTER VOWELL: I have one follow-up for Dr. Johnson.

THE WITNESS: Sure.

SPECIAL MASTER VOWELL: You said chronic glutamate excess would lead to neurodegeneration.

THE WITNESS: To killing of neurons, yes.

SPECIAL MASTER VOWELL: Okay. And is there any particular reason you say that? I mean you stated it but you didn't give a reason.

THE WITNESS: Well, it's been, I mean we use it to kill cells all the time. In culture we kill cells *in vivo* with excitatory cytoamino acid toxicity. And there's also a lot of evidence in Parkinson's and other diseases that, you know, this kind of a chronic glutamate factor, specifically astrocyte dysfunction, and I'm thinking in mind, specifically in mind to ALS, that astrocytic dysfunction is a key component in the presumably cytotoxic death of motorneurons in spinal chord of ALS. And I think that's been shown.

So I mean there is evidence out there in these other disease states where you have an astrocytic dysfunction you end up in the end with neurodegenerative disease or kill-offs of neurons in that region, depending on where that region is, spinal chord, cortex, hippocampus.

SPECIAL MASTER CAMPBELL-SMITH: Any questions generated by Special Master Vowell's questions?

MR. POWERS: No, Your Honor.

SPECIAL MASTER CAMPBELL-SMITH: Thank you,

Dr. Johnson, you are excused.

(Witness excused.)

SPECIAL MASTER CAMPBELL-SMITH: Any additional witnesses to be called by Respondent's counsel?

MR. MATANOSKI: Yes, ma'am. At this time Respondent calls Dr. Jeffrey Brent.

SPECIAL MASTER CAMPBELL-SMITH: Thank you.

And I will just take the opportunity to remind you, Dr. Brent, that you remain under oath.

DR. BRENT: Yes, I understand.

Whereupon,

JEFFREY BRENT

having been previously duly sworn, was recalled as a rebuttal witness herein and was examined and testified further as follows:

DIRECT EXAMINATION

BY MS. RENZI:

Q Good afternoon, Dr. Brent.

A Good afternoon, Ms. Renzi.

Q Could you please state your name for the record again?

A Sure. Jeffrey Brent, M.D., J-E-F-F-R-E-Y B-R-E-N-T.

Q Thank you. Dr. Brent, you've heard

testimony this morning that an essential part of Dr. Kinsbourne's model was that methyl mercury decreases glutamate uptake in astrocytes; is that correct?

A I did hear that testimony.

Q Can that have any relevance to the effects of thimerosal-containing vaccines?

A Absolutely not.

Q And what is the basis for that, please?

A Well, that process of glutamate uptake by astrocytes and effects of mercurial compounds has been extremely well studied. And Dr. Kinsbourne referred to the work of Dr. Aschner who has actually demonstrated that mercurial compounds will indeed at sufficient dosage inhibit glutamate uptake.

Now, when Dr. Kinsbourne presented his hypothesis he was asked about whether the doses that would do that have any relevance to the doses of vaccine. And he said, I think to his credit, that he's not a toxicologist and would therefore defer to a toxicologist about this. Because the issue of dose obviously here is critical.

If you look at the work of Aschner. Bring that up, please.

Q And this would be a different one that the article Dr. Kinsbourne referred to this afternoon or

this morning?

A Right. This is the actual --

MR. POWERS: Excuse me, Special Masters. I'm going to object because this is a dose discussion that we just heard was raised not in his rebuttal today by Dr. Kinsbourne but Dr. Brent just referred to Dr. Kinsbourne's earlier testimony on direct. So again this is, the dose issue was not discussed by Dr. Kinsbourne on rebuttal. And when this did come up during Dr. Kinsbourne's direct and during the cross of Dr. Brent, he testified back then he was not a -- Dr. Brent said that he was not a neuroimmunologist. So this is outside rebuttal and again going back to Dr. Kinsbourne's direct testimony and going back to toxicology issues that Dr. Kinsbourne declined to offer an opinion on. He did talk about dose this morning.

MS. RENZI: I'll let Mr. Matanoski who is more familiar with Dr. Kinsbourne's testimony today.

MR. MATANOSKI: Actually this morning Dr. Kinsbourne was speaking at length about astrocytes. And that's what this testimony is going to, it's going to his description of astrocyte malfunction in his response this morning to criticism that was levied, particularly by Dr. Johnson in the Respondent's case-

in-chief, about Dr. Kinsbourne's reliance on this astrocyte malfunction as a critical element in his theory. He came back this morning and he rolled through his astrocyte malfunction argument again, including reference specifically to the work of Dr. Aschner to try to tie that in, astrocyte malfunction, into mercury. That's the purpose of it in his report, his written report, that was the purpose of it this morning.

SPECIAL MASTER CAMPBELL-SMITH: Let me just inquire. Dr. Brent, are you referring to testimony that you heard earlier this morning?

THE WITNESS: Yes. I, after hearing the testimony of Dr. Kinsbourne this morning I suggested that we could clarify the issue that he raised about astrocytes and glutamate in my testimony that relates to this. So I'm specifically referring to the issue of glutamate uptake by astrocytes that he was referring to this morning.

SPECIAL MASTER CAMPBELL-SMITH: I will allow the question.

BY MS. RENZI:

Q I want to refer you to Petitioners' Master List article 206. And that's another Dr. Aschner article; is that correct, Dr. Brent?

A That's correct.

Q And we're looking specifically at Figure 2?

A That's correct. And this is the actual data, not the review article but the actual data on effects of methyl mercury on glutamate uptake. And it should be noted that ethyl mercury has not been studied in this regard. So everything that we are talking about here in terms of inferring effects on glutamate uptake really is based on data from methyl mercury.

But if we look at the methyl mercury data we see there are two curves on Figure 2. One which is the round, where the symbols are round circles, and one where they are boxes. The round circles represent the inorganic mercury. And as you can see, inorganic mercury is a little bit more powerful in reducing glutamate uptake than is methyl mercury you see effects of lower concentration, the concentrations being on the X axis.

So if we look just at the inorganic mercury, the first statistically significant point where there is a decrease in glutamate uptake is indicated by the first asterisk that you see. And if you follow that down it's at approximately 2 micromolar. Two micromolar. So that is the concentration that is

required of inorganic mercury to reduce glutamate uptake in the astrocytes.

Now, if you will remember from prior testimony, just to put this value in context, the normal amount of mercury in the brain is in nanomolar amounts which is 1,000 times less than micromolar. Quantitatively, 200 micromolar refer, if you do the calculation, works out to about 400 parts per billion. Now, we could put that in context of what we would normally see in the brain. If we could just go back to a slide that I showed earlier which is from Lapham.

Q And this is Respondent's Master List 294. And this is toxic levels of mercury in the brain in development studies. And you referred to this in your direct testimony?

A Yes. Yes, I did. And I just want to put this 400 parts per billion level that is necessary to inhibit glutamate uptake in the context of what is actually seen. And if you will remember, as you can see in the lower three lines, in the general population, the background level of population, the amount of mercury in the brain is in the low parts per billion. You know, anything from 2 or 3 up to about 40 or so. And if we look at the Seychelles study population where we know there are no adverse effects

demonstrable from mercury and yet they have large exposure to mercury through seafood, we see that the amount in their brain is well over 100, 100 or 200 parts per billion without any adverse effect.

So clearly the amount of inorganic mercury that is necessary to inhibit glutamate uptake in astrocytes, which as we saw in the Aschner study in their system was at a minimum of 400 parts per billion, is far above or significantly above the amount that people normally have in their brains and, therefore, could not possibly come from the -- could not possibly be related to anything you would see, for example, from a vaccine where, if you will remember, the extra burden in the brain was 2 or 3 parts per billion.

In addition, the Aschner study, remember, is an *in vitro* study. So as we talk about, and we'll go over it again, *in vitro* studies are studies where the substance being studied, in this case mercury, is simply incubated with the cells you're studying, the astrocytes, and that therefore they are exposed to a relatively high concentration of the astrocytes. Because in the brain if you have 400 parts per billion it's not, the mercury would not just be sitting there interacting with the astrocytes, it would be bound to

all the thiols. And the free concentration of mercury that would be available therefore to interact with the cells would be very, very, very small, or as Dr. Deth puts it, damagingly small.

So that shows that the amount of mercury that is necessary to cause this astrocyte effect is vastly, vastly greater than what could be generated by a vaccine and far above anything that would be expected to be seen in normal human experience.

Q Thank you. We heard Dr. Mumper's testimony today that she wasn't certain that Dr. Rust had actually, actually interviews and gets histories from his patients. But I'd like to talk a little bit about how you as a clinician, as a medical toxicologist see patients. You do regularly see patients, don't you?

A Yes. That's what I primarily do.

Q And you practice in a university setting; is that also correct?

A Yes. I practice in a university setting and I have a private setting as well.

Q And in both your private practice and in your academic practice how are the patients, how do you take histories in the patients that you see?

A Well, thank you for asking that question. I've heard twice now on two separate occasions Dr.

Mumper's description of academic physicians as physicians who don't take histories. And I would like to put that to rest.

I take, and I don't think I am any different than any of my colleagues, I take very extensive histories. I teach medical students, as we all do, that 90 percent of what you learn about a patient comes from the history. The history is an extremely important component of a patient's assessment. And if I, for example, have a complex patient that I am going to see I usually schedule two hours for the initial consultation, of which probably an hour-and-a-half of that is taking the history.

So I think it's important that we dissuade the listeners from any misconception that it is only doctors like Dr. Mumper who take histories. And I was, frankly, a little offended by that. I think academic physicians, physicians in private practice do definitely take histories.

Q And you also see autistic children in your practice; is that correct?

A I do.

Q And are the histories you take of autistic children any less thorough or any more thorough than a regular patient that you would see?

A No. Actually they are very thorough because it's a slow history. It's usually a history from the family. Often the child is there. It's often a difficult chore to take a history. Often they come with an awful lot of questions about things that they have learned on the internet and various kinds of sort of alternative medicine treatments that we've been hearing about today that have been recommended, and they'd like advice about that. So they tend to be very long discussions.

Q Dr. Mumper also discussed today several aspects of chelation therapy. And we heard Dr. Fombonne discuss the efficacy of that treatment. But that aside, as a medical toxicologist do you see any reason for the chelation to remove mercury from either Jordan King or William Mead in these cases?

A Absolutely not. If we could bring up the slide that I think we showed earlier I just want to make one point on that slide. Yeah.

Q This is slide 45 from Dr. Brent's direct testimony.

A If you will recall, the normal pattern of what we see for assessing mercury is that if we take a urine sample of mercury and we simply collect it on a patient there are validated reference ranges, that's

an unprovoked urine, there's no chelator, there are validated reference ranges. And under normal people who are not mercury toxic will have a urine mercury excretion.

If on the other hand we take a normal person, any one of us here in this courtroom, and we add a chelator that urinary excretion will be increased, and often increased out of the normal reference range for unprovoked urine. So that's normally what you would expect to see. And, in fact, our gold standard test for assessing mercury toxicity is a urine mercury level. There is no test in medicine except on the cases of very shortly after an acute exposure where we might look at blood level there is no test in medicine that is more valid for assessing mercury toxicity than an unprovoked urine mercury concentration.

Below that you see the results of Jordan King and William Mead. And here we see that their unprovoked urine concentration is exactly in the normal range.

On the other hand, they have been chelated. And the justification for that chelation with regard to mercury comes from what you see in the righthand column where in both cases four out of five provoked

urine samples have had increased urine mercury. Well, you're supposed to have increased urine mercury with provoked urine -- with provoked samples. Therefore, there is absolutely no indication based here or anything else I saw in the medical records that suggest that there is any mercury effect in these children and, therefore, there was absolutely no reason to chelate them for any mercury-related reason.

Q Thank you.

SPECIAL MASTER HASTINGS: Just for my benefit when I go back to read this, this is slide 46 not 45; isn't that right?

MS. RENZI: I apologize, Special Master.

SPECIAL MASTER HASTINGS: Okay.

MS. RENZI: Slide 46.

BY MS. RENZI:

Q Dr. Mumper also testified today to seeing an increase of lead levels in children and that chelation may help with the adverse effects from lead. Is there any scientific or medical basis for that statement?

A It is true that chelation therapy is the appropriate therapy for lead toxicity. However, the records do not reflect any lead toxicity in the case of either of the two children at issue here, Mead or King. Neither of them had had an elevated live lead

level. And a blood-lead level is the gold standard test for lead toxicity. Because contrary to testimony that was given earlier today, blood lead remains elevated and will be elevated for years in children that have lead toxicity. It equilibrates with tissues and if there is high tissue burden there's going to be high blood burden.

Q So you disagree with Dr. Mumper that the blood levels would only test for acute toxicity?

A That's absolutely wrong. So there was no indication, therefore, for treating either of these two children with a chelator for any lead effect.

Q Is there any other accepted test for measuring lead toxicity other than blood?

A Blood lead is the gold standard. And there are no other accepted tests in medicine now that routinely give blood levels, lead levels.

SPECIAL MASTER CAMPBELL-SMITH: Can I interrupt for just a moment?

MS. RENZI: Sure.

SPECIAL MASTER CAMPBELL-SMITH: I'm hearing a little something in your microphone, Dr. Brent. Can I encourage everybody to check to make sure you're turned off. Oh, and the distance from the microphone.

THE WITNESS: I understand.

(Pause.)

SPECIAL MASTER VOWELL: Dr. Brent, while we're in a pause may I follow up on your comments about the lead levels in the --

THE WITNESS: Please.

SPECIAL MASTER VOWELL: Excuse me, the mercury levels post-chelation --

THE WITNESS: Right.

SPECIAL MASTER VOWELL: -- in both the Mead and the King boys.

THE WITNESS: Please.

SPECIAL MASTER VOWELL: Was there anything about the levels you observed in the medical records post-chelation that would cause you to think that these were extraordinarily high levels of excretion upon chelation?

THE WITNESS: No. You always expect the levels in the urine bumped post-chelation. It would happen to any one of us. There are no validated reference ranges for post-chelation, that's why they're not used in medical practice or there is no valid way of using them. And, in fact, if you look at these two children they've had mild increases in urine-lead excretion as I recall, but they were nothing different than what you would normally expect

to see if you give a chelator to them.

SPECIAL MASTER VOWELL: Have you given chelators to a lot of children?

THE WITNESS: I have chelated a number of children.

SPECIAL MASTER VOWELL: So there's nothing here that would be out of the ordinary from your experience even in the absence of a standard reference range?

THE WITNESS: Well, I have to -- in truth we don't follow urine leads because the correct test is blood leads. So I haven't looked at many blood leads -- urine leads in children that I have chelated. So I can't speak to that from my experience. But I have seen, I have had a number of patients now come to me because of these **[NAME REDACTED]** type of laboratories where which are based on urine, chelated urine, and they always have high leads in their chelated urine. And I tell them, well, let's just do the gold standard test, get a blood lead level, and so far 100 percent of the time they've been normal.

SPECIAL MASTER VOWELL: All right. And let's go back to mercury though.

THE WITNESS: Okay.

SPECIAL MASTER VOWELL: Are the post-

chelation mercury levels in either of these two boys in excess of what you would see or in excess -- I take it there's no standard reference range post-chelation?

THE WITNESS: No standard reference range there. You do tend to see small increases, they've had some minor increases in their mercury excretion over the reference ranges for the non-provoked. It was not, certainly not very dramatic. And it was certainly well within the range of what you would expect to see.

For example, if you look at the studies that I've cited on where they were studying chelators and they would look at the effect of the chelator on urine mercury excretion, now that's a valid time to do a post-chelation mercury if you want to study the effect of the chelator. And if you look at the normal controls in those studies when they give them a chelator you do see some increase in the urine mercury excretion and it's a moderate increase and it's really not very different from what you'd see, what we saw in these children.

BY MS. RENZI:

Q Dr. Brent, I just want to clarify something. When you say you've chelated children you've chelated them for lead toxicity or mercury toxicity?

A Actually both.

Q And under what circumstances did you chelate for mercury toxicity?

A I've had a number, but probably the most common and the most dramatic relates to the fact that I live in Colorado and in the Rocky Mountain area there are people that are still out panning for gold. And the way they do it is they collect gold ore, which is a mixture of gold and other things, and they take advantage of the fact that you can extract the gold from ore using liquid mercury. And so they chop up the ore, they grind up the ore, they mix it up with liquid mercury, they extract the gold and they get into the liquid mercury. They get rid of everything else. Now they have the gold separated, the only problem is it's in all this mercury. And what they will often do to get rid of the mercury is they will heat it. And they will often heat it in their house, in their kitchen for example.

When you volatilize mercury like that a tremendous amount will get into the air. And I've had now a number of families that have become profoundly mercury poisoned because somebody had heated up the mercury in an attempt to do this. Patients that were so sick that they've had to be on -- families that

have had to be so sick that they've had to be on ventilators, they've had protracted stays in the ICU for severe inhalational mercury vapor poisoning.

Q Thank you. So when Dr. Mumper said that she saw mobilization of heavy metals by chelation and then assumed that the chelation was beneficial do you agree with that statement?

A No. That's exactly -- I think what you see is you give a chelator, you look in the urine and there is more than the non-chelated reference ranges for the levels in the urine, and it's what you would normally expect. It tells you nothing about mobilizing stores of heavy metals in the body.

Q Dr. Mumper also talked about supplements and those supplements to increase glutathione to treat mercury toxicity. Do you agree that that therapy is warranted in cases?

A Glutathione, no. Supplemental glutathione to treat mercury toxicity has no validity at all.

Q And why is that?

A Well, the reason for that is that we have very, very, very large amounts of glutathione in our bodies. WE have huge amounts of glutathione in our bodies. And glutathione is never limited in terms of being able to handle heavy metals. It's a defense

that has been put into humans and animals and it works extremely well. And there is no way that some small additional amount of glutathione on top of the already very, very large stores we have, can make the slightest difference.

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

THE WITNESS: Thank you.

SPECIAL MASTER CAMPBELL-SMITH: Thank you. Any questions from Petitioners' counsel?

MR. POWERS: Yes. Thank you, Special Masters.

CROSS-EXAMINATION

BY MR. POWERS:

Q Dr. Brent, my name is Tom Powers. I didn't have a chance to talk to you on direct or cross last time, that was Mr. Williams' privilege, but I have a couple of questions for you now.

A Sure. Please.

Q You were talking about Dr. Aschner's paper on glutamate uptake a little while ago; correct?

A Correct.

Q This is an experiment that was *in vitro* rat cells; correct?

A Correct.

Q And there is some evidence, we've heard testimony, that human cells are often more sensitive than rat cells; is that correct?

A I don't know of any data about human cells being more sensitive to inhibition of glutamate uptake by mercury than rat cells.

Q Can you describe a human model that parallels what Dr. Aschner did with this rat model?

A If there was a very good human model that could be used then Dr. Aschner would probably be studying humans and not rat brains. The problem is that we don't, it's very hard to have cultured human neurons that are -- that have not been so transformed that they're highly artifactual. So unfortunately there's not a really good model for that. And that's why the rat models are typically used.

Q And actually this isn't a rat brain, these are isolated rat cells in a petri dish; correct?

A As I said, it was an *in vitro* culture. It's an *in vitro* experience, yes.

Q And this *in vitro* experiment featured astrocytes; correct?

A Correct.

Q And since it's an isolated culture it would not have microglia; correct?

A Correct.

Q And you understand, of course, that Dr. Kinsbourne's hypothesis is based on the idea that microglial activation releases proinflammatory cytokines that harm astrocytes; correct?

A Correct.

Q So there's nothing about this petri dish that is absent microglia that is at all relevant to Dr. Kinsbourne's position that it's the reactive oxygen species in the proinflammatory cytokines released by microglia that cause the astrocyte damage; correct?

A Well, in fact this is the data that exists on mercurial effect on astrocyte glutamate uptake. I don't know of any data that is specific for this sort of complex scenario that you are describing in your question. However, clearly if you look at the data that was cited by Dr. Kinsbourne for showing that mercury inhibits astrocyte uptake of glutamate, this is the data. And that's the date, therefore, I was referring to.

Q Dr. Kinsbourne also was citing the Vargas and the Pardo papers and the evidence of inflammation that involved proinflammatory cytokines in the possible effect on astrocytes; correct?

A I don't recall him citing anything that suggested that, that showed that proinflammatory cytokines altered astrocyte glutamate uptake in response to mercury.

Q And, in fact, when Mr. Williams cross-examined you on this issue you testified that you were not a neuroimmunologist and you didn't comment on those papers under cross and declined to comment on those papers under cross; correct?

A Well, mostly correct. I don't think we were discussing neuroimmunology. This is not an immunological question.

Q But the inflammatory response --

A Right.

Q -- is an immunological process?

A Right.

Q And Dr. Kinsbourne posits that it's initiated by microglia; correct? And there is nothing in the Aschner paper -- I mean it's impossible for it to address that issue because there were no microglia in the petri dish with the rat brain cells?

A That's true. That's true.

MR. POWERS: No further questions.

SPECIAL MASTER CAMPBELL-SMITH: Any further questions from Respondent's counsel?

MS. RENZI: No, thank you.

SPECIAL MASTER CAMPBELL-SMITH: Any questions from my colleagues?

(No response.)

SPECIAL MASTER CAMPBELL-SMITH: Thank you, Dr. Brent.

THE WITNESS: Thank you, Special Master.

(Witness excused.)

SPECIAL MASTER CAMPBELL-SMITH: Any further witnesses to be called by Respondent's counsel?

MR. MATANOSKI: No, ma'am.

SPECIAL MASTER CAMPBELL-SMITH: We are roughly at 4:00 o'clock. I think this might be a good moment to take a break and let counsel gather your thoughts for the brief closing arguments that, or closing remarks that counsel had indicated that they were planning to make. So how brief would you like this recess to be to prepare your brief remarks?

MR. POWERS: I'm happy with 10 minutes, Special Master.

MR. MATANOSKI: That would be fine for me as well.

MR. POWERS: Maybe just 10 after the hour.

SPECIAL MASTER CAMPBELL-SMITH: Perfect. We are in a brief recess.

(Whereupon, a short recess was taken.)

SPECIAL MASTER CAMPBELL-SMITH: We are back on the record for brief remarks.

MR. POWERS: And, Special Masters, I appreciate a description of this as brief and just remarks. And I just want to acknowledge that, particularly for people who might be listening either live or will download this, what we are going to do here, it's certainly not what I plan to do, is a summary of the evidence and argue with the evidence really not at all, because that's something that in this program, as the counsel and the Special Masters know, is something that happens in the months after the evidence is closed in theses cases and happens largely on paper through motions and pleadings. But we do want to take advantage of the opportunity that you have provided to make some comments about the proceedings here over the last three weeks and the proceedings in the Omnibus Autism Proceeding in general.

One issue that I want to talk about is something that we've heard about and this idea that the Petitioners somehow are wanting to spring surprises, whether it's on the Court or on Respondent's counsel. And I just want to make it

clear, particularly to the Special Masters, that that absolutely is not the Petitioners' intent. We are responding to a dynamic scientific environment. And we do everything we can to stay on top of the literature. We monitor everything we can. And when we find something new we want to bring it your attention to inform your decision in these important cases.

We are working hard to do that. And I can definitely assure you that if we found something helpful we would want to talk about it early and talk about it often. So there is no intent here to slip in a surprise or hide the ball. We want our best and our strongest case in front of you and in front of the Respondent as early and often as we can.

But as I said, we are in a dynamic scientific environment. There is new research going on all the time, some of this during the hearing. There were abstracts presented on some of these relevant issues at international conferences. There were peer-reviewed papers that appeared in journals, some of them were published during this proceeding, some of them only became available in our language during this proceeding.

It's also important to understand, I

believe, that there's an interesting dynamic at work in the Vaccine Program that one does not encounter in traditional civil litigation, and I believe it's intention, and Congress set it up this way. It's important to remember that the Respondent here is the United States Department of Health and Human Services and its related agencies. They have a charge and a public mission and a public obligation and a public duty to stay abreast of the science, to follow the science and, in a sense, to not be surprised by the science. And it's important that in these proceedings the litigation goals of prevailing not be confused with the client's overarching public policy goal of staying abreast of the science, interpreting the science, and getting the word about the science out to folks, whether it's their attorneys that are here in these proceedings to the families of the children here, to the Special Masters, and to the scientific community at large.

I believe that one of the reasons that discovery is not available as a matter of right in this program is in a sense to help address the tension that you see in civil litigation about the interests of the parties. In civil litigation each party in the adversarial system has only its own self-interest at

mind, that is, the only interest they have in the adversary system is to prevail in that litigation and to win in that litigation. But here the Respondent, the U.S. Department of Health and Human Services, has that larger obligation to be doing the scientific research, to fund research, to make data and research available to the public.

So by taking away the contentious adversarial rules of discovery it seems that it helps alleviate that tension and doesn't create a conflict between the litigation defense goals and the public policy goals of not being surprised by the science.

We've heard testimony that a lot of the work that the Petitioners have introduced in this case is work that is in fact funded by the NIH, by the CDC, and by other entities involved with the Respondent, with HHS. To the extent that the Respondent is involved in the science, whether it's doing the science itself, funding the science and monitoring the science, they ought not to be claiming complete surprise when new science does come out. Again, we cannot confuse the litigation goals with the public policy goal and the institutional goal that HHS has. And as I said, I believe that is one of the reasons that Congress wanted this to be a non-adversarial

system and to not have those rules of discovery that for those experienced in civil litigation really turns it into a fight over sometimes every scrap of paper that you are trying to pull from the other side.

So the program should be less adversarial in that way. And I think it's important to remember that. It's also to remember that the program is designed to be less adversarial in order to provide an environment for families who believe that they have legitimate claims to appear and present their case. And that also includes having experts who are willing to come in and testify for them. The experts in this process are obviously critically important because all of the issues that you all have to decide are often very complicated issues of fact that require technical explanation, interpretation, and presentation. And I just think it's a shame that in these Omnibus Autism Proceedings we have seen from the Respondent a regrettable inclination to launch attacks, often unsubstantiated smear attacks, on some of the witnesses involved in these cases. And we saw it with Dr. Kinsbourne in this proceeding.

Again, if the Federal Rules of Civil Procedure were at play none of the issues that Respondent's counsel attempted to impeach the

credibility of Dr. Kinsbourne on would have been allowed in. This is a 31-one-year-old employment dispute that was resolved in his favor but they brought it in. And I argue and Petitioners believe that the lack of rules of the Federal Rules of Civil Procedure applying here explicitly was done by Congress in order to make it less adversarial and to remove some of those adversarial qualities that one sees in the civil litigation system. And that's a system where you commonly do see this type of attack constrained by the rules. But here the absence of the rules shouldn't allow people to engage in conduct that would be barred by the rules in a civil proceeding, and it's regrettable.

Dr. Kinsbourne, obviously, was perfectly capable of defending himself, and he did, and he's made that record. But it is just regrettable that in every one of these hearings, whether it's Dr. Bradstreet being accused of being an exorcist to Dr. Kinsbourne being attacked for the issues he was attacked on here is regrettable and we ought to be able to avoid that in this congressionally-mandated non-adversarial study.

One of the last things I wanted to conclude on is addressing a thematic argument that I have heard

and I think all the Petitioners have heard from Respondent's experts, and that is the idea that the Petitioners' expert witnesses are somehow so fixed on a conclusion that they leapt to that they are willing to ignore contrary evidence, that they are staring through Tycho Brahe's telescope insisting that the Earth is the center of the universe. I think in the testimony that you've heard in this proceeding that absolutely is not the case. And I just want to use the example of Dr. Mumper.

Dr. Mumper is a clinician not a bench scientists, not somebody that does original research, but she is a clinician who has responded to the needs of a significant patient population who weren't being addressed by other doctors, including Dr. Rust. And so Dr. Mumper, even if the Respondent's experts disagree with her conclusions, what you heard from Dr. Mumper is a doctor who is doing her absolute best to follow good science, to keep on top of the science. Here is a pediatrician in Lynchburg, Virginia that is spending her resources to build bibliographies of science, to get that information out to other doctors, to validate her work as scientifically as she can, to bring in the resources to increase the scientific rigor and the scientific integrity of the work that

she's doing.

She is doing that while on the other hand Dr. Rust is so fixed in his telescope, the Tycho Brahe telescope, or the *idee fixe* that what you have here, he testified for at least an hour on Rett syndrome. And it seemed to be his argument that Rett because it's congenital and genetic is a model for autism because if Rett's is genetic and autism shares some of the symptoms of Rett's then autism itself must be genetic.

That line of argument is a faulty syllogism. It's sort of another example of the classic false syllogism that Aristotle is a man, all man are mortal, therefore all men are Aristotle. It's a flawed logic. And it just represents how fixed he is on the idea that this is an inevitable, at inception, predetermined outcome that he is not willing to entertain apparently the idea that environmental factors might be at play, that care and treatment might alleviate the symptoms, that some care and treatment somewhere down the road in an investigation into etiologies that aren't presumed to be genetic are worthwhile. His mind is closed to that.

And those are just two very contrasting and telling examples of the type of, if we're going to be

describing expert advocacy in these cases as the Respondent's experts have attempted to do, that is an example of the Respondent's experts who are so focused on what they think the outcome is that they are willing to spend 114 pages in a PowerPoint really just arguing, as I said, the false syllogism that all autism is like Rett's, and therefore all autism is congenital. That is not supported by the science.

So these are just some observations about this proceeding as we move forth. Again, this ought to be a science-based inquiry. This ought to be a non-adversarial setting. This ought to be the type of setting where families and their experts can come and air their meritorious claims. And whether one disagrees with the conclusion that any particular witness reaches, the idea that at every single one of these test cases there is going to be some one of the Petitioners' experts who is going to be targeted the way that some of these experts have been in earlier proceedings is something that we should avoid and focus on the science, be willing to consider the science that comes in, understand that the science is changing, understand that there is a convergence of science over time, and understand that when we do close the evidence in these cases there probably will

be more information out there in the scientific literature. And the science will need to speak for itself at some point. And as we see the science converge on some of these key issues the Petitioners will do everything that we can to bring that information to the Special Masters, to share it with the Respondent, but ultimately with the idea that litigation strategy in this program is really not what should be driving the consideration of the science but ultimately, again considering the unique position of the Respondent as a party here, reflecting a responsible fulfillment of the mission to keep up to date with the science, protect public health, consider the science and apply it in a way that's going to provide the best information ultimately to the three of you deciding the general issues and the specific issues in all of these cases.

Thank you.

SPECIAL MASTER CAMPBELL-SMITH: Thank you. Mr. Matanoski?

MR. MATANOSKI: Thank you, ma'am.

In putting together my closing remarks, though the time that we have is brief, I feel I would be tremendously an error of my part to not acknowledge the families that were involved here, the King an the

Mead family. Probably the most poignant moments during this trial was hearing their testimony, testimony of MyLinda King and George Mead discussing William and Jordan. We thank them for their participation. Certainly our hearts go out to them and to all of the families that have autistic children. We may be litigating one side of this issue but we certainly have tremendous respect and admiration for all of them.

You have a threshold matter before you that's a scientific matter, however, which you must address. And obviously a scientific question necessarily turns on scientific evidence. And there are certain legal standards that must be applied in this courtroom and every courtroom to how you handle scientific evidence. What, indeed, can even be considered reliable scientific evidence.

The Supreme Court has spoken. It said that it is evidence that must be tested, it's evidence that should be subject to publication and peer review, it's evidence that has general acceptance in the scientific community. On the PSC side of the ledger of the evidence you have not heard that yet, you've heard speculation pure and simple.

What you've hard in terms of comments from

Mr. Powers this morning suggests that that evidence as far as the Petitioners are concerned or the PSC is concerned is still not available. He talks about the dynamics of science, ongoing studies, which in some way may imply a lack of evidence, scientific evidence that is available to the PSC at this point to prevail.

Now, the PSC's case started with a curious approach. Rather than putting on evidence in support of their claim they put on evidence that was to, or put on testimony that was designed to undermine evidence against their claim. That was the testimony of Dr. Greenland. But Dr. Greenland's testimony and his whole postulate depended on a supposition. The supposition was that the Petitioners would prove to you a case that their mechanism applied to clearly regressive cases only. Now, you've heard from Dr. Deth about his hypothesis and he said it did not apply only to clearly regressive cases. You heard this morning from Dr. Kinsbourne who said that he hasn't even looked at whether his hypothesis would have any application on non-regressive cases so he can't even address whether his hypothesis is only limited to clearly regressive cases.

All of the abundant epidemiological evidence that has addressed the precise issue in front of you,

that is whether thimerosal-containing vaccines can cause autism or are associated with autism is back on the table. It never was off. Dr. Greenland's supposition is in error.

If you follow the mechanisms proposed by the PSC here to their logical conclusion, they fail to show that thimerosal-containing vaccines are the cause. They propose that inorganic mercury is the causative agent. Inorganic mercury is not specific to childhood vaccines. It's in what we eat, it's in the air we breathe, it may be if we have poor dental health may be in the fillings in our mouth. They have failed to specify how much inorganic mercury is necessary to cause autism. Their experts consistently refused to say. In fact, when they did say they essentially said any amount. They have pushed the threshold down so that any exposure to inorganic mercury could be a potential cause of autism.

They have described a causal mechanism or mechanisms that are so general they apply to virtually every disease and to every case of autism. Oxidative stress is seen in conjunction with almost every disease. You even see it after trotting or jogging, you even get it after you bang your thumb nailing it, hammering in a nail. Neuroinflammation is seen in a

variety of neurological illnesses, including Alzheimer's and Parkinson's disease, for example. And in the Vargas study every single autistic patient in that study had neuroinflammation, regressive, non-regressive, young and old alike. These are non-specific causal mechanisms that are proposed to you.

In the end, you could just as easily conclude that a tuna sandwich or a dental filling could cause autism as a childhood vaccine. And to flip it around, you can just as easily consider that an 80-year-old man who received a flu vaccine would get Alzheimer's from it.

Mr. Powers commented about what I describe I guess as -- or his description of a smear campaign or heavy-handed treatment of Petitioners' experts. You take the witnesses as they come. Now, perhaps there was an explanation, and you've heard it for the events that transpired with Dr. Kinsbourne's departure from the University of Toronto, but again, you take the witnesses as they come. When Dr. Deth took the witness stand and said that he's willing to come before you and say that his hypothesis, you should rely on that to make a finding of this import even though he's not willing to go to the scientific community and say that it's acceptable without further

testing, I think that bears consideration.

Dr. Kinsbourne when he sat in the witness chair he put his credibility on the line. If he's coming before you saying, rely on me, believe me, trust me as an impartial scientist, because that's how he's coming to testify to you, you deserve to know whether he gets that kind of trust. You know he's known to you, you've seen him appear many times. If you go back and look at the cases that are currently active in front of the Special Master's Office you will find that he's maintained or offered an expert opinion saying vaccines have done harm in over 30 cases. In the past year he's offered one article in a medical journal. I think that tells you whether he's coming to you as a witness who spends his time in the courtroom or as an impartial scientific expert witness who is adding some value to what your deliberations are from a point of view of reliable science.

Now good science and reliable science comes from testing, publication, critical review, validation, verification of results. It's performed by those who work in the field, apply scientific method to their research. The Supreme Court tells us there can't be untested hypothesis, as Dr. Deth has essentially described his causal mechanism. And good

science won't be first revealed in the courtroom, as Dr. Kinsbourne's hypothesis is. But it's going to see the light of day through critical discussions of research among the scientists themselves. It's not reliable science, indeed it's not any kind of science to sit at your computer, take your last litigation-driven report, run find and replace. Find measles vaccine and replace with thimerosal-containing vaccine. A litigation-driven contrivance such as that has no place in this courtroom; the Supreme Court has mandated that.

Now, when the trial began Mr. Powers described thimerosal-containing vaccines as a relic of history. Perhaps that was a reference to allowing some leeway in what your evidentiary standards would be to provide some grading on the curve of the science you'd accept. In fact, they have done everything to make this anything but a relic of history. The day that they said that they held a press conference to discuss the case. Their experts are here telling you that trace amounts of mercury that are in vaccines, the flu vaccine, for example, that's still administered could be enough to cause autism.

This, whether we like it or not, this issue has great importance, the issue before you had great

attention drawn to it. Just last week Time Magazine had vaccines and the safety of vaccines as their cover issue. Many eyes are going to be turned to this Court to see how you handle the scientific evidence before you. What do you make of that evidence? And it's not just from the parents that are front of you with their claims, it's from parents who haven't brought claims who have autistic children and who are wondering if by getting them vaccinated they are somehow responsible for that condition. It's from scientists who work in these relevant fields, it's from those who treat autism, and it's going to be reviewed by parents who are wondering whether they should get their children vaccinated or not.

Now, I'm going to be blunt at this very late hour having brief remarks. Are you going to decide that question on the say-so of Dr. Deth and Dr. Kinsbourne? Or are you going to decide that question on the evidence given to you by witnesses like Dr. Catherine Lord, Dr. Eric Fombonne, and Professor Sir Michael Rutter? Are you going to look at and consider the fact that every reputable medical, independent medical organization that has considered this issue, the Institute of Medicine, the American Academy of Pediatrics, the European Medicine Association, the

World Health Organization have all come to the conclusion that thimerosal-containing vaccines do not cause autism?

Are you going to also consider that every Court that has had to consider this claim before it, or you have considered it in fact, has found that the claim is so lacking in scientific merit that it should not be even presented to a jury?

Reliable scientific evidence at this point is all on one side of the ledger: vaccines don't cause autism.

Thank you. I have no further remarks at this time.

SPECIAL MASTER CAMPBELL-SMITH: Thank you.

At this time we have reached the conclusion of this portion of the evidentiary hearing in the Omnibus Autism Proceeding. And on behalf of my colleagues I am going to make a few brief comments this afternoon.

First, we again thank the members of the King and the Mead families who came to Washington and were with us for part of this hearing. We thank them as well for generously agreeing to have their sons' cases designated as test cases in the Omnibus Autism Proceeding.

We also wish to thank the counsel for both sides who have presented their evidence so ably during this hearing. We know that they have worked enormously hard in preparing and in conducting this hearing. And we appreciate that hard work.

We also thank the expert witnesses who have testified before us.

We thank the United States Court of Claims for the Federal Circuit who have allowed us to use their courtroom. We thank all of the wonderful employees of both of the courts housed in this building who assisted so well in preparing for and conducting this hearing.

Next we want to acknowledge once more certain other people who are also very important to this proceeding, that is the families of all the other 5,000 Vaccine Act claimants who have been diagnosed with autism or a similar condition. Some members of those families have been listening in by means of our teleconferencing system. Others have followed this hearing by downloading the audio from the internet. To all such family members, as to the King and the Mead families, we three Special Masters pledge to you again that we will consider very carefully the evidence put before us at this hearing and give that

evidence our very complete and thorough study. We realize the great importance of the task assigned to us in deciding these cases. And we will give our greatest effort in carrying out that heavy responsibility.

Finally, now that this hearing is finished in this respect some of you may want to know what will happen in these test cases. The answer is that, first, in July we will hear from two more expert witnesses for Respondent who could not be here this month. At that same time we will hear any rebuttal to those two witnesses that the Petitioners wish to present.

We will also hear some case-specific testimony in a third yet-to-be-identified test case related to the same theory, which case will be decided by Special Master Vowell.

In addition, after the July hearing the parties will file written briefs summarizing the testimony in this hearing. That process will likely take several months. Then once the last of those briefs are filed I will issue a written ruling in the William Mead case. Special Master Hastings will issue a written ruling in the Jordan King case. And Special Master Vowell will issue a written ruling in the third

to-be-identified case.

Finally, for updates concerning the progress of all three cases and concerning the Omnibus Autism Proceeding in general please do keep checking the autism proceeding page on the Court's internet website.

With that, I thank everyone involved in this hearing. I wish you safe travels to your point of return. We are now adjourned.

(Whereupon, at 4:40 p.m., the hearing in the above-entitled matter was concluded.)

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REPORTER'S CERTIFICATE

DOCKET NO.: 03-584V, 03-215V

CASE TITLE: In Re: Claims for Vaccine Injuries

HEARING DATE: May 30, 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 30, 2008

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