

**Respondent's  
Exhibit NN**



HEALTH SYSTEM

*Department of Neurology*

ROBERT S. RUST, M.A., M.D.  
THOMAS E. WORRELL, JR. PROFESSOR OF EPILEPTOLOGY AND NEUROLOGY  
PROFESSOR OF PEDIATRICS  
CLINICAL AND TRAINING DIRECTOR, CHILD NEUROLOGY  
CO-DIRECTOR, F.E.DREIFUSS COMPREHENSIVE EPILEPSY AND CHILD NEUROLOGY CLINICS  
PO Box 800394  
CHARLOTTESVILLE VA 22908

U.S. Department of Justice  
P.O. Box 146  
Benjamin Franklin Station  
Washington, DC 20044

I have been asked by the Secretary for Health and Human Services to provide an opinion concerning the medical condition of three young boys, Jordan King, [REDACTED] and William Mead. All three boys satisfy the DSM-IV criteria for autistic disorder (DSM-IV 299.0)<sup>1</sup>. They represent the most commonly encountered combination of findings in children with autism. They are boys (as in 80% of those who satisfy the diagnostic criteria), and they manifested their autistic features prior to three years of age. There is also a suggestion of regression in function. Their manifestations include typical and highly significant impairment of social interaction, communication, and they are observed to have restricted/repetitive/stereotypical behavior, interest, and activities.

Medical science has usually succeeded most reliably in approaching an understanding of illness when a clinically defined group is found to have a particular underlying pathology. This pathologic understanding enables a return to the clinical realm to refine diagnostic criteria and to better appreciate the actual disease mechanisms, and the developmental course and outcome of a condition. In the case of autism, considerable advances have been made over the past few decades. Understanding of the mechanisms of autism has advanced in association with growing evidence of characteristic pathological changes in the brain.

The intellectual rules whereby cause and effect is established in medicine have become quite clear over the past century. The initial stage for most studies of toxins is

---

<sup>1</sup>APA (2000) American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4th ed., text rev. Washington, DC: American Psychiatric Publishing.

epidemiological—demonstration of an association between exposure and an ensuing clinical syndrome. The next phase has been experimental demonstration of the production of a similar toxic syndrome, as well as characteristic pathological changes in an apt animal model. The next stage has been investigation of the mechanisms of injury with the production of a viable explanation for the toxicity, an explanation that makes biological sense. The final stage is application of various pertinent and reliable measures of toxic burden in order to produce reliable tests of intoxication and to refine understanding of the quantitative toxicity of an offending substance. At each stage, an understanding of the concentration of a toxin required to produce that clinical abnormality is further refined.

This scientific method has not been followed in the assertion that thimerosal toxicity is a cause of autistic disorder. Instead, bits and pieces of information have been pasted together to generate an unproven hypothesis. Information supporting this hypothesis has largely been borrowed from better established investigations of toxic substances (e.g. methyl mercury and lead) and their toxic effects. In particular, clinical and neuropathological facts of essential importance in understanding the effects of those toxic elements have been ignored. Presumptions concerning the alleged toxicity of ethyl mercury appear to be drawn by analogy to methyl mercury, as there is no reliable epidemiological data upon which such assumptions concerning ethyl mercury can otherwise be based. A considerable amount of information is available concerning the neurotoxicity of methyl mercury. Both the clinical and pathological aspects of that neurotoxicity are well-defined, and they do not include the clinical and pathological features of autistic syndrome.

With regard to the hypothesis of the pathophysiology of autism advanced by petitioners' experts here, one must explain why all but the tiniest fraction of children develop normally after receiving vaccines containing very tiny amounts of ethyl mercury. The explanation offered by petitioners' experts is an increasingly complex and scientifically awkward collection of presumed vulnerabilities, including an idiosyncratic failure to normally compartmentalize or excrete mercury, as well as exertion of a novel form of mercury neurotoxicity that in no way resembles the known neurotoxicities of mercury. It requires acceptance of the view that this produces autism, and hence the pathology underlying autism, despite the fact that even the known alterations produced by mercury in the nervous system do not produce that pathology. Moreover, no effort has been made to explain how the pathological findings associated with autism reported in the literature result from mercury toxicity.

The hypothesis advanced in support of ethyl mercury toxicity in these three cases further entails a novel form of immunological disturbance and autoimmunity, with an associated abnormality of gastrointestinal function. The clinical data advanced in support of the hypothesis include an alleged abnormal frequency of infections (particularly ear infections) and a persistence of diarrhea. The allegations are made without reference to the frequency of these manifestations in the normal population, or to

the possibility that at least one of these conditions (diarrhea) may actually develop as a secondary manifestation of the autistic disorder itself.

I would add that from the vantage point of nearly thirty years of evaluating and treating children, the frequency of ear infections in the three cases under consideration here is no different from that observed in children without autism. Moreover, it is not clear to me that the many children whom I have evaluated and treated for autism suffer an excessive number of ear infections or other illnesses. The role of autoimmunity and immunodeficiency in childhood neurologic disease has been a major concentration of mine throughout my career, and it entirely eludes me how the novel disorder proposed by petitioners' experts might in any way produce autistic disorder, or what has been repeatedly observed about the pathology of autistic disorder.

My clinical experience in managing children seen either for autism or for frequent, troublesome diarrhea suggests that autistic individuals may be subject to a common cause of frequent stools in early childhood: stool retention with the development of secondary megacolon and overflow diarrhea. This is a well-known condition that comprises a major part of the work done by child gastroenterology clinics. Among individuals who may experience this difficulty are children with autism.

Before discussing each child specifically, some general points that apply to each of the three cases under consideration will now be addressed.

**1. Mercury intoxication has been well studied clinically and pathologically, and it does not present as autism.**

In her reports on each of three children, Dr. Mumper claims there is evidence showing medical problems compatible with mercury toxicity. Jordan King "JK" Exhibit "Exh." 13 at 2; [REDACTED] William Mead "WM" Exh. 16 at 2. This statement is entirely unjustified because in none of the three cases do I find any evidence whatsoever of the known manifestations of mercury toxicity. Nor do I find any evidence of exposure in the quantities necessary to produce injury.

Mercury intoxication presents a clear clinical and pathologic picture, which does not in any way resemble the combination of findings of autistic disorder. Research on the neuropathology of methyl mercury poisoning has shown damage that is not concentrated in the discrete areas of the brain that are implicated in autism.<sup>2</sup> Even with exceptionally high exposures to mercury, as in the Minamata Bay disaster, autistic disorder is not a known outcome. The pathology of infants afflicted with severe neurologic disease in the wake of that exposure, and the associated pathology of the nervous system, in no way resembled autistic disorder. The concentration of mercury in the brain resulted in fetal death or severe static encephalopathies that could not be mistaken for autism. Considerable exposure to quantities of mercury in doses far in

---

<sup>2</sup>Eto K. Minamata disease. Neuropathology. 2000 Sep;20 Suppl:S14-9.

excess of the amount contained in vaccines, such as that carefully documented in the Seychelles<sup>3</sup>, or exposure in children resulting from dental amalgams<sup>4</sup>, have not been shown epidemiologically to be linked with the development of autism. In sum, there is no convincing epidemiological evidence that mercury exposure produces autistic disorder.

Post-natal methyl mercury intoxication results in a higher concentration of mercury in the peripheral sensory nerves, which causes severe motor abnormalities in the limbs. In stark contrast to language function in children with autism, motor functions in autistic children are usually on par with neurotypical children of the same age.

**2. There is no evidence that the small concentrations of thimerosal contained in vaccines produce toxic effects in children.**

Each of Dr. Mumper's reports states that the child has an increased vulnerability to the toxic effects of thimerosal, which is exacerbated by other co-existing factors and other mercury exposures (WM Exh. 16 at 3 [REDACTED] JK Exh. 13 at 3). There is absolutely no reliable support for this statement.

There is no evidence that the small concentrations of thimerosal contained in vaccines produce toxic effects in children, nor for the theory that other conditions of vulnerability increase the toxicity of thimerosal. The clinical evidence cited in support of this point is not based upon any reliable scientific information of which I am aware, nor could I find any such evidence in peer-reviewed publications. Further, there is no reliable evidence, despite Dr. Mumper's assertion (see JK Exh. 13 at 4, "antibiotics exacerbated mercury toxicity") that small amounts of thimerosal in combination with antibiotics cause autistic syndrome.

---

<sup>3</sup>Myers GJ, Davidson PW, Cox C, Shamlaye CF, Tanner MA, Choisy O, Sloane-Reeves J, Marsh D, Cernichiari E, Choi A, et al. Neurodevelopmental outcomes of Seychellois children sixty-six months after in utero exposure to methylmercury from a maternal fish diet: pilot study. *Neurotoxicology*. 1995 Winter;16(4):639-52.

*See also* Davidson PW, Myers GJ, Cox C, Wilding GE, Shamlaye CF, Huang LS, Cernichiari E, Sloane-Reeves J, Palumbo D, Clarkson TW. Methylmercury and neurodevelopment: longitudinal analysis of the Seychelles child development cohort. *Neurotoxicol Teratol*. 2006 Sep-Oct;28(5):529-35.

<sup>4</sup>Bellinger DC, Daniel D, Trachtenberg F, Tavares M, McKinlay S. Dental amalgam restorations and children's neuropsychological function: the New England Children's Amalgam Trial. *Environ Health Perspect*. 2007 Mar;115(3):440-6.

In each of the three reports, Dr. Mumper references the Stern (2005)<sup>5</sup> study in which it is estimated that 1 in 6 children born today has a blood level of mercury high enough to impair neurological development. If this were indeed true, it begs the question why we are not in the midst of an extraordinary epidemic of neurological dysfunction in children; an epidemic that is not documented in the medical literature or observed in clinical practice.

Dr. Mumper's argument that mercury has "myriad" manifestations of toxicity appears to imply that "anything can happen," a common theme underlining many of her opinions. This is in fact *not* true in medicine. There is some variation in relation to mercury toxicity and its clinical manifestations, but the threshold for any clinical appearance of toxicity, and hence, any variation in the expression of symptoms, is only in the context of much higher concentrations of mercury than those contained in vaccines. And Dr. Mumper's assertion by no means proves the validity of the novel hypotheses implicating tiny quantities of ethyl mercury as a cause of autistic disorder.

In the WM and JK reports, Dr. Mumper cites the Stajich, Lopez, et al. (2000)<sup>6</sup> study stating that in one of a number of vaccinated pre-term infants, elevation of blood mercury exceeded the threshold used by the CDC to define risk for mercury intoxication. The CDC definition of mercury intoxication is appropriately conservative. It is intended to be the marker for designation of a population at risk for subtle toxicities, and not the level associated with severe neurological dysfunction. It is intended to be far lower than any as yet demonstrated level proven to produce toxicity. The single infant noted in the Stajich study was a small premature infant, and no such elevation was found in that study in full-term infants. In any event, infantile mercury intoxication produces a known neurological and pathological syndrome that does not resemble autistic disorder, and Dr. Mumper fails entirely to complete the connection between mercury and the development of autistic syndrome.

### **3. It has not been established that autism rates are truly "rising."**

Dr. Mumper's allegation of an "autism epidemic" has not been established; it is at least as valid to conclude that advances in recognition account for increased diagnosis. Many authorities believe that the increase in prevalence of diagnosis is the result of far more accurate and careful labeling that children currently receive for developmental syndromes. There is abundant evidence that disorders such as autism were mislabeled as static encephalopathy or mental retardation, even within our own practices. The same is

---

<sup>5</sup>Stern AH. A revised probabilistic estimate of the maternal methyl mercury intake dose corresponding to a measured cord blood mercury concentration. *Environ Health Perspect.* 2005 Feb;113(2):155-63.

<sup>6</sup>Stajich GV, Lopez GP, Harry SW, Sexson WR. Iatrogenic exposure to mercury after hepatitis B vaccination in preterm infants. *J Pediatr.* 2000 May;136(5):679-81.

true of many syndromes that we now accurately label but did not do so twenty or thirty years ago, such as Williams syndrome, Rett syndrome, and other syndromes with autistic features. In my experience, it remains very common to apply the diagnosis of autism for the first time to children who are followed with other diagnoses.

#### **4. Credible, peer-reviewed literature does not support a link between gastrointestinal disease and autism.**

Goodwin et al., 1971<sup>7</sup> observed that children with autism manifest symptoms suggestive of malabsorption. The idea that this is a frequent problem in autistic children was perhaps skewed by the fact that a number of these studies were carried out in gastroenterology clinics and their populations. Survey studies (e.g. Lightdale et al, 2001)<sup>8</sup> found that half of the children studied with autism were reported by their parents to have had frequent diarrhea or loose stools. A careful epidemiologic study by Fombonne and Chakrabarti,<sup>9</sup> however, identified gastrointestinal problems in only 19% of their identified cadre of children. The studies of Kuddo and Nelson (2003)<sup>10</sup>, Peltola et al. (1998)<sup>11</sup>, and others have considerably discredited the notion that there is a significant association of gastrointestinal disturbance with autism, including data that have refuted an association between autism and gastrointestinal immune dysregulation (DeFelice et al., 2003)<sup>12</sup>.

---

<sup>7</sup>Goodwin MS, Cowen MA, Goodwin TC. Malabsorption and cerebral dysfunction: a multivariate and comparative study of autistic children. *J Autism Child Schizophr.* 1971 Jan-Mar;1(1):48-62.

<sup>8</sup>Lightdale JR, Hayer C, Duer A, Lind-White C, Jenkins S, Siegel B, Elliott GR, Heyman MB. Effects of intravenous secretin on language and behavior of children with autism and gastrointestinal symptoms: a single-blinded, open-label pilot study. *Pediatrics.* 2001 Nov;108(5):E90.

<sup>9</sup>Fombonne E, Chakrabarti S. No evidence for a new variant of measles-mumps-rubella-induced autism. *Pediatrics.* 2001 Oct;108(4):E58.

<sup>10</sup>Kuddo T, Nelson KB. How common are gastrointestinal disorders in children with autism? *Curr Opin Pediatr.* 2003 Jun;15(3):339-43.

<sup>11</sup>Peltola H, Patja A, Leinikki P, Valle M, Davidkin I, Paunio M. No evidence for measles, mumps, and rubella vaccine-associated inflammatory bowel disease or autism in a 14-year prospective study. *Lancet.* 1998 May 2;351(9112):1327-8.

<sup>12</sup>DeFelice ML, Ruchelli ED, Markowitz JE, Strogatz M, Reddy KP, Kadivar K, Mulberg AE, Brown KA. Intestinal cytokines in children with pervasive developmental disorders. *Am J Gastroenterol.* 2003 Aug;98(8):1777-82.

Regarding the so-called “intestinal dysbiosis” to which Dr. Mumper refers, it must first be stated that this is another term and theoretical concept that remains far outside the realm of conventional medicine and medical science. The roots of this alleged “disorder” arose in the late 19<sup>th</sup> Century and have been renewed in various forms. The current iteration is known as “the leaky gut.” Proponents of this theory allege that the intestinal flora are altered in such a way that a combination of inflammation, autoimmunity, malabsorption, and interference with non-gut metabolic pathways produce various diseases. Attempts to demonstrate any pathological correlate to this supposed condition have been unsuccessful, and the concept has not been accepted in the general medical community. Evidence was advanced to support this concept with regard to autism upon the basis of work performed in England some years ago.<sup>13</sup> It has subsequently been demonstrated that the results of this work were misrepresented, the study was redacted,<sup>14</sup> and it has further been demonstrated that the authors of those publications benefitted financially from carrying out and publishing this work in ways that have widely been regarded as highly unethical.

**5. The laboratories used in each child’s case produce unreliable results.**

Elevated mercury levels in children with autism are not documented by laboratories certified with regard to methodology, reproducibility, and integrity of results. The only laboratories to report elevated mercury levels in autistic children are those that are not willing to subject themselves to the scrutiny of agencies that certify the quality of results. Mercury level elevations in children may be found by established and bonded laboratories, but these children do not have autism.

The laboratories that have done the majority of testing on JK, WM, and [REDACTED] have produced astonishing variability in results. The ranges of concentrations in the results differ markedly from what might be termed standard laboratories of university hospitals. We have limited opportunity to make comparisons with the laboratory results obtained from such laboratories as Great Smokies Diagnostic Laboratory or Doctors’ Data, as the tendency has been for these laboratories to be sought out by a particular cadre of physicians whose views of autism fall outside that of the general medical community.

---

<sup>13</sup>Wakefield AJ, Murch SH, Anthony A, Linnell J, Casson DM, Malik M, Berelowitz M, Dhillon AP, Thomson MA, Harvey P, Valentine A, Davies SE, Walker-Smith JA. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet*. 1998 Feb 28;351(9103):637-41.

<sup>14</sup>Murch SH, Anthony A, Casson DH, Malik M, Berelowitz M, Dhillon AP, Thomson MA, Valentine A, Davies SE, Walker-Smith JA. Retraction of an interpretation. *Lancet*. 2004 Mar 6;363(9411):750.

### **Jordan King (hereinafter "JK")**

With the possible exception of the febrile "flu-like illness" that Mrs. King experienced during her fourth month of pregnancy (JK Exh. 8 at 3), JK's course during the first year of life was unremarkable, as is the case for many individuals who develop autistic disorder. Although Dr. Mumper's report states that the onset of regression was at 15-20 months (JK Exh. 13 at 2), JK's father reported in his son's Child Development/Child Psychiatry initial evaluation that he stopped talking at about one year of age. JK Exh. 7 at 8. Although Dr. Mumper's report states that JK's developmental regression is "Clearly documented" as having emerged "between 15-20 months," (JK Exh. 13 at 2) the contemporary records do not so clearly document the onset of regression.

Dr. Mumper's assertion that JK showed "impairment or suboptimal functioning of biologic mechanisms designed to rid [his] body of heavy metals" (Id.) is not supported by the medical records. First, the "biological mechanisms" apparently referred to rest on now thoroughly discredited research, and include a collection of theories that fall well outside the mainstream of medicine and science. Indeed, even if one were to credit the laboratory evidence in this case, the evidence does not confirm the presence of ethyl mercury in toxic concentrations. The laboratory results obtained from Doctor's Data when JK was 3 years of age reflect "above average" concentrations of many heavy metals in his hair, including mercury, and especially antimony and arsenic (specimen obtained 3/29/2000) (JK Exh. 1 at 46). Yet levels of mercury, arsenic, and lead obtained on 4/27/00, done by what appears to be some type of Medical Laboratories in Spokane, Washington, showed levels that were not only normal, but were quite low or undetectable (JK Exh. 12 at 1). Finally, I would reiterate that the "laboratory evidence" available in this case does not in any way confirm the presence of ethyl mercury in toxic concentrations. Any conclusion to that effect must be derived from appropriately supervised and certified laboratories, and there is no such reliable information in the records.

If one were to consider the Doctor's Data results, fecal mercury from a specimen JK provided 5/2/2000 showed mercury concentrations to be greater than the 95<sup>th</sup> percentile for their normative date. JK Exh. 1 at 36. That result would confirm that one of the most important routes for mercury excretion (i.e., fecal matter) is, by Doctor's Data's own standards, intact in JK.

In looking through the series of tests obtained over a long interval, and speaking as a physician, I find it very hard to understand the elevated concentrations of so many different, potentially toxic metals in JK's hair and feces, and their wide variations in concentration over time. This variation makes it difficult for me to accept the view that urine results from Doctor's Data confirm increased excretion of mercury after attempts to "improve detoxification," as stated in Dr. Mumper's report. JK Exh. 13 at 2. I would have preferred confirmation in another laboratory.

In the section of her report entitled "Clinical Evidence," Dr. Mumper points to a number of other environmental exposures that she alleges may have resulted in "synergistic toxicities." JK Exh. 13 at 4. The statements in this section are speculative and not supported by the literature. The mention of tuna (Id.) is another unproven point and uninformative in assessing the burden of mercury to which this child, who in fact had a normal mercury level (JK Exh. 12 at 1), was exposed. Even had JK been exposed to considerable amounts of mercury, the toxic effects of mercury are well-recognized and *do not* produce autistic disorder. Further, pica is usually regarded as a risk factor for autism, and not, as Dr. Mumper asserts, "a known symptom of heavy metal exposure" (JK Exh. 13 at 4). There is some evidence that pica may be provoked by abnormally low metal concentrations (at least insofar as iron is concerned) and improves with iron supplementation.

JK's records do not demonstrate the associated findings of severe mercury toxicity, such as the presumed catecholamine elevation that increases heart-rate, hypertension, flushing, and produces profound lethargy. The medical records do not document sustained excessive daytime or nighttime sweating or excess tearing, so far as I can determine. JK Exh. 13 at 4. Where such symptoms are observed in the literature, the concentrations of mercury are related to exposure to much larger amounts of mercury than are possible to have occurred in this child. The cases cited in the literature concern very high concentrations of mercury from ingested substances, pastes, or exposure to mercury from broken barometers or thermometers. In all such reported cases that I can find, blood mercury levels were markedly elevated, while this young boy's mercury level was in the low range of normal.

The section of Dr. Mumper's report regarding laboratory data, fails to address whether and how mercury causes autistic disorder. JK Exh. 13 at 5. As noted repeatedly, autistic disorder is not among the known effects of mercury intoxication, despite the other and quite severe toxicities this substance may exert when present at sufficiently high concentration in the body.

The manner in which amino acid analysis has been employed by one treating physician, John Green, as reflected in the records, is not in keeping with the standard practices that employ such assays. JK Exhs. 3 at 12-17; 1 at 12-13. It can be stated, in fact, that based upon the records, JK has no evidence of a known amino acid disorder, and shows the usual small variations with no distinct pattern of abnormality that may result from dietary or other environmental variables.

The term "impaired xenobiotic detoxification" (JK Exh. 13 at 5) is not used in any context that is intelligible to me after nearly thirty years of experience in the evaluation of children with neurologic diseases, including those with autism, and aminoacidopathies.

The data concerning the presumed effects on mercury and tin from chelation, as demonstrated by the results provided by Doctors' Data, raises more questions than they

answer. The test reports indicate astonishing levels of various metals alleged to be present in JK's urine and feces and their equally astonishing variation over time. *See, eg.,* JK Exhs. 1 at 35, 36, 42, 43, 55, 56. It exceeds my understanding of biochemical kinetics to allege that such large quantities of excreted mercury could have been produced upon the basis of the tiny amounts contained in JK's vaccines. It further astonishes me to think that so many different, potentially toxic metals could have been found in this child. Tin intoxication, implied in Dr. Mumper's report, is a rare disorder indeed, chiefly experienced in industrial settings. It is particularly rare in children, not only because of the limited access to tin, but because the chief route whereby children might be exposed (i.e. orally) is unlikely to produce toxicity, due to the repellant flavor of tin, and the fact that it is poorly absorbed from the gastrointestinal tract. The combination of such results, as already noted, makes one quite suspicious as to the correctness of the laboratory determinations.

With regard to Dr. Mumper's assertion that JK showed evidence of "intestinal dysbiosis" (JK Exh. 13 at 5), there is no reliable evidence that this process occurs; that it in some fashion impairs the excretion of heavy metals; or that it impairs immune function. There is no evidence in the medical records that this child's gut has manifested such a proposed pathological state or even that his gut flora (bacteria) are particularly remarkable. Interpretation of various fibers and other contents of stool as evidence of pathology is particularly far-fetched as all stool contains such undigested elements.

Dr. Mumper relies upon indirect evidence and inference to suggest the presence of pancreatic insufficiency (JK Exh. 13 at 5), such as fatty "appearance" of stools and the already mentioned persistence of fibrous materials in stool. So far as I can determine, there is no laboratory demonstration of insufficiency of pancreatic enzymes or other assays to implicate pancreatic dysfunction. This allegation of pancreatic involvement has been a persistent element of the aforementioned "leaky gut" hypothesis and remains unproven.

Dr. Mumper alleges "clinical evidence of damage compatible with damage from mercury." JK Exh. 13 at 5. There is no reliable evidence upon which this comment can be based; the concept itself is nebulous, and, as noted, there is no reliable evidence upon which to implicate abnormality of intestinal flora. There is no reliable evidence that the tiny amounts of mercury in vaccines are capable of producing intolerance of gluten or casein. Further, the clinical records do not appear to document that "diarrhea . . . resolved dramatically when taken off gluten and casein." JK Exh. 13 at 5. It cannot be known whether any such improvement may have occurred because of reduction of challenges to digestion related to the very common problem of alterations in the intestinal brush border due to diarrhea. It is clearly true that despite this allegedly effective intervention and other various interventions, JK's gut issues persisted over a long interval. As previously mentioned, it is at least possible that the diarrhea manifested here was an example of what is sometimes encountered in children with autistic disorder and

in otherwise normal children: stool retention with acquired megacolon and overflow diarrhea.

Dr. Mumper discusses observations made by Dr. John Greene. JK Exh. 13 at 6. Once again, however, she fails to provide a scientific basis and employs novel conceptions of disease that fall far outside the bounds of generally accepted medicine and medical science. Moreover, JK's records do not appear to detail a strong history of improvements either in gut or neurological function. Indeed, it appears from the record that the course followed by JK is typical for autistic disorder. We do not as yet understand why it is that some children with autistic disorder (or more commonly autistic spectrum disorders) may in fact improve rather dramatically in the wake of certain interventions. This is not what we see, unfortunately, in the records available for JK.

The first point in the section entitled "Analysis of Jordan's clinical and laboratory evidence with regard to the medical literature," (JK Exh. 13 at 6), cites the work of Grandjean and Jorgenson, well known for studies of the effects of considerable exposures of children to methyl mercury (due to pilot whale ingestion) in the Faroe Islands. These studies have demonstrated that prenatal exposure to methyl mercury may, in some children, affect attention, language, verbal memory, spatial function, and motor speed. They have provided evidence of possible brainstem dysfunction after such exposure. These studies involve large concentrations of a known neurotoxin – methyl mercury – rather than ethyl mercury. Although the studies describe toxic effects, they do not demonstrate a link between mercury toxicity and autistic disorder. These observations are not pertinent to tiny amounts of ethyl mercury exposure due to vaccination.

Reference to the work of James, Cutler, and others<sup>15</sup> concerns evaluations of possible mechanisms of autism upon the basis of indirect measurements of what it is proposed may be happening at the cellular level, and correction of these indirect values with dietary supplementation. So far as I am aware, it remains to be proven that this intervention improves function in children with autistic disorder. It further remains to be proven that this is evidence of what is going on at the cellular level.

Dr. Mumper's supposition that there may be differences in vulnerability (JK Exh. 13 at 8) may be true, but such differences do not address the lack of evidence that thimerosal causes autistic syndrome. Thus, the vulnerability idea is essentially putting

---

<sup>15</sup>James SJ, Cutler P, Melnyk S, Jernigan S, Janak L, Gaylor DW, Neubrandner JA. Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism. *Am J Clin Nutr.* 2004 Dec;80(6):1611-7.

*See also* James SJ, Melnyk S, Jernigan S, Cleves MA, Halsted CH, Wong DH, Cutler P, Bock K, Boris M, Bradstreet JJ, Baker SM, Gaylor DW. Metabolic endophenotype and related genotypes are associated with oxidative stress in children with autism. *Am J Med Genet B Neuropsychiatr Genet.* 2006 Dec 5;141(8):947-56.

the cart before the horse. The final point in this section addresses the issue of the generation of antibodies that may prove toxic to central nervous system cells perhaps pertinent to autistic disorder. Prior studies that have pursued this course of investigation remain quite inconclusive, especially where the same antibodies are often found in first degree relatives without autism. At any rate, one of the best known and most meticulously performed types of investigation for such antibodies was performed in this case (in the Connolly laboratory in St. Louis) and was negative.

I find no evidence in JK's medical records, or in the credible, scientific literature, to support the speculative theory that JK's autism was caused by thimerosal in vaccines.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

The clinical and pathological features of neurological injury due to methyl mercury toxicity characteristically include encephalopathy and not the peculiar intellectual disturbances of autism. They also differ fundamentally from the pathology of autism in brain local, microstructural disturbance, and involvement not only of the central but also the peripheral nervous system. This is neither mentioned nor accounted for by those who propose that ethyl mercury exposure causes autism. It is also important to note that the observed pathological features in autistic patients, on the one hand, and those in individuals suffering from methyl mercury toxicity, on the other hand, make biological sense with reference to the clinical aspects of these two quite different disorders. The fine structure of autistic disorder seen on pathology provides insight into the intellectual peculiarities of that disorder. The pathology of mercury intoxication provides a sensible explanation for the encephalopathy and for the motor disturbances observed in mercury intoxication, both quite different from the abnormalities of autism.

Were there some link between methyl mercury and ethyl mercury toxicities, one would then be required to explain why there is no epidemiological support for this association, and why there is such a major discrepancy between the relative toxicity of these two compounds. The question as to how minute quantities of ethyl mercury might prove so much more toxic than the known neurotoxin methyl mercury has required the elaboration of a series of unproven hypotheses concerning conditions that render the substance more toxic to a tiny fraction of those who have received thimerosal containing vaccines. These include the "perfect storm" of 1) idiosyncratic incapacity to excrete ethyl mercury; 2) idiosyncratic inflammatory changes in metabolism within the gut; and 3) idiosyncratic failure of the immune system to prevent persistent viral infection in non-immunologically privileged areas of the body, areas heretofore not known to be vulnerable to such persistent infection.

In support of these elements of the thimerosal hypothesis, no experimental model has been produced, and no experimental neuropathology has been advanced. Instead, the novel "perfect storm" deficiencies alleged to be present in a tiny number of "vulnerable" children within the vast context of children who manifest no toxicity from thimerosal containing vaccines are "documented" by a series of indirect tests performed in a very small number of laboratories that are preferentially used by those who share the belief

that certain children are vulnerable to thimerosal-related neurotoxicity. In contrast, the test results obtained by credible laboratories at universities show quite different normative data, as well as results that differ substantially in other ways—not the least of which is the failure to demonstrate “toxic levels” of mercury, lead, and many other compounds. It is not only thimerosal that appears to be implicated as a toxic compound in the tests obtained from the former laboratories. Indeed, the results of tests on all three children allege toxic levels of a broad collection of metals and other substances in addition to mercury. These include substances chiefly known to produce toxicity only in individuals with a peculiar sustained and intense exposure to industrial and other such substances.

There is as yet no convincing evidence to support Dr. Mumper’s opinion that coexisting antibiotic administration at the time of immunization would have “increased vulnerability to the toxic effects of thimerosal...” Further, the records provide insufficient evidence to support the statement in Dr. Mumper’s report that the very exotic and poorly studied treatments provided to resulted in clinical improvement. The remarkable array of these treatments primarily includes substances of unknown potential to produce either benefit or harm when viewed from the vantage point of the general medical community. Few, if any, of these treatments have any proven efficacy with regard to improving “methylation biochemistry, cellular redox status, and detoxification systems...” Most of the various substances employed as “treatments” have a long history of use by individuals who subscribe to unproven notions about the mechanisms of human disease. The evidence of improvement in the clinical notes is provided without the precision or quantification that a neurologist or developmental pediatrician is accustomed to employ. Few, if any, of these substances have been submitted to the blinded controlled trials that are the essence of modern medicine. Those that have been submitted to controlled trials have demonstrated no value in the treatment of autism.

Dr. Mumper’s reference to a “thiol profile” is representative of the manner in which data are readily employed to prove a point for which such data have as yet to assume any proven value. Cysteine, methionine, and glutathione values in serum may indeed reflect certain aspects of oxidative stress in the tissues and have recently been employed in studies of human lipid metabolism and risk for heart disease in adults (Giral et al., 2008)<sup>16</sup>. The use of such data only indirectly reflects metabolism in the tissues of the body, and abnormal values may be produced by a wide variety of circumstances. To my knowledge, there are no reliable normative data for the utilization

---

<sup>16</sup>Giral P, Jacob N, Dourmap C, Hansel B, Carrié A, Bruckert E, Girerd X, Chapman MJ. Elevated gamma-glutamyltransferase activity and perturbed thiol profile are associated with features of metabolic syndrome. *Arterioscler Thromb Vasc Biol.* 2008 Mar;28(3):587-93.

of such measurements, except in the setting of known metabolic diseases of children, wherein quite striking abnormalities are required for diagnosis.

The concentrations of these thiol intermediates have recently been used to detect the effects of environmental toxins on fish, but to do so it has been necessary to study tissue samples from fish (Parvez and Raissuddin, 2006)<sup>17</sup>. Moreover, doubts have been raised about the concept that even tissue thiol values are a decisive determinant of total antioxidant capacity of the tissues themselves (Balcerczyk et al., 2003)<sup>18</sup>.

The final point in this section notes porphyrin changes viewed by “the lab” as “moderate mercury toxic effect.” “The lab” in this instance, Laboratoire Philippe Auguste [REDACTED], is one of the small collection of proprietary laboratories that employ measurements, normative values, and interpretations that lie far outside that of credible, university-based laboratories. The concepts here have been borrowed from lead intoxication and perhaps, to some extent, from methyl mercury intoxication. Once again, individuals exposed to these toxic metals in quantities sufficient to produce neurologic injury do not manifest the findings of autistic syndrome.

[REDACTED]

The portrayal of [REDACTED] “clinical picture” as being “consistent with classic descriptions of mercury intoxication” ([REDACTED]) is simply false. No capable neurologist could mistake mercury intoxication for autism. [REDACTED] the discoloration associated with chronic mercury intoxication involves a pink color of the nose, cheeks, and fingers, and is a minor feature of the syndrome of mercury intoxication. [REDACTED]

[REDACTED] Despite the assertions of [REDACTED], there is no reliable documentation for “chronic inflammatory neuropathy.” Such a conclusion requires electromyographic testing. The possible causes of hypotonia, if present [REDACTED] are many, and chronic inflammatory neuropathy is among the least likely to be found. Moreover,

---

<sup>17</sup>Parvez S, Raisuddin S. Effects of paraquat on the freshwater fish *Channa punctata* (Bloch): non-enzymatic antioxidants as biomarkers of exposure. *Arch Environ Contam Toxicol.* 2006 Apr;50(3):392-7.

<sup>18</sup>Balcerczyk A, Grzelak A, Janaszewska A, Jakubowski W, Koziol S, Marszalek M, Rychlik B, Soszynski M, Bilinski T, Bartosz G. Thiols as major determinants of the total antioxidant capacity. *Biofactors.* 2003;17(1-4):75-82.

the neuropathy of mercury intoxication is a toxic axonal degeneration and *not* a form of “chronic inflammatory neuropathy,” as opined by Dr. Mumper. Nor is that form of neuropathy at all likely to be responsive to the “nutritional and medical interventions” given to [REDACTED]

The last section on page five of Dr. Mumper’s report (“Clinical evidence of improvement with medical treatments...,” [REDACTED]) repeats many of the unproven assumptions already discussed and includes the putative benefits of methylcobalamin injections. That form of treatment has known benefits for conditions such as combined systems degeneration (CSD), which is a disease of older adults that bears not the slightest similarity to autism, either clinically or pathologically. Injections have been offered for a bewildering variety of diseases, real or imagined, without benefit and at considerable cost to worried patients. There is no role for treatment with that compound in the established forms of mercury intoxication. Advocacy for this form of treatment may be based upon limited evidence suggesting that methyl mercury may interfere with the transport of cobalamin into the central nervous system. However, the clinical features of mercury toxicity are not those of methylcobalamin deficiency, nor is the pathology that of CSD.

Dr. Mumper’s reference to chelation [REDACTED] raises the important question as to how very tiny quantities of ethyl mercury from vaccines produced, what Dr. Mumper terms, the “extreme excretion of mercury” years after these tiny quantities are alleged to have become resident in [REDACTED] central nervous system. It appears pharmacologically *impossible* to have produced such an “extreme” outpouring of chelated mercury in this child upon the basis of that tiny quantity of ethyl mercury, even were the other highly questionable aspects of the hypothesis of sequestration of mercury true. This is particularly true since the chelation produced by DMSA is unlikely to exert effects within the central nervous system, especially within brain tissue. DMSA crosses the blood brain barrier poorly, if at all (doing so only to a small degree even in rats-- animals with a comparatively inefficient blood brain barrier). Moreover, DMSA, even were it able to enter the nervous system, is unlikely to penetrate the brain, a very fatty tissue. This is because DMSA is water soluble, and water and fat do not mix. Thus, even were it true that persistent mercury in the brain results in toxicity, DMSA would be a markedly inefficient way of removing that mercury. The inefficiency of the remedy would be even greater if the additional, unproven theory proposed by Dr. Mumper (toxicity to myelin) were true, for myelin is one of the most fatty tissues (in essence pure fat) of the brain (which is about 90% fat).

The first full section (entitled “Laboratory evidence of immune dysregulation, endocrine disruption and autoimmunity,” [REDACTED]) contains questionable assertions concerning serum anti-myelin antibodies. First, anti-myelin antibody testing was developed as a possible method of evaluating and following multiple sclerosis, an autoimmune condition that is well-known to involve primarily inflammation of myelin. This approach has long since been discarded because the test proved non-specific and prone to false-positive and false-negative results. Little clinical usefulness became

attached to these studies. Presumably, when Dr. Mumper says “CNS myelin IgG titers” and “CNS myelin IgA titers,” she means “antimyelin IgG titers (CNS myelin)” and “antimyelin IgA titers (CNS myelin).” These types of studies have been employed in highly specialized laboratories concerned with the pathogenesis of multiple sclerosis and have no known relevance to mercury poisoning. In fact, such studies are no longer routinely employed for the diagnosis and management of multiple sclerosis.

Indeed, recent evidence has shown that positive serum anti-myelin antibodies are unreliable diagnostic tests when employed for their original purpose, i.e., predicting the likelihood that an individual has multiple sclerosis (Kuhle et al., 2007).<sup>19</sup> Thus, these studies are of little or no value for their original purpose, and are certainly of no value in trying to establish the unproven hypotheses that: 1) myelin damage occurs in autism and 2) mercury has produced white matter injury. It is also incorrect for Dr. Mumper to conclude that the positive results of these antibody studies on [REDACTED] “[are] compatible with a toxic encephalopathy” ([REDACTED]). These studies provide no information whatsoever about toxicity. Nor do they indicate an encephalopathy, a term that refers to dysfunction not of myelin (brain *white* matter), but of *gray* matter. This is evidence of imprecision and inaccuracy that is troublingly persistent throughout Dr. Mumper’s three reports.

It is unclear whether the “[p]ositive myelin basic protein antibodies,” [REDACTED] [REDACTED] are directed against the central nervous system or the peripheral nervous system. Only if directed against peripheral nerve myelin basic protein would these antibodies be indicative of an autoimmune neuropathy. Here again, however, the laboratory track record and certification in the use of these tests is an essential determinant as to whether such results are to be relied on at all. Moreover, myelin basic protein antibody tests are quite subject to false positive and false negative results, and they are not the manner in which autoimmune neuropathy is diagnosed. No reputable neurologist would make such a diagnosis without first providing electrophysiological evidence, and the pathogenesis of that neuropathy would not be established without nerve biopsy.

Dr. Mumper’s comments concerning anti-thyroid antibodies [REDACTED] do not establish clinically significant inflammation in [REDACTED] thyroid gland. These types of antibodies are positive in a number of other inflammatory conditions. However, even if they were indicative of thyroid pathology, their presence certainly does not establish the unproven hypothesis that mercury has produced this change. Nor do they establish the other unproven hypothesis that thyroid dysfunction somehow potentiates mercury toxicity. Modestly low IgG levels in serum are essentially meaningless, especially within

---

<sup>19</sup>Kuhle J, Pohl C, Mehling M, Edan G, Freedman MS, Hartung HP, Polman CH, Miller DH, Montalban X, Barkhof F, Bauer L, Dahms S, Lindberg R, Kappos L, Sandbrink R. Lack of association between antimyelin antibodies and progression to multiple sclerosis.

the context of the vague arguments and unsubstantiated statements made in Dr. Mumper's report.

Dr. Mumper's reference to Grandjean and Jørgensen (██████████) is both disingenuous and highly misleading. The epidemiological studies of this group do not in any way support Dr. Mumper's assertion, on page six of her report, that "injected thimerosal in bolus doses is associated with more risk of toxicity than a chronic low-dose daily intake of oral mercury" (*Id.*). Contrary to Dr. Mumper's assertion, the studies of this group do not provide evidence of a risk of autism from mercury.<sup>20</sup> The Faroe Island studies<sup>21</sup> did not consider "low dose" exposure, rather they considered levels of mercury exposure far greater than the levels of thimerosal received in vaccines. Grandjean's studies were not designed to provide comparative evidence of toxicity of oral versus injected mercury.

The next point in this section provides bits and pieces of observations concerning metabolism of thimerosal and possible toxicity in concentrations of unknown relevance to immunization-related doses. It does not establish a thread of evidence that proves anything about the alleged role of thimerosal in the risk of developing autism.

Dr. Mumper's statement that "Improvements argue for environmental components" (██████████) is, once again, pure speculation. Improvement in the function of individuals with autistic disorder, or for that matter autistic spectrum disorders, is a highly unreliable way to validate complex biochemical and immunological hypotheses. Virtually all individuals who appropriately bear these diagnostic labels show improvement, and that improvement is at times strikingly rapid. This improvement, and the variable profiles of improvement, remain poorly understood and cannot credibly be used to show that thimerosal is a contributing factor to the development of autism.

Finally, the section entitled "Absence of alternative explanations for ██████████ developmental regression," (██████████) begs the question as to why genetic and infectious, or other explanations, for autism are found in only a minority of cases. Indeed, the minority of cases where such putative causes are identified are typically cases of symptomatic autism that only superficially resemble autistic disorder. ██████████  
██████████

---

<sup>20</sup>Grandjean P, Jørgensen PJ. Measuring mercury concentration. *Epidemiology*. 2005 Jan;16(1):133.

<sup>21</sup>Grandjean P, Weihe P, Jørgensen PJ, Clarkson T, Cernichiari E, Viderø T. Impact of maternal seafood diet on fetal exposure to mercury, selenium, and lead. *Arch Environ Health*. 1992 May-Jun;47(3):185-95.

See also Debes F, Budtz-Jørgensen E, Weihe P, White RF, Grandjean P. Impact of prenatal methylmercury exposure on neurobehavioral function at age 14 years. *Neurotoxicol Teratol*. 2006 Sep-Oct;28(5):536-47.

[REDACTED] The important fact about autistic disorder is the fact that there is such a strong clinical resemblance among individuals who bear that diagnosis, similarities that set individuals with autistic disorder apart from individuals with classical Rett syndrome. Girls with classical Rett syndrome share unique and diagnostic clinical features that lead to a diagnosis after short intervals of observation, the similarities speaking to the likelihood of a genetic basis for the condition.

[REDACTED]

[REDACTED]

Conclusion

Based on my education, training, personal experience as a clinician, and thorough review of the literature, I cannot endorse the view that exposure to thimerosal in vaccines has produced autism in any of these children.

March 12, 2008

Date



Robert S. Rust, M.D.