

Respondent's Exhibit X



DEPARTMENT OF MEDICINE
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April 23, 2007

Vincent Matanoski
Assistant Director
U.S. Department of Justice
Civil Division, Torts Branch
P.O. Box 146, Ben Franklin Station
Washington, D.C. 20044-0146

Re: Dr. Arthur Krigsman's Medical Report in the Autism Omnibus/Cedillo case

Dear Mr. Matanoski:

At your request I have reviewed the medical report and accompanying references provided by Dr. Arthur Krigsman pertaining to Michelle Cedillo. I am pleased to provide a rebuttal to his assertions that the patient has inflammatory bowel disease caused by measles virus.

According to Dr. Krigsman's report, the patient developed symptoms consistent with a viral syndrome approximately one-week after receiving the MMR vaccine ("high fever for 4 days accompanied by vomiting, irritability, and lethargy"). She then became afebrile and, one week later, developed "fever and a rash" that were treated by a pediatrician with an antibiotic "for an unspecified illness." He reports that "the fever resolved after a few more days but her vomiting and irritability worsened...coupled with the onset of diarrhea....alternating with periods of being unable to pass stool despite much effort and straining." Further, he states that the "straining was often accompanied by panting sweating and vomiting with the eventual passage of loose, mucoid, yellow, foul smelling stool...(and) her abdomen became distended."

I should, initially, point out the the above are NOT symptoms of inflammatory bowel disease (IBD) or enterocolitis, but instead of an "irritable bowel" and what will be shown later to be gastroesophageal reflux. Indeed, Dr. Krigsman describes a gluten free and casein free diet being prescribed for "worsening diarrhea and constipation" a syndrome that is NOT associated with enterocolitis or IBD.

Dr. Kringsman described her first formal gastrointestinal evaluation in 2000 (five years after MMR exposure) for “a history of vomiting, gastroesophageal reflux type symptoms ...along with diarrheal mucoid stools from 2 to 7 times per day.” At gastroscopy she had esophagitis with a mild eosinophilic infiltrate (*neither enterocolitis nor IBD*) and the stomach “demonstrated a patchy but heavy eosinophilic infiltrate (*neither enterocolitis nor IBD*) and the esophagitis was treated successfully with acid reducing therapy (*demonstrating the typical response in gastroesophageal reflux, not IBD*).

Due to persisting “diarrhea, abdominal pain, irritability, and worsening anorexia’ an upper a lower endoscopy were performed two years later in January, 2002, demonstrating “lymphonodularity of the distal esophagus, duodenal bulb, terminal ileum and sigmoid colon.” He reports that a “diagnosis of colitis was made” and the patient was started on Pentasa. *Of note, these findings are all NORMAL in children with no pathological significance and I cannot find rationale for a diagnosis of “colitis” without description of inflammation in the colon that would form a basis for “colitis”.*

Dr. Kringsman first evaluated the patient in 2003 and a colonoscopy revealed “an aphthous ulcer...in the sigmoid colon” but biopsies “revealed no significant inflammatory pathology” although “Serology demonstrated an elevated anti-ompC” and she was treated with corticosteroids that “normalized the stool”.

These findings are not sufficient to diagnose enterocolitis or IBD. Aphthous ulcers may be typical of Crohn’s disease (IBD) but are in no means SPECIFIC. They can be seen in normal individuals, after exposure to bowel preparations for colonoscopy, or related to the use of anti-inflammatory medications. The observation that the biopsies revealed “no significant inflammatory pathology” is CONTRARY, by virtue of definition, to a diagnosis of either enterocolitis or IBD.

A subsequent evaluation in 2006, again revealed “an aphthous ulcer in the transverse colon (*totally non-specific*) and lymphonodular hyperplasia of the distal colon (*normal in a child and NOT indicative of enterocolitis or IBD*). *Despite a capsule study demonstrating multiple aphthous lesions of the small bowel (normal in 15% of the population) and terminal ileal lymphonodular*

hyperplasia (normal in children) biopsies reviewed at UCLA were "unremarkable"! Hence, at a tissue level, despite non-specific lesions noted at endoscopy, there is NO EVIDENCE OF enterocolitis or IBD.

Thus, there is insufficient evidence from Dr. Kringsman's report to make a diagnosis of either (chronic) enterocolitis or IBD. While Dr. Kringsman relates the eye lesions (uveitis) and arthritis to IBD, there is no rationale for such a conclusion. There are other possible explanations including HLA-B27 associated eye and joint manifestations that are independent of a diagnosis of IBD that would respond to similar anti-inflammatory therapies including steroids and Remicade.

I have reviewed the medical literature regarding a possible association between measles virus and the MMR vaccine with inflammatory bowel disease and there is no acceptance in the medical community of such a linkage. The reports of autism-associated gastrointestinal disorders describe a wide spectrum of symptoms and findings with no specific pathophysiological syndromes. The "finding" of measles virus by RNA in tissue samples also does not; provide any specific explanation for her symptoms, define IBD or enterocolitis, or for viral enterocolitides as described by Dr. Kringsman. Viral enterocolitis are "self-limited" and do not induce chronic symptoms and the description of a "mild, diffusely patchy nonspecific lymphocytic infiltrate of the gastrointestinal mucosa" (*not described in this patient!*) "coupled with lymphonodular hyperplasia" (*again, a normal finding in children*) "is precisely the inflammatory pattern seen in viral infections of the bowel." *Indeed, since these findings are "non-specific" and are "normal" in children and adults, the association with viral syndromes is neither an acceptable nor substantiated conclusion.* Further, the composite medical literature does not support an association between measles virus, nor the MMR vaccine, with the development of IBD.

Sincerely,



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