UNITED STATES
COURT OF FEDERAL CLAIMS

HAZLEHURST,	)	
	)	
Petitioner,	)	
	)	
v.	)	Docket No. 03-654V
	)	
SECRETARY OF HEALTH AND HUMAN SERVICES,	)	
	)	
Respondent.	)	

REVISED AND CORRECTED COPY

Pages: 555 through 699

Place: Charlotte, North Carolina

Date: October 18, 2007

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IN THE UNITED STATES COURT OF FEDERAL CLAIMS

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	)	
	)	
Respondent.	)	

Courtroom 6330
North Carolina Superior Court
832 East Fourth Street
Charlotte, North Carolina

Thursday,
October 18, 2007

The parties met, pursuant to notice of the Court, at 10:30 a.m.

BEFORE: HONORABLE PATRICIA CAMPBELL-SMITH
Special Master

APPEARANCES:

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C O N T E N T S

E X H I B I T S

PETITIONER'S EXHIBITS:	IDENTIFIED	RECEIVED	DESCRIPTION
2	578	578	Pediatric record of Yates Hazlehurst dated January 18, 2002

P R O C E E D I N G S

(10:30 a.m.)

THE COURT: We are back on the record in the matter of Hazlehurst v. Secretary of the Department of Health and Human Services, Case No. 03-654. Respondent to call your next witness, please?

MS. RICCIARDELLA: Yes. We'd like to call Dr. Christine McCusker.

THE COURT: Dr. McCusker right here. Would you like to pour yourself a cup of water, and I'll administer the oath.

DR. MCCUSKER: Thank you.

THE COURT: Would you raise your right hand please?

Whereupon,

DR. CHRISTINE MCCUSKER

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

THE COURT: To proceed.

MS. RICCIARDELLA: Thank you.

DIRECT EXAMINATION

BY MS. RICCIARDELLA:

Q Good morning, Dr. McCusker. Would you please state and spell your name for the record?

A It's Christine McCusker, and the last name

is spelled M-C-C-U-S-K-E-R.

Q And what is your profession?

A I'm a pediatric immunologist.

Q And what is your current title?

A I'm an Assistant Professor of Pediatrics and Research Director at McGill University and Montreal Children's Hospital.

Q Doctor, would you briefly describe your educational background?

A I did a bachelors in microbiology and immunology at the University of Toronto, and following that, I did a masters in molecular virology at McMaster University followed by three years of a PhD in immunology also at McMaster.

Following that I did my medical degree at McMaster University and then moved to McGill University where I did a residency in pediatrics followed by a fellowship in allergy and clinical immunology and then followed that with a two-year postdoctoral fellowship in fundamental immunology research at Meakins-Christie Laboratory at McGill.

Q And are you board certified?

A I am certified in the Royal College of Physicians and Surgeons of Canada in both pediatrics and allergy and immunology as well as the CollŠge des

M,decins due Qu,bec in Canada as well I have board certification in pediatrics in the United States.

Q Doctor, would you briefly highlight some of the honors that you have received in your career?

A During my postdoctoral fellowship I received a Salary Award from the Canadian Society of Allergy and Clinical Immunology for two years to support my work. I've also a Recherche Clinique CA -- I'm sorry, habit. A Clinician Researcher through the -- I'm going to have to say this one in French, Fonds de recherche en sant, du Qu,bec, the Foundation for Health Research in Qu,bec where they have supported me with awards twice now. They're two- to four-year awards.

Q And of what professional organizations are you a member?

A I'm a member of the Canadian Allergy and Immunology Society, the CSACI. I'm a member of the Allergy and Immunology Association of Qu,bec. I'm a member of the Royal College of Physicians and Surgeons of Canada. I think that might be about all.

Q And do you hold any teaching positions in your specialty?

A Yes. I'm Assistant Professor at McGill University, so my teaching requirements include

teaching undergraduate students basic immunology in the science microimmuno program. I also teach the medical school students, both basic and clinical allergy and immunology, and I teach graduate students and postdoctoral fellows in the graduate school at McGill.

Q Do you hold any laboratory positions?

A I'm the Clinical Director of the Clinical Immunology Laboratory at Montreal Children's Hospital.

Q And what are your research laboratory responsibilities?

A My appointment is 50 percent of clinical duties and 50 percent research duties, and I'm a Research Director at the Meakins-Christie Laboratories, where I run a fundamental research lab working on immunoregulation of the immune system through development, so in a model of infancy through adulthood.

Q What division of your time is spent between your research and your clinical work? Is it 50/50?

A Theoretically.

Q Approximately how many patients to you see per month?

A On a monthly basis to break it down it's probably in the order of 200 to 300 depending on the

month.

Q And are the majority of those patients children?

A Almost all of them are children.

Q And do you have a general pediatric practice as well?

A I work both in two different practices for general pediatrics. The first is at a private clinic where I fill in for doing what's called emergency visits or walk-ins, and the second is through the emergency room, where I act as an Emergentologist.

Q Approximately how many of those patients do you see per week?

A It varies depending on the week, but it's probably about 50 patients a week.

Q Are you an examiner for any licensing boards?

A I'm an examiner for the Royal College of Physicians and Surgeons of Canada for allergy and clinical immunology.

Q And what does that mean to be an examiner?

A Well, you're asked to or invited to participate on the examination boards. You have to be nominated by your peers in the specialty, and then you're invited to be an examiner on the boards, and

you're responsible for the development of examination

questions for the specialty as well as the oral exam component where you're examining the fellows who have completed their training and who are asking to be allowed to practice as specialists.

Q Okay. And have you published in the field of pediatric immunology?

A Yes.

Q Are those publications referenced on your CV?

A Yes, they are.

Q Are they all peer-reviewed?

A Yes, they are.

Q Are you a reviewer for any scientific journals?

A Yes, I am.

Q Which ones? Name a few.

A I've been a reviewer for the Blue Journal, which is the American Journal of Respiratory and Critical Care Medicine. I've been a reviewer for the Journal of Immunology. I've been a reviewer for the Journal of Allergy and Clinical Immunology. I've been a reviewer for Clinical and Experimental Allergy, Clinical and Experimental Immunology, the Annals of Allergy and Immunology. There might be a couple more.

Q Have you ever testified as an expert witness

in a legal case?

A Yes, I have.

Q Approximately how many times?

A This would be my fourth case.

Q And did you testify in the Cedillo case?

A Yes, I did.

Q After turning to this case, did you review Yates' Hazlehurst medical records that had been filed?

A Yes, I have.

Q And did you review the expert report of Dr. Corbier?

A Yes, I did.

Q And do you agree with Dr. Corbier that Yates has a weakened immune system or a compromised immune system?

A No, I do not.

Q Does he have a dysregulated immune system?

A I see no evidence for a dysregulated immune system.

Q Based on your review of the records, do you believe that Yates' immune system is at all abnormal?

A No, I do not.

Q In your opinion, Doctor, did the vaccinations that Yates received cause or contribute to his autism?

A No, I do not think so.

Q Would your opinion change if it was determined that Yates' developmental regression began at 12 months as the family and Dr. Corbier allege?

A No.

Q I'd like to turn specifically to the facts of this case, and before you took the stand, did I hand to you Petitioner's Exhibit 16 for the record?

A Yes, you did.

Q Okay. Before we get to that, I'd like to talk about the upper respiratory tract infections that Yates had during the first two years of his life. Do you recall seeing those notations in the record?

A Yes, I did.

Q Is this evidence to you of a weakened immune system?

A No.

Q Why not?

A As I elucidated in my report, I looked at the frequency of infections that this child experienced and found that he did not have a frequency of infection that was any more or less than his peer group. His frequency was somewhere in the order of four physician diagnosed upper respiratory tract infections and seven ear infections, five of which

were associated with documented viral illnesses.

That is entirely within keeping with a normal range of infection or a normal frequency of infection in a child of his age.

Q Could you briefly describe or explain the immune system of a child up to two years old? In a nutshell.

A Briefly?

Q I know that's your profession, but in a nutshell?

A Essentially, when a child is firstborn, obviously their immune system, although partly protected by maternal antibodies, their immune system is essentially having to learn from first principles how to fight and combat infection and to remember how these infections look like so that they can fight them again should the need arise, and so usually in the first four months, children don't have that high a frequency of infection, but as the maternal antibodies begin to wane, the infection frequency increases.

Now, in this particular child, for example, he was the third child in the family, so there would have been more circulation of viruses.

Q I believe he was the first-born child.

A Is he the first-born?

Q He's the first-born child. There are some cousins, but in the immediate family, he is the first one.

A Well, the circulation of viruses begins fairly early on in a child's life, usually between the ages of four and six months is when they start to catch their first infections. From the age of six months to the age of somewhere, and it depends on the child, threeish, two to three, a child will catch probably in the range of six to 10 infections per year. That's the average that a general pediatrician would look at as within the normal range.

Some children have a few more, some children have a few less, but that's sort of the range. In that time period, their immune system is learning, and what it's learning to do is it's learning to recognize the infections and fight them and to generate what's called immunological memory. That immunological memory allows them the next time they see the infection to fight it without apparent illness.

That doesn't mean that they don't see the viruses, they don't come into contact with the same number of viruses because obviously they do. It's just they don't manifest the illness as frequently as

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they would early on in the first two years of life, so somewhere between the ages of two and six, the frequency of infection begins to decrease significantly.

So by the time a child is sort of through the first year of school, past grade one, you see that their school absences and their frequency of infection markedly decreases, and that's because their immune system has learned, and so they're not manifesting illness quickly.

Q Now, you briefly touched on Yates' otitis media infections. Approximately how many otitis media infections do you see documented in the medical records? Approximately how many?

A I actually counted seven in the first two years of life.

Q Is that a normal amount?

A That's within the normal range.

Q Okay.

A Some children have more, some children have less.

Q Now, Yates had tubes put in his ears, correct?

A Yes.

Q If Yates' immune system were abnormal or

weakened, what would you expect would be the clinical course of future infections following the installation of tubes?

A As a general rule, you put tubes in the ears to allow the ear canals to drain freely because the eustachian tube is blocked from usually the mucus in the nose, so you put the tubes in the ears to allow the mucus and the accumulated liquid from the inner ear to drain out to the outside, and that prevents or reduces the frequency at which those kind of blocking of the nose will allow the bacteria or the virus to grow in the ear and manifest itself as an ear infection, so you put the tubes in.

You will expect to see a decrease in the frequency of infection following the installation of tubes.

Q Is that with a normal immune system?

A Yes.

Q What about if one's immune system were abnormal or weakened, and he or she had tubes put in. What would you expect the clinical course of infections to become?

A As a general rule in the patients that we follow with primary immunodeficiency, who have documented problems with their immune system, the

installation of tubes may somewhat reduce the frequency of ear infections, but does not completely eliminate it. The tubes frequently block because the amount of inflammatory mediators generated is generally much higher in those patients, so they often have trouble even with the installation of tubes.

In addition, their immune system is compromised, and it's compromised from birth, so their frequency of infection does not change. It's just the characteristics of the infection changes, and these children go on to have more sinusitis for example, and they also go on to have lower respiratory tract infections such as pneumonias, so what you see in a clinical course is you'll see a baby, who has many otitis media developing to pneumonia to sinusitis.

Q Did you see evidence of that in the medical records of this case?

A No, I did not.

Q Now, Dr. Corbier in his report states that Yates developed chronic, and I'm going to butcher the word, lympha --

A Lymphadenopathy?

Q It's easy for you to say, yes. Swollen lymph nodes, right?

A That's correct.

Q Did you see evidence of this in the medical record?

A No, I did not. There was one episode where the parents brought Yates in because they were concerned because they could feel some lymph nodes in the child's neck, but it was noted by the physician to be within normal. I'm just looking for the -- It's about nine months of age. There was one note. I don't actually have it written in my notes because it wasn't considered normal, but there was one, and it would be in the record.

Q Are swollen or palpable lymph nodes normal in young children?

A Yes.

Q Okay. Doctor, if lymph nodes are indeed swollen, is that a sign of a healthy immune system?

A It's a question of degree. Certainly, we expect that especially in the first years of life that you will have what's called palpable lymph nodes, particularly in the back of the neck or the posterior cervical chain, and that's in part a sign that the immune system is responding normally to the onslaught of infectious agents that it's seeing, and also it's in part an issue of children that actually don't have a lot of subcutaneous tissue in their neck, so you can

feel the

nodes much easier than you can in an adult.

We expect in pediatrics to palpate, touch, lymph nodes, particularly in the back of the neck, sometimes in the front and all the way down just above the clavicles here, and that's considered to be normal. It's the draining lymph nodes from the head and neck and to be able to feel them as small shotty nodes is normal.

THE COURT: For the record, the reference to mom and the lymph nodes, Petitioner's Exhibit 2, 22, and that's at about seven months.

THE WITNESS: Seven months.

THE COURT: September 5, 2000.

THE WITNESS: Thank you, and it was noted I think by the doctor to be normal. Sorry.

BY MS. RICCIARDELLA:

Q Doctor, there's also been testimony in this case that Yates' head felt constantly hot after his first birthday. It was described as possibly a low-grade fever. Does that have any clinical value to a pediatrician or pediatric immunologist?

A I would say no. In truth, children have a temperature range, and it's quite broad ranging in celsius anywhere from 36 to 38.5, and in fahrenheit, that would be up to 101.3 as core temperature, and

that's considered normal, and our normal variations are some children run sort of around 100. Some children run at the classic 98.6 and some children run at 97 and a little bit lower than your classic core body temperature, and it's within normal.

As long as it is below 101.3 or 38.5, it is not fever, and it is not abnormal. It's just normal metabolic rate and normal metabolic variance. Parents sometimes come in to me and say I brought him in because he feels hot, or I brought him in because he's sweating, or every time I put a blanket on him, he kicks it off because he's too hot, and all those things are concerns that parents will raise to you as a doctor, and you go and you measure the child's temperature core, and it's completely normal.

You evaluate the child, and there's nothing wrong with the child, so feeling hot is not significant unless it correlates with the presence of fever. Children as a general rule, if they are truly feverish, have a change in their behavior such that they tend to be more sleepy, they tend to be more quiet, they tend to be less interactive, so the parents note that usually before they note the feeling warm.

Q Now, the records also reflect that Yates had

several episodes of candida or thrush. Do you recall seeing those records?

A Yes.

Q How many documented episodes of thrush do you recall seeing?

A I counted three that were documented as a notation in the notes as seeing a thrush, and then there were two others that I found a reference to, but couldn't find the actual physician note saying what they saw, and so I qualified those as sort of possible or probable, and then there was the episode where he was treated because of the dermatitis of his thumb, which was treated "in case" in the physician note.

Q Assume for purposes of argument that there were five episodes of thrush, would that be abnormal?

A In a child, with absolutely nothing, who is five or six years old, that's abnormal. In a child, who is between the ages of zero and two, that is considered to be something that happens. I think that it's something that you would note, but you wouldn't necessarily worry about, especially in a child who such as in this case was a thumb sucker because that promotes the adherence of the candida to the oral mucosa, and as well in the case of a child who required a lot of antibiotic use.

Q What is candida or thrush?

A Candida is a yeast or a fungus. It's colonized, found in our mouths, and in most children they're found colonized with candida in the oral mucosa. It's a commensal organism. It usually is competed out by other organisms in the mouth, so you usually don't get an "infection" with it.

Q Is it normal in young children?

A Very common in young children.

Q Are developmentally delayed children more prone to candida?

A It seems that children with developmental delay have more frequency of candida, yes.

Q Why is that.

A There's several different theories on that. Most of the feeling is it has to do with the mouthing behaviors, but it's largely unknown.

Q And does the chance of developing candida increase with antibiotic use?

A Yes, it does. That's considered a risk factor.

Q Is Yates' experience with candida evidence of a systemic immunodeficiency or a compromised immune system?

A Yates' frequency of candida infection, with or without the fact that we know his immune system is

normal from the immune workup, the frequency of candida infection is there. It's not zero.

In the face of the frequent antibiotic use, you could explain it, but in and of itself that would be something that might warrant examination of the immune system to ensure that there is no underlying other cause, other than the ones that we already know, the mouthing behaviors and the frequent antibiotic use, so the answer is I guess yes and no. In the face of the immune workup that was done, the child's immune system was completely normal.

And any abnormality that you would be looking for in a child, who as recurrent thrush, which is abnormalities in the functioning of the T-cells really wasn't found.

Q In fact, that's exactly what the pediatrician questioned. You were presented today with a new record dated January 18, 2002, a pediatric record. Is that correct?

A Yes.

Q What was reflected on that record to the best of your recollection?

A The family had come in questioning the frequency of the child's infections with thrush, and the physician felt that it, while again explainable by

the extant

circumstances of the child's first two years of life was enough to warrant a further immune evaluation.

THE COURT: Pardon me. For the record, just so what we know what that record is, I'm going to designate that as Petitioner's Trial Exhibit 2.

(The document referred to was marked for identification as Petitioner's Exhibit No. 2 and was received in evidence.)

MR. WEBB: Absolutely.

BY MS. RICCIARDELLA:

Q And then immune function testing was done, correct?

A That's correct.

Q And that was tested in August 2002 by Dr. Blaiss? Is that --

A Yes, that's correct.

Q And I'm referring to Petitioner's Exhibit 16. Do you have a copy of that in front of you?

A Yes, I do.

Q I'm specifically referring to Petitioner's Exhibit 16 at 3. What do the medical records say about Yates' immunoglobulin levels?

A According to the medical records, they're

entirely within normal limits for age.

Q And what's the purpose of testing immunoglobulin levels?

A The immunoglobulin levels themselves are a fairly reasonable screen to determine whether or not there's a profound immunodeficiency. In and of itself, it's just a level, and it doesn't necessarily denote function. You can have children who have normal levels but poor function, so it is a good first step, and it denotes that his body was able to make antibodies and to maintain a level.

The more important study or results is the fact that when his immune system was asked to make an immune response so that when he received his diphtheria and tetanus vaccine, and he was asked to make a response to tetanus, he was able to do that.

Q For the record, are you referring to Petitioner's Exhibit 16 at 9?

A Let me just verify, but I believe so. It's repeated a few times during that. Yes. Essentially, when you're doing an immune evaluation of a child, you are asking two different questions: The first question is do we have the building blocks. Are the numbers of all the building blocks, that means the T-cells, the B-cells, the other cells of the immune

system and the antibody

levels, are they within a normal range? That's your first step.

Then the next question, and really for an immunologist the more important question is it doesn't matter if you have a thousand T-cells if none of them function, so what you really want to know is can we make these T-cells and B-cells talk to each other, and can we make them function to generate immunity that's longlasting?

What the tetanus antibody tells me is it's actually a very good screen because in order to make tetanus antibody, in order to have a level, you actually have to have a fairly comprehensive immune system. You have to have B-cells that are present, and the B-cells have to be able to make antibodies, but most B-cells can't make antibody by themselves.

They actually have to be told what to do, so what you really need to do is you need to have the T-cells that are there and that can recognize the tetanus in this case and tell the B-cells okay, go ahead make the antibody, so what the presence of that specific antibody tells me is that his body was able to see these antigens. They were able to recognize them as something that you should make an antibody to.

The T-cells were able to talk to the

B-cellS,

and the B-cells could do their job, so that tells me you have a very comprehensive functioning immune system from a specific or adaptive point of view.

Q What were the findings for Yates' compliment levels, and I'm referring to Petitioner's Exhibit 16 at 4?

A He had normal compliment levels and as well, they also did the compliment function that told hemolytic compliment, and again levels are interesting, and they're very helpful, and if they're abnormal, they tell us something, but normal levels in and of themselves don't necessarily tell us that the immune system is competent, but Dr. Blaiss here went the step further, and he said can I make it function? If I demand this compliment system to work, will it function, and it did completely normally.

Q What were the findings for the T and B cell numbers?

A They were entirely normal for age.

Q Doctor, did the testing of Yates' immune system in August 2002 show any evidence of immune dysfunction?

A No.

Q Or immune compromise?

A No.

Q Are you satisfied with the testing that was done by Dr. Blaiss in August of 2002?

A Yes, I am.

Q Doctor, was Yates also tested for antibodies to candida?

A Yes, he was.

Q And I'm referring to Petitioner's Exhibit 17 at 3. What were the results?

A They were negative.

Q Does that mean he did not have antibodies to candida?

A It means that he did not have an infection of candida that was invasive. Children with primary immunodeficiency, when they do have problems with candida, their candida tends not to remain in the mouths. It tends to become invasive, and so invasive candidysis is a sign of a compromised immune system. In that situation, the children will make antibodies to candida.

If it remains local, sort of just on the skin or in the oral mucosa or even in the diaper area, you do not make antibodies to candida, and there are papers that are quoted in my report that have looked at that in normal children.

Q Doctor, turning to the date of vaccination,

February 8, 2001, the medical records reflect, and there was testimony that Yates was sick that day that he received his vaccinations. Is being sick with an upper respiratory infection and a fever contraindication to vaccination?

A No. The Redbook, which is sort of the infectious disease bible that's used by many physicians does not recommend withholding a vaccine from a child because of an upper respiratory tract infection, with or without fever.

Specifically, when they look at the live viral vaccines, specifically the MMR, studies have shown that the presence of fever and upper respiratory tract infection do not compromise your ability to mount an immune response to measles, mumps or rubella under those circumstances, and so particularly for the live viral vaccines, it is not a contraindication.

If the child is considered to be severely ill, then the vaccine is withheld, but a child with a cold and an ear infection needing some antibiotics would not warrant withholding vaccine.

Q Doctor, if Yates had or has an immunodeficiency as Dr. Corbier opines, what would you expect to be his clinical course throughout the seven years of his life?

A If you have a primary immunodeficiency, it's something you're born with. The immune system will struggle to try and keep ahead of the infections, but essentially over time, the child will become sicker and sicker and sicker with recurrent infections, and that's really what we see.

While children with immunodeficiency can have ear infections in the first year of life, by the time they're two or three, they've already had one or two or three pneumonias because their immune system just cannot cope with the flood of virus and bacteria that they're being exposed to, and it gets weaker and weaker and weaker, and eventually they present and are diagnosed with primary immunodeficiency.

That's children who have more subtle immunodeficiencies. Obviously, those that have severe combined immunodeficiency, where their immune systems don't work at all, present very early on in life, usually within the first year, and those children are very sick and will die without medical intervention, so when we're talking about the more subtle immunodeficiencies, what you really find is that you have a child, who maybe in the first two years of life was sick, maybe a little bit more sick than his peers.

As time goes on, they continue to be sick.

They don't have that period where they're well, and really these children are never well.

Q Did you see any evidence of that in the medical records in this case?

A No, I did not. This child followed the normal course of few infections in the first two years of life, and a slow or a predictable reduced frequency as he aged, at least in the records that I reviewed.

Q Doctor, would an immune defect ever resolve or dissipate over time?

A A true primary immunodeficiency does not, and that would be something that has clinical relevance.

Q Is there any evidence in your experience as a pediatric immunologist that as Dr. Corbier states immune mechanisms are implicated in autism?

A No.

Q Is there any reliable medical evidence in the peer-reviewed literature that immune mechanisms are implicated in autism?

A Not that I have been able to find.

Q In your practice, have you tested the immune profiles of autistic children?

A Yes, I have.

Q Approximately how many?

A At least 100, perhaps more. It's hard to know exactly.

Q Over what time period?

A About eight years.

Q And among the approximately 100 autistic children that you have tested, how many have had a immune deficiency?

A One.

MS. RICCIARDELLA: I have no further questions.

THE COURT: Mr. Webb?

MR. WEBB: Thank you. I'm sorry for the interruption.

CROSS-EXAMINATION

BY MR. WEBB:

Q You were asked some questions about whether there was some significance to the fact Yates' grandmother reported that he seemed constantly warm during his second year of life?

A Yes.

Q Can a low-grade fever that persists for a long period of time be an evidence of chronic infection?

A I have never seen a report of that. I guess it would depend on what you would define as low-grade

fever. I would say off the top of my head no.

Q You indicated that there was a fairly broad or you're saying a variety of normal temperatures for individuals?

A Yes.

Q But if the child was in fact beyond that normal range for six months --

A Yes.

Q Would that merit some kind of evaluation?

A I suppose it would merit some kind of evaluation, except that I've never seen a case report of a child with documented fever for more than six months. I mean, during those six months, one would presume that this child had been seen by his pediatrician, and there would have been a note of it in the case history, but I failed to find a note to fever of the significant frequency of fever in the case history notes.

I'll give you an example. We've recently followed a child, who does have a primary immunodeficiency, who presented to our hospital with a history of fever for a month. Now, that child had had weight loss, that child had had significant symptomatology associated with that and did have what's called an immune activation syndrome and

macrophage activation syndrome that was clearly and easily documented by the testing that was done.

But that was after months of fever, and this child was quite sick and very close to death at the time when she presented to the hospital, so six months I think would be unbelievably unusual and would warrant a case report.

Q Would warrant some kind of immunological evaluation?

A Absolutely. Absolutely, but I would think that six months of daily fever to that extent, even "low-grade," which would be 38.5 and above core would significantly debilitate the child. It wouldn't just be a child who felt warm. It would be a child who didn't grow.

Q How about kids that develop sinusitis? Am I pronouncing that right?

A Yes.

Q Sinus infection.

A Yes.

Q Those infections persist for months, do they not?

A The mucosal thickening can persist for a long time. The bacteria can remain in the sinuses for a while, but clinical sinusitis is actually a

relatively acute event. There are two different etiologies: There's acute and chronic sinusitis. Acute sinusitis is the one that's characterized by facial pain and fever. Chronic sinusitis is the one that's characterized by chronic congestion, and it's usually in the absence of fever.

Q Usually? Does that mean that there are cases that unless you have a chronic sinusitis in which there is a fever despite the absence of acute infectious symptoms?

A No. In fact -- when I say usually what I mean is that a patient will come in -- I mean as an allergist, I see a lot of sinusitis. A patient will come in, and there will be a history of nighttime snoring, poor sleep, chronic congestion, a nasal voice, not being able to breath through the nose, anosmia, which is unable to smell, which is really a sign of a chronic congestion of the sinuses, and so you would call that child to have chronic sinusitis.

Now, sinusitis doesn't necessarily mean infection. It means inflammation, so you would have inflammation of the sinuses, but the reason they're coming to you because the parents assume it's just a snotty kid and don't think that it's worthy of coming to the doctor, so the reason the child comes to you is

because now he's developed a fever and green nasal

discharge and now has an acute sinusitis over top of what really is a chronic inflammation of the sinuses.

When the child presents to medical attention, it's when the symptoms become acute as opposed to when they're chronic. Kids with chronic sinusitis who present because they do too. It's true. It's because they've been waking up at night. They have poor sleep and things like that, and that's usually a sign of inflammation of the sinuses and is often related to the present of allergens in the environment and things like that and not related to acute infection.

Chronic sinusitis in particular is usually not an infectious process.

Q Do you have a sense of what percentage of children develop a thrush infection, a candida infection in their first year of life?

A There's something in the order of one in three will have thrush in the first year of life. It's quite common, 30 percent.

Q And how many did you count in the first year of Yates' Hazlehurst's life?

A I counted as I mentioned three documented thrush, not in the first year. Sorry. Three documented, two probables in the first two years.

Q How many did you say?

A Sorry. Three documented that I was able to find documentation for, and two more probable infections in the first two years of life.

Q Three and two, did you say?

A Yes, five.

Q Five? Do you have any idea how many children would develop five in the first two years of life?

A The studies have not been done, so no is the short answer. The long answer is in a child who receives antibiotics, it's not unusual for you to have a problem with thrush.

Q One thing you did say when you were discussing thrush was that some of the findings would be different for a child who sucked his thumb more than those who didn't. Is that correct?

A No, I didn't. I actually said that children who mouth, so who suck their thumbs or suck soothers or have a blanket that's always in their mouth or something like that, who tend to be mouthers, that's a risk factor for recurrent thrush, so it's just a risk factor.

Q So your opinion wouldn't change based on the extent to which Yates sucked his thumb?

A It's like everything else in life. It's a risk factor. It cumulates or not.

Q Now, I'm going to hand you again a document dated January 18, 2002, physicians visit that's been marked as Petitioner's Trial Exhibit 2, and I again apologize for having only the one copy. I guess the question I have is do you agree with the note in the pediatrician's records that you should consider an immune evaluation in this child's case if this kind of problem continues to persist.

A Yes, I agree. I also should note that we see these patients all the time. In my practice as a clinical immunologist, we're referred patients who have recurrent otitis media, we're referred patients with recurrent thrush, we're referred patients with recurrent pneumonias even, and we will see 15 patients a week referred in to evaluate their immune system.

We will diagnose primary immunodeficiency six, maybe 10 times a year, and 10 times a year would be considered a banner year, so that means that I evaluate hundreds of children for immune "deficiencies" based on the history of their infections and the type of infections they have. These are even children who have severe invasive

infections, meningitis and septicemia, and they don't have a bad immune system.

They just got a bad bug, so the incidence of primary immunodeficiency while from my point of view I think it's important, from the general population point of view, we evaluate a lot of normal children with the same history.

Q That's the fundamental question I had, and you said that 10 or 15 a week that you looked at that might be someone like Yates Hazlehurst in his first two years of life. Is that right?

A That's correct.

Q And so there are large number of children who merit an immune workup?

A Yes.

Q Because they fit a profile somewhat like Yates Hazlehurst?

A It's not really because they fit a profile. It's because our thinking about immunodeficiency has changed, and it's a bit philosophical, and I'm going to get on a soap box I hope you don't mind about this, but the truth is that in the '80s and '90s, the frequency of the time from onset of first infection to diagnosis of primary immunodeficiency was somewhere in the order of five to six years, and immunologists

looked at that and said well, that's not right,.

Really, essentially children had to follow that pattern that I talked about where they had to have the frequency of infections in the first two years of life and then it just not go away, not go away, and they were getting more and more debilitated, and then finally somebody looked at their immune system. What has happened is that through campaigns to make primary caregivers aware that primary immunodeficiency should be examined, children are referred earlier for looking at their immune system.

Now because we don't know what's going to happen after age two or age three whether or not they're just going to behave like every other kids, or whether they're going to have this downward spiral, it's better to catch them at 18 months or age two and start treatment if you can. That's really the goal, so the purpose of having a lot of these evaluations and my knowing that when I walk into clinic on Tuesday morning I'm going to see 15 kids and probably all of them will be normal is that I pick up that one, and then I make an improvement in that one child's life, but the truth is, based on history alone, you can't make a diagnosis of immunodeficiency because infections happen, and so the

frequency in infections happen, and it's not an indicator of a primary immunodeficiency. It's an indicator that maybe you should look.

Having said that, I have children who I diagnose at nine or 10 with a primary immunodeficiency who have really nothing from zero to 10, so infection is a sign, and it should be examined, but it doesn't make the diagnosis. It doesn't even say the child's immune system is abnormal by any means, and it may not even be there in a child who has clearly abnormal immune system, so in and of itself it's helpful.

It gives us information, it warrants a consult, and it warrants an evaluation, but the evaluation when done is clear.

Q This is what I'm trying to ask, and maybe I misheard it. Did you say that some of these 15 or 30 or 90 that you see that end up not having primary immune deficiencies might have an efficient immune system?

A Might have what? I'm sorry.

Q I thought you said something about bad immune systems as something different than primary immune deficiency. Am I incorrect there?

A Yes. I'm sorry.

Q Do I understand that kids that have primary

immune deficiency that this is a serious and often lifelong condition that requires attention because they can't deal with infection?

A Yes, it's always lifelong unless you intervene.

Q As opposed to these children, are there some children that just don't deal with infections well, but don't have a primary immune deficiency?

A I'm not sure I know the answer to that question. There is a range of what is considered normal, so if you have a child who has 10 infections in a year, is your child not dealing well with infection versus the kid who only had three? That's hard to know, or did they just come into contact with a virus at a different time. It's multifactorial, and really in pediatrics, what are you looking at? You have to look at the child.

You have to say is he growing? Is he missing a lot of school? Is he not missing a lot of school? Is the infection frequency decreasing or not? Is it continuing and persisting? Is it affecting his activities of daily living over the long term rather than in the acute first two years of life. All those things you have to ask yourself before you say it's outside normal because we all have to go through it.

Anybody in this room, who has children, knows that kids go through a series of infections in the first two or three years of life. Especially if they're in daycare, especially if they go to parks, if they go to malls, if they're brought outside through the family unit. It's just normal, and it's what their immune system is supposed to do. It's supposed to learn when we're young, and we have a little bit of plasticity.

Q Can there be selective immune deficiencies?

A Yes, there can.

Q Are there selective immune deficiencies that would not have been detected by the immune workup that was done in Yates' Hazlehurst case?

A Yes, there are.

Q And does the ability to develop a specific immune response to tetanus tell us with certainty the ability to develop a specific immune response to other bacteria?

A As a general rule, it's a very good indicator. There is one exception to that rule, and that's what's called polysaccharide antibodies, and those are four encapsulated bacteria such as pneumococcus, which in children who have a specific immunodeficiency to pneumococcus, or polysaccharide

antibody deficiency is what it's called, you're unable to form antibodies against encapsulated organisms such as strep, pneumonia, neisseria meningitides and others in that group.

Those children present with severe infections, pneumococcal septicemia, pneumococcal pneumonias, meningitis caused by pneumococcemia or pneumococcus, and they're evaluated because of recurrence of those types of infections, and they are unable to perform those antibodies. There is a vaccine now that allows us to get around that somewhat, but it's not perfect.

Q Are there specific immune deficiencies to viruses or certain viruses?

A Not that have been reported to specific viruses.

Q I just seem to remember in another case looking at a report of a child that had a specific immune deficiency to varicella, for example, that couldn't generate natural killer cells that would deal with varicella. Does that ring any bells or not?

A It's not exclusive to varicella. It's to --

Q That was my recollection.

A Okay. Sorry.

Q No. I'm not saying --

A NK cell dysfunction exists. Usually, you have a very low NK cell number. Yates has a normal NK cell number, and it leaves you at risk for acute viral illnesses and tumors and cancer, and these are invasive viral illnesses, so not your typical upper respiratory tract infections, but things that will invade and will cause, for example, a viral encephalitis or a viral pneumonitis.

They're related to defects in the cascade related to the NK cell function, and usually related to low NK cell numbers and also can be related to specific T-cell dysfunction.

Q Is there any significance in your mind to the physician's decision to change from nystatin for the thrush early in Yates' life to the Diflucan later?

A Fluconazole?

Q Does that mean anything?

A Because nystatin has been used a lot, there is some resistance to nystatin in the environment. At the time when Yates was a child or young, diflucan or fluconazole came out as an easy to give medication, so it was easy. It's a couple of doses, and it eradicates candida, so a lot pediatricians started using it in place of nystatin because they were getting some treatment failures because of resistance.

That's sort of been put aside now because we want to use it for other things, and we don't want fluconazole resistance, but at the time, it was one of those things that would have been used more frequently.

Q If a child is moderately ill with otitis media, is that a contraindication to giving the MMR vaccination?

A I guess it would depend on what you'd define as moderately ill. The Redbook says that a physician can choose not to give the MMR vaccine if a child is moderate to severely ill but excludes the idea of upper respiratory tract infections and their complications as being an indication. Otitis media is a common complication of upper respiratory tract infections.

Q What is the recommendation for the vaccination with MMR vaccine? When should a child receive the MMR vaccine?

A It actually varies depending on where you live in the world. Certainly, in North America our first MMR is given at 12 months. In underdeveloped countries, the MMR is pushed back a little earlier and can be given at nine months of age. The reason that it's not here is that you don't develop perfect

immunity at nine months of age to MMR.

They want children to be at the older end because we have herd immunities so that the risk of the measle, mumps of rubella disease associated with waiting the extra three months is significantly less, but in the underdeveloped world where measles kills millions of children, it can be given earlier because even though you're not going to cover all children, you'll reduce the death rate during an outbreak.

Q Do you see anything in Yates' medical history up through the age of one year that indicated that he couldn't have waited for three months to receive the MMR vaccination at 15 months rather than 12?

A I see no indication that he couldn't have waited. I see no indication that he should have waited.

MR. WEBB: That's all the questions I have.

MS. RICCIARDELLA: I just have one redirect question, Special Master.

REDIRECT EXAMINATION

BY MR. WEBB:

Q Doctor, is there anything in Yates' clinical picture or the immune testing that was done to indicate that he needed further immune testing for

selective immune deficiencies?

A No. Yates' infection history markedly decreased. If he has an important primary immunodeficiency, he would continue to have infections at a frequency that would increase, and you would predict the severity would worsen as well if he was following that path.

MS. RICCIARDELLA: Thank you. That's all I have.

THE COURT: Mr. Webb?

MR. WEBB: Nothing further.

THE COURT: Thank you, Dr. McCusker. You're excused.

(Witness excused.)

THE COURT: Is this your trial exhibit here, Mr. Webb?

MR. WEBB: Yes.

DR. MCCUSKER: I'm sorry.

THE COURT: Let's hold onto that. We're going to need that.

MS. RICCIARDELLA: Can we just take a quick five-minute break between witnesses?

THE COURT: Five minutes? We're in a five-minute recess.

(Whereupon, a short recess was taken.)

THE COURT: We are back on the record anticipating Dr. MacDonald as Respondent's next witness. Dr. MacDonald, would you raise your right hand, please?

Whereupon,

DR. THOMAS T. MACDONALD

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

THE COURT: To proceed.

MS. RICCIARDELLA: Yes.

DIRECT EXAMINATION

BY MS. RICCIARDELLA:

Q Hi, Dr. MacDonald, would you please state and spell your name for the record?

A Thomas T. MacDonald, M-A-C-D-O-N-A-L-D.

Q Dr. MacDonald, what is your current profession?

A I'm Professor of Immunology and Dean for research at Barts and the London School of Medicine and Dentistry.

Q Doctor, would you please briefly describe your university and graduate education?

A I'm an Immunologist, but when I started off doing immunology many years ago, immunology wasn't a discrete course, and so as an undergraduate took the

only option to learning immunology which is a parasitology course. After I graduated, I worked on my doctorate, and I wanted to do immunology, so I did a doctorate on how immune reactions particularly T-cell mediated immune reactions could damage the human and mouse gut.

I got my PhD in 1976 and the title of my PhD was called Delayed Hypersensitivity Reactions in the Small Intestine, and subsequently I did postdoctoral training in upstate New York at the Trudeau Institute in Saranac Lake, New York, where I went because I really wanted to learn about T-cells from one of the world's leading laboratories, and the person I worked with was actually particularly interested in the way in which the normal microbes in the gut could influence T-cell function.

Q And would you briefly describe your work history in the field of immunology?

A I have been a researcher in the Laboratory for Medicines that's actually been doing experiments since 1973, and have been publishing papers throughout this period. I run an active research group, which is funded by external bodies and peer-reviewed external bodies including the European Union, the Medical Research Council of the UK and the Biotechnology

Science Research Consulate in the UK.

Most of my research work these days is now studying the human gastrointestinal immune system instead of the Murine gastrointestinal immune system, so I like to try and look in people, especially children, to try and find what is causing these terrible devastating diseases, inflammatory bowel disease particularly.

Q Doctor, did you work for a time for Merck?

A Yes, I did actually. I had a very interesting time at Merck. I was working in Philadelphia as an associate professor at Jefferson Medical College, and I don't know what happened. I think I was seduced to go to north Jersey and work in Rahway, and when I went on my interview the sun was shining, it seemed very good to me to go there.

In fact, when I got up to Rahway, I discovered that not only Merck was not a particular sort of place I wanted to work in, but also I didn't want to live in north Jersey, so I had to make a decision what to do, whether to go back into academia in the U.S., and I was offered a position at Yale, but then for personal reasons, I decided to move back to London, really for family reasons.

Q And what is your current position at the Barts and London?

A I'm a Professor of Immunology and Dean for

Research in the Medical and Dental School.

Q And what is your research budget?

A The research budget of the Medical and Dental School, the spend last year, was $76 million.

Q And would you just describe some of your responsibilities in your position?

A Okay. I run a lab where I do research on inflammation, mostly in the human gastrointestinal tract, but most of my time these days is actually taken up with looking after and administering the research portfolio of the Medical and Dental School, which has six institutes with 300 independent researchers, about 2,000 staff in total.

It covers a whole range of medical disciplines from diabetology to cardiology, inflammation biology, surgery, microbiology, immunology, so I have a broad portfolio. Essentially, I'm in charge of the research direction of the School of Medicine and Dentistry and also ensuring performance standards to make sure that our research meets the standards that it needs to be competitive in the 21st century.

Q Do you teach at the Barts in London?

A Yes. I'm in charge of all the immunology

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teaching, and I teach about inflammatory bowel disease and gastroenterology. I teach the undergraduate medical students. I teach the undergraduate science students in a very popular course, and I teach the PhD students, the postgraduate students doing MSCs and PhDs. I also teach the immunology to the young trainee doctors, who graduated from medical school because we have a different system in the UK, which is medicine is not a postgraduate degree.

It's an undergraduate degree, so after five years, they have to go into further training, and there I teach them in immunology subsequently to try to get them up to speed.

Q Have you published articles in the field of gut immunology?

A Yes, I've published many, many articles in the field of gut immunology over many years.

Q Your CV lists 158, and you had refereed articles. Is that the same thing as peer-reviewed?

A That means peer-reviewed.

Q Have you written a book on gut immunology?

A Yes, I've just published a book called gut immunology. It's actually called Immunology in Gut Disease because I felt that there was a problem.

Immunology is a rather complicated discipline anyway, and gut immunology is a little part of that, and that's also quite complicated, and I felt that there was a need for quite a simple book that explained the basic aspects of immunology and gut immunology and then showed how these mechanisms were important in gut diseases.

I also set up an A to Z of gut diseases starting off with allergic colitis and going down to yersiniosis, so if someone wanted to know what was happening in say ulcerative colitis or Crohn's disease, they can read a bit about the immunology. They just go to C, flip open, and there would be the key things about Crohn's disease in a very easily digestible fashion.

Q How many books have you edited on the immunology of the gut?

A Seven or eight I think actually, and I'm doing another two at the moment.

Q Have you written any book chapters or other publications?

A I've written hundreds of book chapters.

Q Do you currently or have you ever served on the editorial board of a scientific journal?

A Yes, I was on the editorial board of the

British Center for Gastroenterologies official journal Gut, from 1996 to 2003. I was also on the editorial board of the American Gastroenterological Association's Journal, "Gastroenterology" the top journal in its field from 2000 to 2006. I'm also currently an associate editor of the journal of the Crohn's and Colitis Foundation of America. The journal is called Inflammatory Bowel Diseases, and I've also been on various other smaller, less significant journals.

Q Are you a reviewer for any scientific journals?

A Yes, I review all the time actually. I review a lot for Gastroenterology because I feel that the quality of the journal depends on good and adequate refereeing to make sure that things that are bad don't get into the literature, but I also review a lot for Science and Nature, PNES, GX Med, so all the top notch scientific journals in the world. If anything comes up that's vaguely gut associated that goes to Nature Medicine, the premier journal in medical research, I tend to see it.

I also do papers for the Lancet. I did one for the New England Journal of Medicine once.

Q And do you sit on any research panels?

A Yes. I sit on the physiological systems

panel of the medical research council of the UK, which is the panel that reviews grants on the organ-specific diseases of the gut, the airway and the skin, so traditionally actually medicine, so I'm also on the MRC's experimental medicine panel.

Q What is the MRC?

A Sorry. The Medical Research Council of the UK. It's the UK's equivalent to the NIH with a much smaller budget, of course. I also sit on other smaller grant giving bodies as well such as the Crohn's and Childhood Research Association. A grant giving body of which I'm on the medical advisory board also.

Q Do you have any learned society memberships?

A Yes. Actually, I'm a Fellow at the Royal College of Pathologists, which is an honorary degree that's given for people who have published lots of papers in an area. I got that in 1995 on the basis of the quality of my published works. The thing I'm most proud of though is I was elected in 2002 to be a Fellow of the Academy of Medical Science in the UK, which I think I'm the only gut immunologist on it.

It was a body put together as sort of a side-by-side with the Royal Society of Britain, which actually is all science. It was actually to put up a

learned body of experts in medicine, who could help the government and advise on policy and give them a source of really authoritative opinions on medical issues of the day, so I was elected to that in 2002.

Q And do you speak frequently on the topic of gut immunology?

A I speak on gut immunology and inflammation and inflammatory bowel disease all the time. I was in Dresden last week talking at a folk symposium on inflammatory bowel disease. In a few weeks I'm going to talk at the inflammatory bowel disease think tank, which the Swedish government have put forward to think about new ways in which we can think about treating these diseases and the understanding of these diseases.

I do this thing all the time. I also work very closely with industry to try to develop new therapies for treating inflammatory bowel disease.

Q Doctor, did you participate as an expert witness in the MMR litigation in the United Kingdom?

A I didn't get to the witness part. I only got to the expert part because the litigation was stopped after expert witness reports were submitted to the Legal Aid Board.

Q What role did you have during the expert

part of that litigation?

A I was approached in 1998 by Lovells, a law company representing Merck against the litigation in the UK, for the idea that MMR was associated or caused autism, so my role in that was to evaluate essentially the evidence that measles virus was present in the gut of autistic children using techniques of immunohistic chemistry and PCR and also to talk about whether in fact there was such a thing as gut inflammation in autistic children.

In other words, really does autistic enterocolitis exist, so it was an interesting time because there really wasn't any literature until the 1998 paper came out, which is the Wakefield paper. But then subsequent in the next five years actually, it sort of rolled out as the data came along and more papers were published. I'm familiar with these papers.

Q Doctor, you said you didn't get to the witness part. Have you ever testified in Court before?

A Never.

Q Turning to this case, what material did you review in preparation for your testimony today?

A Well, I read Dr. Buie's report. I reviewed

Krigsman's report in the Cedillo case, and I reviewed Corbier's report, and I reviewed lots of relevant publications, newer publications, later publications, older publications, so essentially it had been mentioned in either Krigsman or Buie's report or Corbier's report, I went over these papers again just to refresh my memory.

Q Did you review the medical records of Yates pertaining to any of his GI issues?

A Yes, I did. Yes.

Q Do you agree with Dr. Corbier that Yates likely has an immunological disturbance affecting his gut?

A No.

Q Now, based on your review of the records, has Yates experienced gastrointestinal symptoms?

A Yes.

Q And in your opinion, are those symptoms causally related to the MMR vaccine?

A No.

Q Does Yates have inflammatory bowel disease?

A No.

Q In your opinion is Yates' autism causally related to the MMR vaccine?

A No.

Q Would your opinion be different if his regression into autism had an onset at 12 months?

A No.

Q Let's look at the basis of your opinions and start with the medical records that have been filed in this case. Did you review the medical records pertaining to the upper endoscopy and the colonoscopy that Dr. Buie performed on April 17, 2003?

A Yes.

Q For the record, I'm referring to Petitioner's Exhibit 20. Did I hand you before you took the stand a copy of Petitioner's Exhibit 20?

A Yes.

Q If you could please turn to page 2?

A Yes.

Q Is this the report of the upper endoscopy?

A Yes.

Q What were the findings?

A When the endoscope was put down, he saw some inflammation from an endoscopic point of view in the esophagus. The stomach was normal, and the upper duodenum was normal, and then some biopsies were taken of stomach, of the duodenum and of the esophagus to be sent for histopathology.

Q Was reflux esophagitis found during this

upper endoscopy?

A Reflux esophagitis cannot be found during the -- reflux esophagitis is a functional thing in which acid goes back up. When you see inflammation in the esophagus of a child, and this is actually a rather common observation that is seen by a reddening of the mucosa, which is consistent with reflux esophagitis, but doesn't actually show reflux esophagitis.

Q And a biopsy was taken of the esophagus?

A Yes.

Q I'm referring to Petitioner's Exhibit 20 at 8, which is the pathology report of the biopsy taken.

A Yes.

Q What was the pathology finding of the esophageal biopsy?

A It was no diagnostic abnormality recognized.

Q Doctor, if you could please turn to Petitioner's Exhibit 20 at 4 through 6?

A Say that again?

Q Four and really through 6.

A Page 4?

Q Four. Right. Is this the report of Yates' colonoscopy?

A Yes.

Q And what were the visual findings of the colonoscopy?

A The mucosa was normal of the colon, and the ileum was also normal, but what was noted was some nodular lymphoid hyperplasia at the sigmoid colon and the rectum.

Q Doctor, have you ever observed a colonoscopy?

A Yes, I've seen hundreds and thousands of colonoscopies.

Q Now, you mentioned that nodular lymphoid hyperplasia was found at the sigmoid colon and the rectum. What is lymphoid nodular hyperplasia?

A Lymphoid nodular hyperplasia is actually an enlargement of the lymph nodes in the small intestine and the colon. Children generally have a more abundant immune system than adults. They have larger lymph nodes. This is particularly true in the gastrointestinal tract because children are not only susceptible to upper respiratory tract infections, but they also suffer lots of gastrointestinal infections.

So it's extremely well-documented that if you look into the intestine of a child compared to the intestine of an adult, there are more lymph nodes as part of the normal situation. Lymphoid nodule

hyperplasia is a very subjective assessment, in which it is felt by the endoscopist as they're looking through that these are larger or more prominent than would normally be seen, and it's very much a subjective assessment.

Q Is it a pathological diagnosis?

A No.

Q would you please explain why that is?

A The histopathology or the histology of lymphoid follicles in autism, in lymphoid hyperplasia is identical to the histopathology of the lymphoid follicles in all healthy individuals. Just to prepare for this actually, I went over some of the older literature, and this is something, which is really well-acknowledged. For example, this is a paper of the normal histology of the colon in the American Journal of Surgical Pathology quite a long time ago.

It says, "One to two mucosal lymphoid follicles or lymphoglandular complexes may be present in the normal colorectal biopsy and should not be mistaken for increased mononuclear density due to inflammation. It's extremely well-recognized actually that lymphoid follicles are part of the normal component of the gastrointestinal tract.

THE COURT: Dr. MacDonald, would you note

1 the author's name?

THE WITNESS: Yes. Certainly, so this is the paper by Levine and Haggitt, and I'll just leave it. It's not controversial actually. I shall just leave it here.

THE COURT: Okay. And the page numbers that you read from?

THE WITNESS: Okay. That was pages 978 to 979.

THE COURT: Thank you.

BY MS. RICCIARDELLA:

Q Doctor, does a finding of lymphoid nodular hyperplasia mean that one has an inflammatory bowel disease?

A Absolutely not. In fact quite the reverse.

Q Is a finding of lymphoid hyperplasia mean that one has an inflammatory condition at all?

A No.

Q Is the finding of lymphoid nodular hyperplasia in the lower bowel of a child considered an abnormal finding?

A No.

Q Doctor, did you review the medical records in this case pertaining to Dr. Buie?

A Yes.

Q Did Dr. Buie anywhere in those medical

records state that the finding of lymphoid nodular hyperplasia in Yates indicated an inflammatory bowel disease?

A No, because that would be wrong, and he's a very good physician, and when endoscopists and pathologists see lymphoid follicles in either tissue section or through the endoscope, they note it, but it is of no diagnostic significance.

Q Did you review the expert report submitted by Dr. Buie in this case as Petitioner's Exhibit 50?

A Yes,

Q Does Dr. Buie in that report state that the finding of lymphoid nodular hyperplasia is evidence of inflammatory bowel disease?

A No.

Q In fact, does Dr. Buie state that lymphoid nodular hyperplasia is evidence of inflammation at all?

A No.

Q I'd like to turn to the pathology that was taken of the biopsies of the colonoscopy. If you could please look at Petitioner's Exhibit 20 at 8? What was the pathology findings of the biopsy taken of the ileum?

A It was completely normal.

Q And is the ileum part of the small bowel?

A Yes, it's the end of the small bowel, just before the ileocecal valve before the food goes into the colon into the cecum.

Q And what were the pathology findings of the biopsies of Yates' colon?

A Would you like me to say these individually or actually through summation? His colon and his cecum, which is the first part of the colon scattered into epithelial eosinophils and increased cellularity of the lamina propria. In colon transverse biopsy, essentially the same. In the sigmoid colon, which is just before the rectum, the same thing. Also, in the biopsies of the rectum were fragments of unremarkable colon mucosa.

I think it's important to note that actually there is some slight differences between the comments at the top and in the note in which there's some important information talking about the eosinophils in the lamina propria, which is not mentioned. That is the area of tissue below the epithelium, and particularly the pathologist looked to see if there was some of the more characteristic features of allergic enterocolitis such as eosinophils in the crypts.

And these were not seen after examination at

multiple levels, so the pathologist made a good effort trying to look to see if this was a really severe eosinophilic colitis, but could not find them, so the comments at the end was a mild eosinophilic colitis, perhaps related to food allergies.

Q Let's break down what the pathology findings were. What are intraepithelial eosinophils?

A Okay. Eosinophils is a type of inflammatory cell, which moves into tissues usually during allergic diseases. Eosinophils live in the blood normally at low levels, and when you have an allergic response for example in the airway of the skin, eosinophils move into the tissue. It's very much a nonspecific cell, so, for example, ulcerative colitis, a classical inflammatory bowel disease, there are more eosinophils in the gut wall because it is inflamed.

People tend to see eosinophils in a colonic biopsy. The bells start saying allergy of some sort, which is why the pathologist cut through the tissues to look for real more evidence of severe allergic enterocolitis.

Q Is a finding of intraepithelial eosinophils evidence of inflammatory bowel disease?

A No. It is not pathogenomic of inflammatory bowel disease.

Q Are intraepithelial eosinophils found in developmentally normal children?

A Yes.

Q And do you have a slide on this?

A Yes, if you go to the first slide, this is a study for Lano, which is one of the largest studies from the Royal Free Hospital, which has the largest experience of looking at the gastrointestinal tract of autistic children, and this is Table 2, and this is a very interesting study because it looked in autistic children, which is you see the left, normal control subjects, that's children without gastrointestinal inflammation, but the next column is children with lymphoid hyperplasia control subjects.

These children did not have lymphoid hyperplasia, but were colonoscoped because they had severe, intractable constipation. That was a clinical reason for undergoing an endoscopy, which is a fairly serious procedure. When biopsies were taken of all of these children, what you can see is interesting, which is that actually the colitis score on autistic children is 1.4, which is significantly higher than normal control subjects, but it's not different from the children with lymphoid hyperplasia, which is 0.6.

Importantly, in terms of what we are saying

here, if you could look at the lamina propria eosinophils, it's 0.9 in the autistic children, zero in the normal subjects, and 2.1 in lymphoid hyperplasia, children who have severe and chronic constipation. These children are developmentally normal, and their problem is not inflammatory bowel disease, but they have constipation.

What this shows quite clearly is that an increase in eosinophils in the gut is a consequence of constipation and the inflammation caused in the gut wall by having impacted stools.

Q In the second pathological finding that you read out were increased cellularity of the lamina propria. What is that?

A It almost certainly means, but doesn't specifically say, that it is what's called a mononuclear cell infiltrate, slightly more lymphocytes and macrophages in the gut wall, which was the finding of the autistic children in this case actually. By and large the colitis score was nearly all due to increased mononuclear cells in the lamina propria, some more lymphocytes, sometimes perhaps more T-cells.

Q Are findings of increased cellularity of the Lamina propria found in developmentally normal children?

A Yes.

Q Are they also found in children who do not have inflammatory bowel disease?

A Yes.

Q And do you have a slide on that?

A Okay. This is a study that I performed with Professor John Walker Smith when I came back to England in 1985. I worked with Professor Walker Smith, and Simon Murch was my graduate student at this time. We did a very big study, which published in Gastroenterology in 2004, which looking at the levels of a cytokine called tumor necrosis factor alpha, which treatment against tumor necrosis factor alpha has been the major breakthrough in treating inflammatory bowel disease for -- essentially in the last 30 years.

This paper has about 250 or 300 citations in the medical literatures. It's extremely well cited. John Walker Smith when I worked with him was a very caring man, and he felt it reasonable to assess children to give parents of children with gut problems an exclusion diagnosis.

He felt it was quite good if a child came along with some gut symptoms that there was a tremendous relief to them to say well, actually it's

fine. We looked at quite a lot of normal children, and this is a list of the 46 control children, who we studied in this paper.

What we did here actually because we essentially transcribed the histopathology, the reports from the pathologists, onto this table, and so we're looking at the last 15 children and you'll notice that some familiar tabs come up, lamina propria eosinophils, eosinophils and follicles, eosinophilic ileitis patient No. 36, prominent follicles, chronic inflammation, which actually is another way of saying an increase in mononuclear cells and nuclear density.

Mild follicular inflammatory cells, these words keep on coming up. These children were sent home as non-IBD and never came back again because it is part of the normal range that you see in children, who are getting gut infections, who are get all sorts of strange things that we don't understand and when you do a colonoscopy you see a mild increase in inflammatory cells, and it's part of the normal range.

Now, it is quite difficult to actually say this is the normal range for children who undergo colonoscopy. The question really would be do absolutely normal children have an increase in inflammatory cells sometimes, and that question will

never be answered. There was a very recent paper that's just been published from Bernstein. It had just come out in the American Journal of Gastroenterology, which I have here someplace.

They have gone to a great deal of effort to biopsy the gut of completely healthy adults, and what they find is actually that in completely healthy adults, the diagnosis of nonspecific colitis can also be made, and if I can find the paper -- excuse me a moment. The title of the paper, which is by Paski et. al. that appeared in the American Journal is the Importance of Recognizing Increased Cecal Inflammation in Health and Avoiding the Misdiagnosis of Nonspecific Colitis.

They were concerned that actually this phrase "nonspecific colitis" actually may be part of the normal range and have shown in adults, but not in children, that in fact it is normal.

Q Doctor, who is the first author?

A This is Paski.

Q Could you spell that please?

A P-A-S-K-I.

Q And what journal is that found in?

A American Journal of Gastroenterology.

Q And it was published recently?

A It was published recently, which is between the time when I saw the first papers and this came out.

Q Now you said that the question will never be answered in children. What do you mean by that? Why?

A Because it is unethical to biopsy and give a general anesthesia to a normal child to find out what the gastrointestinal tract is like. There are clear guidelines set by the North American Society for Pediatric Gastroenterology and Nutrition as to what the justification for a colonoscopy is. The only way that people can get round is actually to look for biomarkers of inflammation.

It's also interesting why it's probable that the Wakefield studies from the Royal Free will never be repeated ever again because it's unethical to do endoscopy on children with autism whose primary problem is constipation, so we have to look at biomarkers to see if there's inflammation, and there is really a number of papers now suggesting actually that if you use these biomarkers of inflammation that autistic children don't have any inflammation in their gastrointestinal tract.

Q Doctor, are increased cellularity of the lamina propria found in children with constipation?

A It appears so based on the previous slide, yes.

Q Slide one?

A So if you go back to actually this colitis score, actually you can see that. You can look at lymphoid hyperplasia control subjects, 0.6 is their colitis score, but as the autistic children at 1.4, there's no significant difference, and in the text of this paper, it makes the point that actually six out of the 10 children with developmentally normal children with constipation and lymphoid hyperplasia had some nonspecific colitis, and that wasn't significantly different from autistic children.

If you look in children with chronic constipation, which again is very unusual to do, and the reason why it's justified in these cases is that sometimes, really very rarely, there are developmental problems of the gastrointestinal tract, so the functional problem with the bowel actually that's more serious than just chronic constipation, so occasionally they do colonoscopy and they find that they have lymphoid hyperplasia.

A reasonable hypothesis is that actually the constipation causes lymphoid hyperplasia, which causes the mild inflammation if it's there at all.

Q Doctor, in this case, Dr. Corbier talks about different biologically plausible mechanisms in the development of Yates' autism, and one such mechanism that he advances is that the MRI vaccine played a significant role in his development of autism, and in support, he cited the work of Dr. Andrew Wakefield, and in those studies, Dr. Wakefield described a phenotype of autism that he has termed "autistic enterocolitis." Are you familiar with that term?

A I am familiar with the term.

Q And are you familiar with Dr. Wakefield's work?

A I am very familiar with Dr. Wakefield's work?

Q How did you become familiar with his work?

A Where can one start actually? There's been great advance in understanding inflammatory bowel disease really since about 1989, and Wakefield first came into public prominence in 1989 when he published a paper in the Lancet with an accompanying press conference and media interviews where he said that Crohn's disease was not due to an immune response in the gut wall, but in fact was due to lots of small blockages of the blood vessels along the gut wall,

which stopped the blood getting into the gut and the gut died, sort of like little heart attacks along the bowel wall, and so this paper received a huge amount of attention.

Q Are you talking about the 1993 Wakefield paper?

A No, the 1989 paper.

Q 1989. Okay.

A Now, this was sort of put aside as something well, an interesting idea, but just wrong. We just ignored it, but then in 1993, he really put the cat amongst the pigeons when he took this hypothesis further and said that these little infarctions in the gut wall were caused by measles virus, and that was the 1993 paper.

MS. RICCIARDELLA: Dr. MacDonald is testifying about Respondent's Exhibit BB at 1098 in the Cedillo case.

THE WITNESS: That's right.

BY MS. RICCIARDELLA:

Q I'm sorry. Go ahead.

A So this paper again received a huge amount of media attention, and again when it was looked at closely by those of us in the field, we felt that it was lacking how can I say important controls and

1 important things

that a credible, decent scientist would feel duty bound to do but actually hadn't been done. There was a huge furor about this, and Wakefield continued to publish papers in 1995 and 1997 saying that measles virus was causing Crohn's disease.

He actually had moved onto the stage actually saying that measles vaccine was causing Crohn's disease. This caused such problems in the UK with the publicity that the Medical Research Council of the UK had a special meeting to evaluate the quality of Dr. Wakefield's work, that there was measles virus in Crohn's disease.

The conclusion of this report, which was published in 1998, was that a lot of his studies were done using reagents identifying measles virus with reagents that weren't specific for measles virus and also leaving important controls that were on the manufacturers instructions when you used the techniques. He didn't bother to do them.

He was asked to repeat the studies by the Provost of his then employer, Royal Free Hospital, who wrote to him and asked him to repeat these studies because of the problems. He agreed to do this in 1999, but actually they have never been repeated.

Q Doctor, how does the scientific community

today view Dr. Wakefield's claim that he found measles virus in Crohn's disease?

A Well, the thing about Crohn's disease is Crohn's disease is a relatively common disease, and it's really quite easy to get tissue from other patients to repeat what Wakefield has seen. The first rumblings that there's something wrong was when he sent the antibody that he used to detect measles virus in the 1993 paper, and he sent it to a very good researcher in France, who used this antibody in other Crohn's disease samples, and said it stained all tissues.

In other words, it wasn't specific for Crohn's disease, so it saw ulcerative colitis, it saw a normal bowel, and this was published. Then a Japanese group, who actually wrote a letter to the Lancet saying they used PCR and there was no measles virus in Crohn's disease, and this Japanese group then went on to show that the other antibody that Wakefield had used to identify measles virus in fact also saw a human protein.

Then between about 1996 and 2000, there's a number of publications showing that measles virus was not present in Crohn's disease, and finally Wakefield was persuaded to publish the results of his graduate

student, Nick Chadwick, who since 1994 had been failing to find measles virus in the gut of Crohn's disease patients, but actually this information had been suppressed while Wakefield was still publishing other papers using other techniques.

It's now realized quite widely that this was either a case of Wakefield being too enthusiastic over his interpretation of the flawed data, or there was perhaps something slightly more sinister behind it, and that there was some degree of scientific fraud behind it also.

Q Doctor, Dr. Wakefield published a paper in 1998 in the Lancet that's been the subject of a lot of discussion in these cases, and I'm referring for the record to Petitioner's Exhibit 37 at Tab C. Could you briefly describe what that paper, the study entailed?

A That study entails investigating a group of 12 autistic children, who were investigated at the Royal Free Hospital for gastrointestinal symptoms. The gastrointestinal symptoms in the paper were abdominal pain and food intolerance. I think there was something else, and they were colonoscoped, and Wakefield claimed to find an unusual condition in these guts.

It was called ileo small intestinal

lymphoid hyperplasia and a mild nonspecific colitis in the 12 children. It was an observational study of 12 children, and the controls for the study were provided by a doctor, a colleague of mine, called Dr. Paula Domizio at Barts Hospital, who was asked to supply normal samples to him as controls, but the study had no controls. It was probably the worst paper that's ever been published in the history of the journal.

Q Is this the paper that he coined the term autistic enterocolitis?

A No. Actually, not really, no. Autistic enterocolitis sort of evolved. The disease that these children have sort of popped along. The title actually of the paper is Ileal-Lymphoid Hyperplasia. Autistic enterocolitis sort of popped out a bit later on actually. He didn't start using it until about 2000 or so, so that paper was about nonspecific colitis and Ileal-lymphoid hyperplasia.

Q And did he describe this ILNH as a new variant of inflammatory bowel disease?

A I think there was some allusion towards that, but most of the discussion of the paper was actually nothing to do with inflammatory bowel disease. The discussion of the paper was about measles and MMR and GI problems and patients with

them.

Q Doctor, did you prepare a slide today about what ILNH is?

A Yes.

Q This is now Slide 3.

A Yes, so on the upper left, and you can't actually see. I don't suppose we could put the lights out. Can we put the lights out?

Q No. I'm afraid not.

A Okay. So the Panel A and B are taken from the Wakefield publication of ileal-lymphoid hyperplasia, so in A it's not actually quite sure what that big white thing in the side is, but if you look in B, you can perhaps see I put some arrows on it. I should have made them white instead of black to identify the little lymph nodes in the gut wall. There's one on Panel A to the left.

Can you see that arrow on the left-hand side? On Panel B, to the top right-hand side, underneath the line, there's a little lymphoid follicle. The one on the bottom is actually one of my pictures of the lymphoid follicles in a developmentally normal, healthy child's ileum, and the reason I picked this picture is I have a research program funded by VSRC and funded by a number of other

people.

We biopsy these tissues and take them out and study the immune function, so I'm very familiar with actually these things, so I think you can see rather easily that in children lymphoid follicles are present in the gastrointestinal tract.

Q Doctor, what were some of the problems that you found with the 1998 paper published by Wakefield in the Lancet?

A Well, it was an observational study. It was a minor paper reporting some slightly unusual changes in the gut of autistic children, which probably deserved a place lower down in the publication ranks, but would have been worthy of other investigation. The problem with the paper is it was accompanied by a news conference and a video by the Royal Free suggesting that these changes were caused by MMR, but there was no evidence actually that the pathology was caused by MMR.

The only part of the paper that dealt with MMR was to say that actually that colitis occurred shortly after the MMR in a nonobjective way. Just asked the mothers, and they said yes, and that was what most of the discussion was, and this paper really caused a huge furor in the UK because it was vastly

overinterpretated and caused drops in vaccination rates and essentially a worldwide health scare, and it's a modest little observational paper.

Q Were you satisfied with the controls that Dr. Wakefield used?

A There was no controls. It's difficult to say actually, but if you read the paper of what was wrong with the children to justify colonoscopy because it's not entirely clear that the children fulfill the criteria for having a diagnostic colonoscopy, but putting that aside, the paper talked about the children having abdominal pain and food intolerance. That in fact wasn't the gastrointestinal problem these children had.

As was revealed several weeks later in the correspondence section of the Lancet in a report from Simon Murch, Mike Thompson and John Walker Smith, who were the pediatricians looking after the children, it's important to realize that Wakefield is a surgeon. He's not a pediatrician. He's not a immunologist. He's not a histopathologist, so the physicians in charge of these children told us what was wrong with these kids.

And what they're say here is, "Plain radiography confirms severe constipation with acquired

mega rectum in almost all affected children, despite many receiving treatment for constipation. Most parents note a honeymoon period of behavioral improvement after the bowel preparation for colonoscopy, and this is maintained if recurrent constipation can be prevented."

Q And what are you reading from, Doctor?

A I'm reading from a letter to the Lancet by Simon Murch, Mike Thompson and John Walker Smith in response to the scathing criticism of the Wakefield paper.

Q What's the date of the letter?

A It was published on March 21, 1998.

Q Thank you.

A It's my belief that in fact if it had been noted that the children were severely and chronically constipated, knowing that any decent referee would have said well, before we go ahead and publish this, we need to know what's happening in developmentally normal children who also have this severe constipation, and as I pointed out before in my earlier table of the other three, when you look in developmentally normal children, you'll get LNH and chronic constipation.

They also have ILH and some inflammation, so

this is what was wrong with the children, and I think this --

THE COURT: I'm sorry. Go ahead.

THE WITNESS: That's okay. Sorry.

THE COURT: Just for clarity so that we're clear as to what we've referred to, the first article that you made reference to with respect to the colon and the Levine article, pages 978.

THE WITNESS: I'm sorry. Can you say that again?

THE COURT: The first article that you had?

THE WITNESS: Which one?

THE COURT: The first one. I think it said the normal histology of the colon?

THE WITNESS: Yes. Okay. That's Levine.

THE COURT: Levine.

THE WITNESS: That's Levine and Haggitt.

THE COURT: Okay.

THE WITNESS: And then I pulled another one, which is Paski, et al.

THE COURT: And the third one is your 1998 letter from the Lancet?

THE WITNESS: It was, although this was in my report.

//

THE COURT: Right.

THE WITNESS: This is actually part of the record.

BY MS. RICCIARDELLA:

Q So just to be clear, Doctor, what in your opinion was wrong with the children, who were the subject of this 1998 paper?

A I think they had abdominal pain because of severe and chronic constipation. I think the physicians in charge of the children made this quite clear that there was an improvement after colonoscopy, and of course before you can do a colonoscopy, you have to flush out the colon, you have remove all the stools.

This is actually confirmed again in subsequent papers from the Royal Free Hospital where they've actually noted that most of these children were severely and chronically constipated, and actually in other papers where they have mentioned that the abdominal pain that these children undoubtedly suffer and which gives them a terrible time is relieved by the bowel prep for colonoscopy or evacuation of the bowels.

Q Now, before we leave this paper, Dr. Wakefield in the 1998 Lancet paper articulates a

theory as to how the MMR vaccine causes autism?

A Yes.

Q And you prepared a slide to show this?

A I have a slide of this.

Q And this is Slide 4.

A This was the slide that underpinned the UK litigation, which was that children, who receive measles, mumps and rubella because mumps and rubella were in the vaccine, that they somehow interfered with the immune response against measles and allowed measles virus to persist, and it went to the gastrointestinal tract.

When measles infected the gut, and therefore measles had to be present in the gut, this measle infection caused gut inflammation in lymphoid hyperplasia. The gut inflammation made the gut leaky, and therefore this leaky gut allowed things called opioid peptides, or products of digestion, to go through the gut wall, and these peptides from the damaged gut enter the bloodstream and damage the developing brain and cause autism.

This would have happened in the first few weeks after MMR presumably for there to be a temporal association between the MMR vaccination and the development of the autism, and when we're looking at

children as in Yates many years afterwards and in the children in the UK many years after, what we're looking at is essentially a shadow of this event, which happened and precipitated the autism.

It requires a number of actually highly improbable events to occur. This is the Wakefield hypothesis, and of course it's critically dependent on children having gut inflammation, children having measles virus in the gut because children have an increased permeability, and if none of these things happen, the whole case falls apart, and I think you heard from my colleague, Professor Bustin, about the quality of the evidence of the measles virus in the gastrointestinal tract of these children.

Q Doctor, as a gut immunologist, do you find this theory credible?

A Credible or incredible?

Q Either. Which one?

A It's incredible. When I was first approached to work for Lovells for Merck, it was with absolute incredulity that anyone could possibly take this seriously as a hypothesis for serious diseases such as inflammatory bowel disease and a serious disease such as autism. When I told my colleagues in the academic community about this, they were

gobsmacked. I'm sorry, I shouldn't say -- they were surprised that this should form the basis for litigation that cost lots of money in the UK.

Yes, it is fantastic, improbable and also I think most importantly not based on any data or any hypothesis. The theory was made up in January 1997 by a lawyer, Richard Barr, a woman called Rosemary Kessick and Andy Wakefield before they had seen a single patient.

Q Doctor, I'd like to turn next to Dr. Wakefield's paper he published in 2000, and for the record I'm referring to Petitioner's Exhibit 37 at Tab D. Would you briefly describe what this study entailed?

A This is a study in which instead of the initial 12 patients, another 48 patients have been studied. Sixty autistic children were studied, including the original 12, so it's not a completely new study. Importantly, this study had some controls, which was children who were turning up to the Royal Free Hospital and were having a colonoscopy, and there was 37 controls.

They were examined, and what they were specifically looking for really was look for ILH, they looked for large lymphoid follicles in the ileum as

evidenced endoscopically, and they also looked for nonspecific colitis for these inflammatory changes that they had seen earlier on, so it's essentially a larger study, but no different really from -- how can I say it -- an intellectually previous study.

Q And what were the claims made in this study?

A Well, the claims were that enterocolitis was seen in children with developmental disorders, which is the title of the paper, and so these claims are actually unsustainable. Do you want me to elaborate on that?

Q Sure.

A Enterocolitis is an inflammation of the ileum and the colon.

Q And by ileum, is it the same thing that we call ileum?

A Yes, ileum and the colon, the end of the small intestine. This is well-recognized by histopathologists when they take biopsies, so it was very important for this theory here that there is a small bowel inflammation so that the peptides can cross because the small intestine is the organ of digestion, not the colon, so these children had to have had inflammation of the ileum.

If you look at this paper, you discover of

the 60 children, who were analyzed, only eight of them had what pathologists considered to be inflammation, and that was no different from the 37 normal controls, a few of whom also had mild inflammation of the colon. However, the paper said that 88 percent of the children with autism had pathology in the ileum, and that's because they had ILH.

What Wakefield did is he called ILH pathology so he could say they had small bowel pathology so that he could substantiate this argument. The other problem with the paper was that they invented new pathological abnormalities which were not recognized by anyone in the world.

When pathologists look at specimens, it's really quite important that pathologists are very rigorous because they're often diagnosing colorectal cancer and important diseases, so they recognize patterns, and so in this paper, they invented some, which was interesting, they invented disruption of the epithelial basil lamina, condensation of the lamina propria, loss of stratification within lamina propria, and most importantly they put down normal lymphoid follicles as pathology.

They actually said this is a pathological abnormality. Now, I've told you earlier on that large

lymphoid follicles are not a pathological abnormality, so by essentially double counting they were able to say that these children had an enterocolitis when in fact they didn't. So this is something that Professor Paula Domizio and I felt really quite strongly about and published an article that appeared actually earlier on this year about this, which we consider actually to be something of a deception.

THE COURT: Dr. MacDonald, would you give us a page cite for the record please?

THE WITNESS: Okay. That was on page 2287.

THE COURT: Thank you.

THE WITNESS: I think the deception in this paper goes further than this. If I can have the next slide?

MS. RICCIARDELLA: We're on Slide 5.

THE WITNESS: Okay. All right. From this paper, the top image is taken from the paper, and it says, "Grade 2 Lymphoid Hyperplasia in the Ileum of an Autistic Child." I think it's better on the black and white copy. You can see that the bottom picture is a picture of mine, so I would think that any reasonable person would say -- actually the lymphoid hyperplasia is more abundant in the bottom picture than the top picture.

The bottom picture is from a child who was admitted to St. Bartholomew's Hospital, seen by Professor John Walker Smith in my presence and discharged and sent away with ileum lymphoid hyperplasia, not as a diagnosis, as an observation, who never came back. This is a normal finding in children. Go to the next slide.

BY MS. RICCIARDELLA:

Q Slide 6?

A Yes. This was something that I only actually noticed quite recently because I was dealing with a photocopy and not an original, and where you couldn't see the letters. Can you see that actually this is supposed to be taken from this publication? Panel A is normal ileum. In other words, this is what normal children should look like. Panel B is, I think it's better on your copy actually.

Panel B is Grade 1 lymphoid hyperplasia. Panel C you've seen before is Grade 2 lymphoid hyperplasia, and Panel D is Grade 3 lymphoid hyperplasia, but if you look at the times that these were taken, you'll see they were taken 03-03-97. They took Panel A at 10:00 in the morning, 36 minutes past the hour and 50 seconds, and the panel of the Grade 3 lymphoid hyperplasia was taken one minute and 54

seconds later.

A colonoscopy takes about 20 minutes if you're really fast, so in fact what's happened is Panel A is not normal ileum. Panel A is cecum, it's the end of the large intestine just prior, one minute and 54 seconds before the endoscopist put the tube through and took the picture, and so I think this is quite symptomatic of the quality of this publication, in which as soon as you start digging below the veneer of the numbers, you realize actually that there is some strange things happening.

This may be a mistake. I think it's highly unlikely it's a mistake.

Q Doctor, there are problems with the controls in this 2000 paper?

A Yes. They didn't use constipated controls.

Q And what's the significance of using the constipated controls?

A Well, if you do an observation in children with autism and who've got -- as is admitted by the attending physicians -- severe and chronic constipation, and you find some changes, ileal lymphoid hyperplasia, which I'm quite willing to accept is more abundant in autistic children. I have no doubt about that. It's trivial, and you find some

inflammatory cells. A scientist of any repute would say well, what I've seen could be due to two things.

It could be due to the autism, or it could be due to the gastrointestinal problem of severe constipation, and you would then study constipated children as the appropriate control before you really went on to overinterpret results and say it was associated with autism. Science is about being conservative and safe and careful and making sure that before you go out into the world that you've actually covered all your bases, and this was not done in this case.

Q Doctor, I'd like to move on to a paper published by Dr. Uhlmann in 2002 that we've also heard a lot of discussion about, and I'm referring to Petitioner's Exhibit 37 at Tab E. What did that study entail?

A The Uhlmann paper appeared in probably the worst journal that has ever been seen, a journal which is subsequently no longer in existence. It claimed to detect by PCR and by a technique called in-cell PCR that measles virus was present in the gut of autistic children but not present in controls. A number of experts looked at this in the UK, and you have Professor Bustin, talked about the PCR.

My job as an expert witness in UK was to look at the technique called the in-cell PCR to determine its validity, but I'm not privileged to discuss this.

Q Right. Under the UK laws, you're not at liberty to discuss your findings?

A I cannot discuss this.

Q We understand. Does the scientific community find the 2002 claims made by Dr. Uhlmann in that paper credible and reliable?

A No, no. Again, this is one of the worst papers. I think you have to realize the tempo and the way in which these publications were coming out into the literature. The litigation in the UK was being driven by the hypothesis that I showed you, that measles was present in the gut, and this had been claimed since 1998, and the defendants have repeatedly asked the claimants where's the evidence for measles virus in the gut?

And it was always forthcoming; the big breakthrough was always coming through, and there was no publication. As we got nearer to 2003 and the trial date, the pressure increased, and I certainly personally felt that the Uhlmann paper was essentially just an attempt to try to get something into the

public domain, to get something in publication that claimed there was measles virus in the gut of these children despite the fact that the paper was essentially untenable.

There had to be measles virus in the gut of these children for the UK litigation to go forward, so I think it was by and large a device.

Q Doctor, I'd like to look at the paper published in 2003 by Ashwood, and I'm referring to Petitioner's Exhibit 63 at Tab 4 in the Cedillo case.

A Yes.

Q What were the claims made in this 2003 paper?

A Could you read the title actually? I can't remember the title, but I've got the date here in my head. I know the paper.

Q I don't have the title written down.

THE COURT: Just a moment. I can get it for you.

THE WITNESS: I think I got it. It's called Intestinal Lymphocyte Populations in Children with Progressive Autism, Evidence for Extensive Mucosal Immunopathology.

BY MS. RICCIARDELLA:

Q And what were the claims made in this paper?

A The claims made were that if you took biopsies from autistic children and biopsies from normal children and then use a technique called flow cytometry to count the number of T-cells and B-cells. In the samples that the autistic children in their gut had many more T- and B-cells than the control children. It's indirectly related to histopathology, but it's just another way of looking at the same thing.

The paper appeared in a journal of really no great significance, but it's the paper which does mention our observations that gastrointestinal symptoms peak prior to bowel evacuation and are relieved by the latter observed in a clinical setting of bowel preparation for a colonoscopy are a clue that they may reflect visceral pain.

This is a paper where they say that actually the abdominal pain in the children is due to the constipation and not due to the inflammation, but the important problem with this paper is that if I can just sort of say -- this is actually quite incredible. We have lymphoid tissue. We have lymph nodes because lymph nodes are where the immune system recognize antigens, and there are accumulations of lymphocytes, so, for example, if you go back a picture and look at

the bottom of that picture?

Q Slide 5.

A Okay. Go to that bottom picture. If you take a biopsy of that little lymph node, it will contain lots of lymphocytes, so in other words if you biopsy the tonsil, which is a lymph node, you get lots of lymphocytes in the same ways if you biopsy the spleen you'd get lots of splenocytes. It's an artifact of the --

You grab these little things, and you take them out, and you say wow, there's lots of lymphocytes, but you then grab a little bit from someone who doesn't have that, you're not grabbing the same bit of gut. You're grabbing a bit of gut mucosa, which doesn't have many lymphocytes, so the whole thing is a sampling artifact due to the fact that they went and grabbed these little things.

I know this is the case because one of the cell types they saw increased was CD19 B-cells, and CD19 B-cells are only present on these little follicles but not present in the rest of the gut, so it's just an artifact actually. It's quite clever the way they managed to do that, but the paper has no validity at all.

THE COURT: Dr. MacDonald, just for the

record, in the Ashwood article, would you reference the page from which you read?

THE WITNESS: Well, I think it's actually the whole paper.

THE COURT: It was the particular part that you read?

THE WITNESS: So that was on page 504.

THE COURT: Thank you.

THE WITNESS: That was the aside. I could mention they were also by then quite aware that abdominal pain in the autistic children is related to constipation and bowel movements.

BY MS. RICCIARDELLA:

Q Now, Dr. Ashwood published another paper in 2004, and I'm referring to Respondent's Exhibit E at Tab 3.

A Yes, I have that.

Q What's the title of that paper?

A Spontaneously Mucosal Lymphocytes Cytokine Profiles in Children with Autism and Gastrointestinal Symptoms Mucosal Immune Activation and Reduced Counter Regulatory Interleukin-10.

Q What journal is this published in?

A It was again the Journal of Clinical Immunology.

Q Is the published article the only version of this paper?

A No. I saw a previous version of it when it was submitted for publication to another journal.

Q And is the published version the same as the version you saw?

A No.

Q What does the published version claim?

A The published version has omission of the data and the original version that made the paper unbelievable, so the first version of the paper I saw, they were claiming cell yields and some various technical things that could not possibly be true. When the paper appeared in this other journal a few years later, these had been omitted.

Q And what are the claims made in the paper that was ultimately published in the other journal?

A The claims made were really quite remarkable. What this study is about is to try to look at the molecules made by the immune cells in the guts of autistic children and normal children using a technique called intracellular flow cytometry. They claim that in the gut of autistic children they find the same levels of these molecules called cytokines as one finds in children with Crohn's disease.

Crohn's disease is a very severe lifelong condition of extensive mucosal inflammation, and it is not biologically plausible for Crohn's disease patients who get severe inflammation and children with so-called autistic enterocolitis who by Wakefield and his colleagues' own admission is a mild and subtle disease to have the same results. It is just not biologically plausible.

The reason probably for the results is it's a very difficult technique. I think they didn't really use the appropriate controls, and you can make that data appear any way you wish it.

Q Dr. Ashwood published another paper in 2006, and I'm referring to Petitioner's Exhibit 37 at Tab G.

A Yes.

Q What were the claims made in this paper?

A This is almost exactly the same as the 2004 paper. The 2004 paper studied the lymphocytes from the duodenum and the colon of autistic children. This study reports results from the ileum and blood of the children. Same problems, same critiques. It's the same cohort of patients. The experiments were done at the same time. I think you have to remember that this paper came out in 2006, but the last experiments were done at Royal Free Hospital at least five or six years

before.

Q Dr. Wakefield published another paper in 2005, and I'm referring to Respondent's Exhibit T at Tab 35 in the Cedillo case.

A Yes. This is a paper called The Significance of Ileocolonic Lymphoid Nodular Hyperplasia in Children with Autistic Spectrum Disorder. This sort of appeared as an abstract a couple of years before with different authors, and the authors were the physicians at the Royal Free Hospital, who were in charge of the children who were being studied.

That's primarily Simon Murch and John Walker Smith. They were on the abstract, in fact were not present as authors on this paper. It's my understanding they withdrew their names from the publication and did not want to be associated with this publication. Again, I think you have to remember that this is four years, five years after all work has finished, and essentially this is the 12 in the Lancet paper, who have then been republished as 12 of the 60 kids in the 2000 paper.

Q Is that proper to do that, Doctor?

A No.

Q Why not?

A Well, you can't keep on putting the same

children into different studies and claiming that it's new because it's not, so half the children in this study had been reported before. In fact, the repetition in this paper is actually so remarkable. In fact, they've actually just reproduced some of the original work as tables.

They've actually just done it again, and so when this paper came out, I wrote to the editor of the journal pointing this out because when you publish a paper, you have to sign a form saying the work is original, has not been published before. I felt it was a bit of a problem that the tables and the children had been published before.

Q Doctor, one of the named authors on this paper is Kirstin Limb. Who is Kirstin Limb?

A Kirstin Limb, at the time the paper was submitted was working for a charity called Visceral, which was the charity which had supported Wakefield's work over many years. I think she may be a lawyer or paralegal.

Q Is she a scientist?

A No.

Q Does she have a relationship with one of the attorneys from the UK litigation for the particular plaintiff?

A I think she's the partner of Richard Barr,

the attorney, who actually worked with Wakefield and who retained Wakefield in February 1996 to act as an expert witness in the UK litigation.

Q Doctor, in your report, you state that the slides of the alleged enterocolitis allegedly seen by Dr. Wakefield and his colleagues have never been made available for "anonomized objective examination by independent experts."

A Yes.

Q What did you mean by that?

A What I mean by this is if you have done a study that has huge public health implications, and the worldwide implications that one of the pillars of public health policy in the developed world, the MMR vaccine is causing an inflammatory bowel disease that is also causing autism, this is not a little thing.

This is actually a hugely, hugely important thing of worldwide significance given that autism is such a serious condition with a lifelong problem, and inflammatory bowel disease is a very serious condition, lifelong problem, incurable, and also because the gastrointestinal inflammation can cause colorectal cancer, so we're not talking about something that's really quite a little bit of academic argument. This is a very, very big thing.

If this was me, and if it was me, and I had said this, the first thing I would want would be to get somebody to say yes, you're right because it would take the weight off your shoulders. It would show confirmation. It would show acceptability amongst the community. If you showed the slides to somebody else and said well, actually you're right. There is a new disease here -- so these slides have never been passed around.

The slides exist of the original Lancet 12. They're being examined at the moment in the UK because Wakefield and colleagues are under fitness to practice procedure, but it would seem to be common sense to try to get some independent corroboration of his observations.

Q And when you use the word "anonomize," is that the same thing as what we refer to as blinded?

A Blind. It would take about a day. All you do is you tape over the slides, send them to somebody and say what do you think? It's not hard. It's really easy.

Q Are these studies by Drs. Wakefield, Uhlmann and Ashwood currently viewed by the scientific community as credible and reliable?

A No, completely incredible and unreliable.

Everything that Wakefield has done now is actually considered to be -- unreliable I think is the best way to say it.

Q Has Dr. Wakefield's data ever been confirmed?

A No. In fact, it's quite the reverse. Everything Dr. Wakefield has done has always been not confirmed wherever it is possible to do it.

Q Now, you've published this year an article analyzing these studies, and I'm referring to Respondent's Exhibit A at Tab 1. Why? Why did you feel the need to publish that article.

A I think my co-author was Professor Paula Domizio. There was a great deal of frustration in the UK when after five or six years of a lot of work and a lot of effort, the expert witness testimonies of the claimants and the defendants were in October 2003 when the case collapsed after the legal aid in the UK decided to withdraw support for the UK litigation.

I personally was very keen from my report and for what I had found going over the primary data of Wakefield for this to get to the public domain. I was particularly concerned that despite this in the UK that Wakefield had been continuing to promulgate this idea that these children had this serious disease.

Paula Domizio and I -- Paula, who was also involved in this because she supplied the samples for the original autistic enterocolitis study and actually felt rather bruised -- felt that the good thing for us to do was just to systematically analyze the papers, and I make no bones about it, this was lifted from my expert witness report, but I was possible to do it because these papers were in the public domain, so we felt that we had to reach out to a broad --

Q You mean your expert witness report in the UK litigation?

A That's right. That's right. We felt that we had to reach out to a broader audience and just point out to people the difficulties with this idea of so-called autistic enterocolitis, about whether this is a disease or not or whether in fact it was merely an invention for the UK litigation, and I think this is perfectly valid.

Wakefield had a chance to answer. He made some comments in response to the article, and we have another letter coming out in our response to Wakefield's comments.

Q Doctor, in your opinion, is there credible medical evidence showing that there exists a phenotype known as autistic enterocolitis?

A No.

Q Doctor, you've been privy to more information about these studies than what you wrote in your article and shared today in the courtroom. Is that correct?

A Yes, very much so.

Q And are you allowed to discuss the additional evidence that you've been privy to?

A No.

Q Why not?

A Because it's still sub judice in the UK. If I wish to discuss it, I think we'd have to make an appeal in the same way as Professor Bustin was allowed to discuss his expert witness report. I'm not allowed to discuss it.

Q Doctor, I'd like to bring this back to the facts of this case, and Dr. Wakefield claimed to have found an enterocolitis in a subset of autistic children, and he termed the phenotype autistic enterocolitis, and Dr. Corbier invokes this phenotype as a plausible biological mechanism for Yates' autism. What is enterocolitis?

A Enterocolitis is inflammation of the small intestine and colon.

Q So to have enterocolitis, one has to have

inflammation of the ileum, small bowel and of the colon, correct?

A Yes, yes.

Q According to the medical records, did Yates have inflammation of the ileum?

A No.

Q In fact, did Dr. Buie find lymphoid nodular hyperplasia in the ileum?

A No.

Q So Dr. Corbier's claim that Yates has autistic enterocolitis, yet Yates' clinical profile doesn't even fit this made-up definition of autistic enterocolitis. Is that correct?

A Yes.

MS. RICCIARDELLA: I have no further questions.

THE WITNESS: Thank you.

THE COURT: Thank you. Mr. Webb?

MR. WEBB: I thought this would be a good time for lunch and give me an opportunity to prepare my cross-examination as well?

THE COURT: My thought would be that you not only prepare your cross, but you also give some thought to your closing we may do after your cross and some time for redirect, but I would anticipate we'd

sort of roll right in to complete.

MR. WEBB: Absolutely.

THE COURT: I'm sorry?

MR. WEBB: I will also say that we will have a very brief rebuttal testimony from Mrs. Hazlehurst.

THE COURT: Okay. All right.

MR. WEBB: So I can understand schedule-wise, my cross-examination will not be lengthy.

THE COURT: We are in recess. Eat and prepare, think, and we'll return at 2:00 p.m. Thank you.

(Whereupon, at 1:00 p.m., the hearing in the above-entitled matter was recessed, to reconvene at 2:00 p.m. this same day, Thursday, October 18, 2007.)

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A F T E R N O O N S E S S I O N

(2:00 p.m.)

THE COURT: We're back on the record. Dr. MacDonald, you are still under oath. If you would come back?

Whereupon,

DR. THOMAS T. MACDONALD

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

THE COURT: Mr. Webb, to proceed.

CROSS-EXAMINATION

BY MR. WEBB:

Q You're not a medical doctor. Are you?

A No, I'm not.

Q You don't treat children?

A No.

Q How much were you paid by the defendants in the UK litigation?

A Over I think a five-year period I think I received about 70,000 pounds.

Q Over what period of time?

A Five years.

Q Thank you.

A 1998 to 2003. It's actually probably six

years, inclusive.

Q Have you been an expert witness in any other vaccine injury litigation?

A No.

Q Did I understand your testimony that the article critiquing the various articles from Dr. Wakefield and his colleagues relied upon some of the work that you had done in the UK litigation?

A Yes.

Q Do you believe that lymphoid nodular hyperplasia is a normal finding?

A Yes.

Q If you might turn to its -- Attachment 19 in your report, the Kokkonen and Karttunen article?

A Can I just have a moment to dig this out?

Q Sure. If I can figure out, I'll tell you where it is in your report as well.

A Is it the Turunen and Karttunen article? The Lymphoid Nodular Hyperplasia and Cow's Milk Hypersensity in Children with Chronic Constipation?

Q Yes. Lymphoid Nodular Hyperplasia of Mucosa of the Lower Gastrointestinal Tract in Children?

A No. I've got --

Q An Indication of Enhanced Immune Response.

A I don't have that one.

MS. RICCIARDELLA: We have a copy; we'll just give it to the witness.

THE WITNESS: Okay. Thank you. Yes.

BY MR. WEBB:

Q And do you have your report in front of you as well?

A Yes.

Q Did you cite the Kokkonen and Karttunen article that's Respondent's Exhibit A, Attachment 19 for the proposition that lymphoid nodular hyperplasia is a normal finding?

A Yes.

Q Did the authors of the Kokkonen and Karttunen article believe that lymphoid nodular hyperplasia was a normal finding?

A No, I wouldn't say that. No. What they said was it was weakly associated with food allergy. They said, "In conclusion we find formal evidence that lymph node hyperplasia on the mucosa of the colon is not just an innocent bystander. If detected on the colon it seems more suggestive of gastrointestinal food allergy being diagnosed in the terminal iliem. It also may relate to a variety of immunological states. The analysis also presents options to pediatric endoscopists that the TI should always be reached."

Q Excuse me. Lots of us couldn't hear that.

A I was just summarizing what the conclusion was.

THE COURT: We'd like a page cite and the court reporter --

BY MR. WEBB:

Q Could you point to what part of the article you're reading?

A I was reading the conclusion at the end of the discussion.

Q And could you now read it a bit slower?

A I'm sorry. I'm Scottish, so I was speaking Scottish, not English.

THE COURT: And a page cite please?

THE WITNESS: It's on page 46, "In conclusion, we find formal evidence that lymph node hyperplasia on the mucosa of the colon or terminal ileum is not just an innocent bystander, et cetera, et cetera." I think in terms of where you're going, I think actually I would go back to the title of the paper which has a question mark.

BY MR. WEBB:

Q I was scrolling down when you stopped reading. That whole conclusion reads, and tell me if I'm incorrect, "In conclusion, we found formal

evidence that LNH on the mucosa of the colon or TI is not just an innocent bystander. If detected on the colon, it seems more suggestive of gastrointestinal FA. Being diagnosed on the TI, it may be related to a variety of immunological states. The analysis also presents options to pediatric endoscopists that TI should always be reached."

A Yes.

Q Do you believe that lymphoid nodular hyperplasia in autistic children is caused by constipation?

A I think if I was to weigh up the wealth of evidence of what the cause of it was, I would actually say that it's more likely that it's due to constipation and something of contents in the colon and the ileum because it fits the immunology better. It fits the variety of other related pieces of evidence together.

I think that when you're faced with the presence of lymphoid hyperplasia, and you look at what constipation, autism, measles virus and look at the relative evidence for these things, I believe the evidence is much, much stronger that it's related to constipation because there's a very good immunological reason for why that should be.

Q Now, in your report I'd like to turn now I think it's Article 26. No it's not. That's Thilman. The other one by the Finns is 25.

A 25.

Q That is Respondent's Exhibit A at Tab 25, the authors are Turunen, Karttunen and Kokkoren?

A Yes.

Q What did you cite that article for?

A I think this is a very interesting paper actually because I think the children presented with constipation -- so the children came to the hospital, and talked -- I know he examined them because of the constipation, and when he went into their bowel and their upper bowels, he found lymphoid hyperplasia -- they then tried to find out what was causing the lymphoid hyperplasia.

And they produced some evidence, but not fantastically good evidence that actually the constipation was associated with food allergy because when they put the children on a cow's milk-free diet, the constipation went away.

Q So the article doesn't say that lymphoid nodular hyperplasia is a normal finding. Does it?

A I'd have to check. I think that they don't say that, but I'd just have to check, but I'll take

your word for it,

yes.

Q They were of the opinion that the lympho nodular hyperplasia was caused by milk allergies. Weren't they?

A No, I don't think so. I don't think so. I don't think they can make that statement. The children were investigated not because of food allergy but because of chronic constipation. You've got to think about where they started and not where they ended.

Q What do you think caused Yates Hazlehurst's lympho nodular hyperplasia?

A Well, first of all it depends. He doesn't have ileum lympho nodular hyperplasia. He has some enlarged lymph nodes in his colon, and I think it looking at the records it appears as though he falls into that group of children actually who are probably constipated and have some overloading of the colon. The immune system of the gut is there to respond to the things that are present in the gut.

If you have blockages where it's stopping up things, there's constant stimulation, and you see some lymph nodes getting a bit bigger.

Q When you say -- let me just ask you if you're aware of any evidence in the record that Yates

Hazlehurst has

problems with constipation?

A Well, I think he clearly had chronic diarrhea and bloating and a swollen abdomen, and I think that is the picture that was seen in many of the children, who went to the Royal Free, and the papers also in the Royal Free when they actually evaluated over 100 of these children who went to the Free, although many of the children didn't appear to be constipated, in fact were passing frequent watery stools probably because of overflow diarrhea and some of them were treated for constipation as well.

In fact, it turned out they were constipated, so I think the data from the Royal Free was fairly clear. In fact, they said many times that before they did a formal constipation study that all the children were severely constipated. Actually, I looked, and it doesn't actually say anywhere that Yates was chronically constipated. I agree with that.

MR. WEBB: That's all the questions I have.

MS. RICCIARDELLA: I have just a few followups.

REDIRECT EXAMINATION

BY MS. RICCIARDELLA:

Q Just following up on the last question that Petitioner's counsel asked you, what is overflow

diarrhea?

A Overflow diarrhea is when you get fecal impaction and the lumen of the gut, so as the water that comes down and the fluid that accumulates leaks around the bulk of the stool and sort of essentially leaks out through the anus, and you get this constant, and because it's watery, it appears to be the classical-type diarrhea, but it's a diarrhea that's associated with constipation rather than the diarrhea that you see in patients with inflammatory bowel disease.

There is not an issue here about differentially diagnosing the diarrhea that's seen in patients with a real inflammatory bowel disease, and this diarrhea is seen in the so-called autistic enterocolitis. Autistic enterocolitis actually was renamed by Wakefield lymphocytic colitis to take into account the fact that they were claiming that there were more lymphocytes, more mononuclear cells, increased density of cells.

Patients with lymphocytic colitis have profuse watery diarrhea, which is not -- and they also happen to be 60-year-women who usually gets the disease, so I think there's no problem in distinguishing these types of diarrhea.

Q Petitioner's counsel also asked you about

the genesis of your 2007 article that you published with Paula Domizio?

A Yes.

Q And whether or not you relied upon evidence that was adduced during the UK litigation?

A I wasn't asked that. I was asked if that was part of my evidence, and as I think of it, the answer was yes. There was nothing contained in the article that wasn't in the public domain. I didn't rely on anything that was revealed to me in the courts for that article.

Q And what specifically were your duties as an expert in the UK litigation?

A My duties were to the Court and not to Merck or to Lovells. My duties were to look at the data independently. I'm a Presbyterian Scotsman. I have -- I show allegiance to no one. I looked at the data and came to an opinion on it and reported that to the Court.

MS. RICCIARDELLA: Thank you very much.

THE COURT: Mr. Webb?

RE-CROSS-EXAMINATION

BY MR. WEBB:

Q Who paid you the 50,000 pounds?

A Sorry, the 70,000 pounds?

Q I'm sorry?

A Sorry, it was 70,000 pounds.

Q I'm sorry. I heard you wrong. Who paid the money?

A Lovells paid it to me.

Q I'm sorry.

A Lovells, the law company.

Q Do you think that it was inappropriate -- that any of Dr. Buie's care for Yates Hazlehurst was inappropriate?

A No. I think Dr. Buie is a very good doctor. I have a lot of faith in Dr. Buie. I know that unit very well. We send our trainees over to work with his boss, Professor Allen Walker, for many years, and I got a lot of time for Dr. Buie.

MR. WEBB: That's all the questions I have.

THE COURT: Respondent?

MS. RICCIARDELLA: No more.

THE COURT: Thank you very much. You're excused, Dr. MacDonald.

(Witness excused.)

THE COURT: Mr. Webb, did you care to call --

MR. WEBB: We'll call Mrs. Hazlehurst back to the stand.

THE COURT: Mrs. Hazlehurst, first we're

going to open your oath back up to the stand.

Whereupon,

ANGELA HAZLEHURST

having been duly sworn, was called as a rebuttal witness and was examined and testified in rebuttal as follows:

DIRECT EXAMINATION

BY MR. WEBB:

Q Mrs. Hazlehurst, was Yates sick when you saw his pediatrician on February 8, 2001?

A Yes, Yates had been sick for approximately two weeks. He had fever and a purulent discharge.

Q Now, did he have a fever that day?

A I'm not aware if he had a fever the day of the visit. His temperature was not taken. However, previously throughout the two weeks, he did have fever.

Q Can you quantify how sick he was?

A I would say moderate.

Q And is that your judgment or the pediatrician's?

A That's a mother's judgment, and that judgment was based upon the amount of amoxicillin that was given to Yates I believe to be 400 milligrams by mouth BID twice a day for 10 days. At some point I

took it upon myself -- I'm not a doctor,

obviously. However, I did take it upon myself to look in the Physician's Desk Reference, otherwise known as the PDR, and found that the weight of Yates, of 24 pounds and the dosage given of amoxicillin was that of a moderate to severe illness.

Again, I'm not a doctor, however we have seen numerous physicians, and every physician that we've seen that we've shared Yates' medical records and pharmacy records who have expressed an opinion there's five to eight that I can name off the top of my head have all expressed that that was indeed a contraindication for vaccination on February 8, 2001.

Q Was Yates' face expressive during his first year of life?

A Yes, sir. His face was very expressive. Again, I go back to testimony of day one. We all thought Yates would light up a room. Photos taken of him at Christmas and Christening are unbelievable the smile. I only can compare -- I have a second child, and in comparison, Yates was probably more expressive than my second child.

Q Your second child is, what's her name?

A My second child is Sarah Alexander Hazlehurst.

Q When was she born?

A Sarah was born August 21, 2002. I was actually seven months pregnant with Sarah when Yates was diagnosed with autism.

Q How was Sarah's development?

A In comparison of Sarah's development to Yates in the first year, I would say they developed very similar except at the end of the year, it was obvious Yates had developed a little more advanced with imitation, pretend play, and his vocabulary was much larger than Sarah's at the end of her first year. Sarah Hazlehurst is now attending her first year of kindergarten and is doing quite exceptional in a typical classroom as a normal child.

Q Did Yates' autism ever affect his gross motor skills?

A As seen in many, many, many, many occupational and physical therapy reports, it is well documented, and we are very well aware that Yates' motor skills were affected by autism and continue to be affected by autism. One particular memory I would like to point out, I think it was on June 17, 2002, post-autism diagnosis, Tennessee Early Intervention as well as the Kiwanis Development Center came to our home.

They came to evaluate Yates, and he had

actually lost his ability to -- his balance was so off

he couldn't walk up and down stairs, and I noted on those reports their goal was to teach Yates to relearn how to walk up and down steps so that he could play in the back yard.

Q How are Yates' gross motor skills now?

A Yates' gross motor skills are still somewhat delayed.

Q In what way?

A He has an awkward gait. He would still not be able to function in sports. There's still -- our last visit to Dr. Corbier we were worried about Yates' motor skills because his balance was off.

MR. WEBB: Those are all the questions I have.

THE WITNESS: Special Master, I'm sorry. I did forget to mention something with the visit on February 8 with Yates being sick. I apologize. On that day that I mentioned that Yates had a moderate illness, that day, any previous day and any subsequent day we were never given a VIS form.

MS. RICCIARDELLA: I have no questions.

THE COURT: Thank you, Mrs. Hazlehurst.

THE WITNESS: Thank you, Special Master

(Witness excused.)

THE COURT: Mr. Webb, are you prepared to

make your closing remarks?

MR. WEBB: Yes. I don't have a lot to say.

THE COURT: To proceed.

MR. WEBB: What we hoped to do this week is demonstrate the nature of Yates Hazlehurst's autism, and provide a profile of children in whom the onset of regressive autism after MMR vaccination suggests a causal relationship.

What we have demonstrated I hope, is that Yates Hazlehurst developed normally for the first year of his life, that he received an MMR vaccination and a few other vaccinations just before his first birthday, that he was sick at the time and that he remained sick for the next couple of weeks and about 10 days after, he had a rash. More importantly, in terms of critical factors he began regressing.

The first symptoms of his autism occurred in March with his wild behavior, his reduced interest in his mother, reduced interest in his cousins, reduced interest in his toys, and that regression -- he continued to regress during the spring, summer and fall. By June he was self-limiting his diet and we saw in the video tape in the very first of July some of the few symptoms -- the very end of June, first July some of the first symptoms of self-stimulatory

behaviors.

By the fall, he had a great deal -- many self-stimulatory

behaviors. His speech declined beginning sometime maybe late spring early summer and that by fall his functional language had been replaced by what might be described almost as a savant level of interest in vocabulary and letters and numbers.

I think that what we have done -- also of importance in terms of the profile that we maintain suggests a causal relationship is that late June early July, the first time that it was noted was the trip to Norway, he developed serious, clinically significant gastrointestinal symptoms that were chronic for the next almost three years, and that is the combination that we think suggests the causal relationship between the MMR vaccination and the autism.

Normalcy before, onset within a few months after, and the presence of clinically significant gastrointestinal symptoms that are chronic. We also believe that Dr. Corbier said on the stand that the case for thimerosal contributing to Yates' illness is less powerful, but he testified that laboratory values in profuron (sic) and glutathione suggests that Yates had an excessive exposure to mercury, which could affect him both immunologically and neurologically.

I believe that the evidence on, if you will, what happened to Yates Hazlehurst is very clear. The

much harder question of course is whether in fact that profile does in fact suggest cause and effect. It's a highly controversial area. I believe that Dr. Corbier explained our position very well. I believe his demeanor and his understanding of the issues made his testimony highly reliably and highly credible.

I also believe, and though I don't claim to be objective, that we've heard testimony from the Respondent's experts which was reflected a willingness to overstate their case. Dr. Wakefield's work is controversial, and many doctors have rejected it. It has not been thoroughly discredited. There are works by independent laboratories and physicians, which collaborate parts of his work.

There are substantial numbers, though I suspect a minority of the medical community that considers it important and reliable work. Now, the point by point analysis of whether the theory is reliable certainly requires the kind of detail that we could provide in posthearing briefs, but the point I want to make is that, this is not just Andrew Wakefield's theory.

It is a profile that many other reliable, honest, hard-working doctors believe suggests a causal relationship between vaccination, specifically the MMR

vaccination and regressive autism, and we think when you have an opportunity to evaluate all of the evidence, including that from the Cedillo case and this case and presumably some additional evidence from the Snyder case, it will demonstrate the fact the MMR vaccine, in concert with thimerosal-containing vaccines in fact caused Yates' autism.

THE COURT: Thank you, Mr. Webb. From Respondents?

MR. MATANOSKI: Thank you. I'll be presenting the closing argument. May it please the Court, ma'am. During the lunch break, one of our paralegals here pointed out to me that the Boston Globe yesterday had an article in it. The article reviewed immunization rates I believe in Vermont. I haven't read the article.

The interesting thing to take away from that article was that immunization rates were going down, and the article talked about the 1998 Wakefield study as one of the reasons why those immunization rates were going down. Now, it isn't that physicians or physician organization like the American Academy of Pediatrics or health organizations such as National Institutes of Health or the World Health Organization believe that there's any link between MMR vaccine or

even thimerosal-containing vaccines in autism.

But there is a belief that's being perpetuated and particularly acutely in this country, so what we're dealing with in this case is vitally important just as it was in Cedillo. This is going beyond our usual cases that are specific a one-time condition that we're looking at, a one-time claim of an autoimmune disease or something of that nature. This is actually has extremely great relevance to what's going on in this country at least right now.

Petitioner's here set out to prove that MMR vaccine or thimerosal-containing vaccines or perhaps both caused Yates Hazlehurst autism. They failed. They failed on several counts. They failed both on the general causation, which of course you had before you with both the Cedillo information on that as well as the new information you've heard here from Dr. Corbier as well as Drs. McCusker, MacDonald and Rust.

They also failed on a factual basis, that is even accepting the premises that they laid before you, the profile if you will as Dr. Corbier called it. The facts don't fit that. With respect to thimerosal-containing vaccines. Whether there's a good scientific basis for believing that they can cause autism, where do we stand now after Cedillo having

heard from Dr.

Corbier. He didn't add anything new.

Instead, he looked at the same studies that had been looked at by the experts for the PSC in Cedillo, but we have heard a little bit different view now, another way of looking at that question from Respondent. Dr. Rust framed it analytically in an interesting fashion and used evidence to support that analytical framework. He said let's think about this from a neuropathological standpoint.

What does the neuropathology look like in these children who have autism, because there's been work done by Drs. Baumann and Kemper looking at patients who have autism. Now, these were older individuals to be certain, but as Dr. Rust explained, the architecture is in place, though observed at autopsy in these older patients, that brain architecture was in place at the age that we're considering right now, the age soon after birth up to one, two and three years.

So, it is relevant to look at that pathology and try to draw some conclusions if you will about what the brain looks like in an autistic individual. The structure as he explained is very different from the structure you see in a toxic insult case, so that doesn't really fit the hypothesis that's before you

that thimerosal-containing vaccines can cause autism. The pathology doesn't support it. He also said let's think about this from a clinical standpoint.

From a clinical standpoint, what happens if you are exposed to heavy metals and have brain damage? You have deficits to be sure, and sometimes those deficits can be in quite specific areas, and I know that we've had articles submitted in the Cedillo case, works by Drs. Magos and Clarkson that talk about mercury and what you can expect when there's a toxic insult to the brain from the mercury exposure. There are some specific neurologic symptoms that one could expect, a narrowing of the visual field, for example.

There are no savantisms. There are no paranormal behaviors, and that is one of the specific unusual features of autism that sometimes these individuals very frequently develop behaviors and abilities that are beyond our understanding because they seem to transcend some of the abilities or the functions that other individuals have that are not afflicted with that terrible condition.

We heard -- it's interesting that it came up in this case because we heard in this case about Yates' extraordinary abilities at a very young age in counting and identifying letters. I would also put in

that category some of the fascinations that autistic children and later individuals have to fascinations with spinning, turning wheels, tires. These are very specific behavioral aspects. You don't see them with an insult that's damaged an area of the brain and just taken out function.

Dr. Rust explained how this clinical picture is very specific to autism and very different from a clinical picture from a toxic insult. With respect to MMR alone, Dr. Corbier really didn't add anything there that you hadn't heard in Cedillo. It was the notion that measles virus persists and somehow it gets into the brain, affects the brain. Now, interestingly, that isn't actually Dr. Wakefield's theory of MMR causing autism, but it is the theory that you heard in Cedillo and here once again.

There's no support for that. There's no support for -- the model that Dr. Corbier went to is the same model that was used in Cedillo. It's SSPE, subsclerosing panencephalitis or measles inclusion body encephalitis. Yes those are models of persistent measles virus. Those models actually work against the claim that it can cause autism. First of all, SSPE and MIBE do not result -- I believe I was moving away from the microphone.

I just got a look from the court reporter.

They don't result in autism. If we saw that, then we ought to see autism after measles epidemics, right? We ought to see that when SSPE occurs. That isn't what happens. You heard quite clearly again from Dr. Rust that it coordinated with what you had heard already by preeminent virologists, Dr. Griffin and Dr. Ward.

The result in SSPE and MIBE is death. That's what happens to the individual who suffers that. The timeframe that Dr. Corbier used for SSPE showed that he does not have a very good understanding of the condition. He said he believes that it occurred at one to eight months afterwards, and that was one of the building blocks for his profile that he introduced in this case. It doesn't happen one to eight months after exposure to measles virus. It happens years later.

You also heard on this notion that the MMR can cause autism. You've heard now from Dr. MacDonald. Dr. MacDonald added to the evidence that you had heard previously in the Cedillo case. He has had firsthand review of the data, and unfortunately because only a limited amount of what he can say has been made available, he cannot share with the Court fully what he's been able to look at.

But the words that he used, which echo, and he wasn't here to hear Dr. Rust, but they echoed the words that Dr. Rust used: Scientific fraud. Now, for two individuals, who are engaged in scientific research such as Dr. MacDonald and Dr. Rust to use those very strong terms, people who I think you can tell Dr. Rust and Dr. MacDonald are not given to overstatement. They actually have to feel very strongly about the evidence to use those terms.

This isn't just an interpretation of data. I think one of the things you saw today is something that was similar to what happened when Dr. Bustin when through categorically the information. Dr. MacDonald pointed out to you that series of panels from one of the articles, A, B, C, D, and he in closely looking at them had seen that there are dates and times on those panels. Well, if you've gone through a colonoscopy, you know it's not a quick procedure. It is a time-consuming procedure.

Panel A in that article was represented as a normal child. Panel D was represented as a child, who had significant involvement in his colon. They are the same individual. It was the same colonoscopy. It was merely the device being moved further along in the same individual. Now, how can it be both normal and

abnormal.

This is the kind of data that's out there if you look hard enough and examine what Dr. Wakefield has put out, at least in public what one can see. Dr. Wakefield received 50,000 pounds from a lawyer. He received most of his patients in that initial 1998 study from that same lawyer. He then set about doing a study after receiving that money and publishing the results. Before he even published those results, he took out a patent for measles-only virus vaccine.

As I've said in the last case, he not only financially gained from his participation before he ever published a single word on measles virus causing autism, but he had his financial interest in implicating MMR vaccine and creating a market for a vaccine that he patented, a measles-only vaccine that he patented because his theory said that somehow the three working together cause autism, allows measles virus to replicate in the gut and then cause autism.

It has taken years to unravel that in England. The litigation fell apart, which unfortunately meant that much of the information that made the litigation fall apart never saw public light. They're still recovering from the public health scare that was created there. We are undergoing in our

country right now and maybe are yet to reap the whirlwind from that public health scare that he initiated there many years ago.

There's no disease of autistic enterocolitis. It's an illusion that was conjured up by Andrew Wakefield to try to somehow make nonspecific gut findings into a condition that he could call significant. It's not accepted by anyone of any repute in the gastroenterological field. You can't go to a DSM and get a classification and put a classification down that will say autistic enterocolitis.

We unfortunately have to continue to deal with this though until the scientific community has at least already to the extent they can put this to rest, and we're going to have to deal with it in this courtroom and eventually put it to rest. Now, Dr. Corbier really didn't give much of an explanation of how the two combined, MMR and thimerosal-containing vaccines, can cause autism. I think he used the word synergism. I don't really think that it was very well explained.

If you look back at Cedillo, the idea I believe was that thimerosal-containing vaccines made one more immunologically suppressed, and therefore

there was a greater chance of measles virus could grow in the gut and then somehow make its way to the brain. There's no support for that, but beyond that if you look at the facts of this case, there's certainly no support that the immune system here was compromised. We've heard some testimony that Yates had a certain number of infections.

We've also heard from Dr. McCusker and Dr. Rust for that matter that those aren't beyond the expected norm, but beyond that, there was diagnostic testing done. Diagnostic testing that was normal, so there's absolutely no support that thimerosal-containing vaccines affected Yates' immune system in any way, if that happens to be the theory, though again was very poorly explained, at least in my view.

I think you have to at this point take a step back and lay the relative credentials of the experts that you just heard before you and go through who do you think represents the better take on reliable science here. Is it Dr. Corbier, or is it Drs. MacDonald, Rust and McCusker. I'll go through a little bit of Dr. McCusker. She represents, she a clinical -- she's a clinician in immunology, a pediatric immunologist.

She's a research director at her

1 institution. She sees hundred of kids each year for

immunological diseases. She's a teacher. She teaches medical students at McGill University. Dr. MacDonald, research director as well. As a matter of fact, he's Dean of Research, attended on thousands of colonoscopies. He's authored over 150 articles.

He had direct access to data relating to the reliability of the Wakefield studies and the Unigenetics lab, practicing for many years. Dean of Research; I just want to focus on that for a moment. Dean of Research means that he directs as he said the research direction of a major research institution with a $75 or $75 or $78 million annual research budget.

It's important to think about in the terms of what I laid out in our opening statement about what's reliable science, where is reliable science in these issues. He needs to figure out where the money is spent. Where should we start doing research? Where are there good avenues to follow, so I think his views in that regard bear particular attention.

Dr. Rust, he's Child Neurology Society's Man of the Year. He's done years of clinical practice at a major university. He's published over 100 articles. He's really an esteemed educator of doctors. Now, you asked a question of him, Special Master, and one of

the beauties of this inquisitorial process is that there is direct involvement with the bench, and it was a question I wish we had thought of because the answer that you got was I thought very enlightening on the issue of reliability of the evidence.

You asked Dr. Rust what did you mean by conventional peer-reviewed literature. He told you what I mean is the literature that's sufficiently reliable if you will that we should pay attention to it, that our time is well-spent reading it, and our time and our research efforts are well spent following up on the types of things that are being reported in that literature.

His view was that the conventional peer-reviewed literature does not support any of these hypotheses. They're not worth following up on. In other words, they don't represent the view of reliable, reputable scientists. I'm almost done. I'd really appreciate your indulgence. I did want to mention one thing about an expert, who did not appear here, but his name has been mentioned several times, and that was Dr. Zimmerman.

Dr. Zimmerman actually has not appeared here, but he has given evidence on this issue, and it appeared in the Cedillo case. I just wanted to read

briefly because his name was mentioned several times by Petitioners in this matter. What his views were on these theories, and I'm going to quote from Respondent's Exhibit FF in the Cedillo case, which is part of the record in this case as I understand it.

"There is no scientific basis for a connection between measles, mumps and rubella MMR vaccine or mercury intoxication in autism despite well-intentioned and thoughtful hypotheses and widespread beliefs about apparent connection with autism and regression. There's no sound evidence to support a causative relationship with exposure to both or either MMR and/or mercury."

We know his views on this issue. Now, that's on one side. I understand, but we are observing that that side is where reliable science is on this issue. On the other side, and I don't want to sound like I'm going to run down an expert for the Petitioner, but unfortunately I think it will sound like that. On the other side, what you've had added to the evidence that you had in Cedillo is Dr. Corbier's testimony.

I said I don't want to sound like I'm running somebody down, but I believe this is vitally important to lay the credentials of the scientists

against one

another. Dr. Corbier has been a doctor all of seven years. He's affiliated with no university. He's never held an academic position. He's the author of zero papers on autism and peer-reviewed literature, of zero papers on immunology and peer-reviewed literature, of zero papers in gastroenterology and peer-reviewed literature, in fact in any literature.

He's gotten his name in print by virtue of paying for it. He's added nothing to the scientific community's understanding of autism, immunology or gastroenterology. If you have any question about where his views are, his book is actually a manifesto of beliefs. If you have any question about -- if you entertain an idea that his views represent the views of scientists, researchers and medical professionals, who follow scientific principals in doing their research, I commend his book to you for reading.

Where does reliable science stand? Does it stand with Dr. Corbier, or does it stand with Drs. Rust, McCusker and MacDonald? Thank you.

THE COURT: Thank you. This concludes this aspect of the proceedings in the Hazlehurst case. The parties will have an opportunity to submit posthearing briefing, and the schedule for such filings has already been addressed with the parties. A read-only

transcript of this proceeding and an audio version of this proceeding will be available on the autism portion of the website of the Court of Federal Claims after five working days.

Before we depart, I want to thank the Hazlehurst family for sharing during this proceeding your experience with Yates. I extend to you my sincerest sympathies for the challenges that you face with Yates. I also want to thank counsel and the experts who have testified on behalf of the parties for your careful preparation in connection with this hearing. Lastly, I wish you all a safe return to your points of origination. We are adjourned.

(Whereupon, at 2:54 p.m., the hearing in the above-entitled matter was concluded.)

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REPORTER'S CERTIFICATE

DOCKET NO.: 03-654V

CASE TITLE: Hazlehurst v. HHS

HEARING DATE: October 18, 2007

LOCATION: Charlotte, North Carolina

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: October 18, 2007

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