UNITED STATES
COURT OF FEDERAL CLAIMS

THERESA CEDILLO AND MICHAEL CEDILLO, AS PARENTS AND NATURAL GUARDIANS OF MICHELLE CEDILLO,	)	
Petitioners,	)	
v.	)	Docket No.: 98-916V
SECRETARY OF HEALTH AND HUMAN SERVICES,	)	
Respondent.	)	

Pages: 299 through 575

Place: Washington, D.C.

Date: June 12, 2007

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IN THE UNITED STATES COURT OF FEDERAL CLAIMS

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SECRETARY OF HEALTH AND HUMAN SERVICES,	)	
Respondent.	)	

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

Tuesday,
June 12, 2007

The parties met, pursuant to notice of the Court, at 9:02 a.m.

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

APPEARANCES:

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C O N T E N T S

WITNESSES:	DIRECT	CROSS	REDIRECT	RECROSS	VOIR DIRE
For the Petitioners:					
Theresa Cedillo	306	378	--	--	--
Arthur Krigsman	408	491	556	--	--

E X H I B I T S

PETITIONERS' EXHIBITS:	IDENTIFIED	RECEIVED	DESCRIPTION
1	478	--	Dr. Aposhian's presentation
2	478	--	Dr. Krigsman's presentation
3	478	--	Poster presentation on autism
4	478	--	Calendar
5	567	567	Document entitled "Autism Speaks Hosts Gastroenterology Workshop"
6	569	569	Dear Doctor letter

E X H I B I T S

RESPONDENT'S EXHIBITS:	IDENTIFIED	RECEIVED	DESCRIPTION
1	573	573	Pages from the Thoughtful House website
2	573	573	Minutes regarding licensure in Texas

P R O C E E D I N G S

(9:02 a.m.)

SPECIAL MASTER HASTINGS: Let's come to order this morning. Good morning to all, and thank you for being here.

We're here for the second day of the Cedillo hearing, and where we left off yesterday was during the middle of Mrs. Cedillo's testimony.

Before we start with her, I just want to advise counsel and witnesses today we did understand that a number of the people listening in were having trouble hearing, so I really want to stress to counsel and witnesses to speak as loudly as you can into the microphones.

I'm told nearly 750 people were listening in at some point yesterday, different phone connections, so it's very important that they can hear what we're saying so please do speak up so everyone listening at home can hear as well.

With that, Ms. Chin-Caplan, did you want to start in with Ms. Cedillo again?

MS. CHIN-CAPLAN: Could we just have about five minutes? We're having a little trouble with the video here.

SPECIAL MASTER HASTINGS: All right.

MS. CHIN-CAPLAN: If we cannot restore the sound I'm just going to bring Mrs. Cedillo back for a little bit, but unfortunately we'll have to go with the unedited version of the DVDs, and we'll fast forward through certain scenes.

SPECIAL MASTER HASTINGS: All right. For those of you at home, we'll be having about a five minute delay here before we start.

(Pause.)

MS. CHIN-CAPLAN: Special Master?

SPECIAL MASTER HASTINGS: Yes?

MS. CHIN-CAPLAN: We are ready to resume. What I would like to do would be to bring back Mrs. Cedillo for a very brief direct.

SPECIAL MASTER HASTINGS: All right.

MS. CHIN-CAPLAN: Then we're going to run the video.

SPECIAL MASTER HASTINGS: All right. Ms. Cedillo, please take the witness stand. You've already been sworn yesterday, so please take a seat.

Whereupon,

THERESA CEDILLO

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

THE WITNESS: Can you hear me? Can you hear me okay?

SPECIAL MASTER HASTINGS: I believe so.

THE WITNESS: Okay.

SPECIAL MASTER HASTINGS: Thank you again for being with us.

Ms. Chin-Caplan, please go ahead.

MS. CHIN-CAPLAN: Thank you, Special Master.

DIRECT EXAMINATION RESUMED

BY MS. CHIN-CAPLAN:

Q Mrs. Cedillo, yesterday we were discussing Michelle's inflammatory bowel disease. Is she currently under treatment for her inflammatory bowel disease?

A Yes, she is.

Q And who is treating Michelle's inflammatory bowel disease?

A Dr. David Ziring at UCLA Children's Hospital.

Q When did you start to consult with Dr. Ziring?

A In November of 2006.

Q And when you first saw Dr. Ziring, what did he tell you?

A He told me that Michelle was very sick.

Actually, the first time he saw her he wanted her to begin anti-TNF therapy.

Q And do you know what TNF stands for?

A Tumor necrosis factor, so it would be an antitumor necrosis factor therapy.

Q And did he tell you what the purpose of this anti-TNF therapy was?

A It is to control the bowel inflammation, and he had hoped it would also control the secondary arthritis and eye problems, uveitis.

Q So was it your impression that when Dr. Ziring saw Michelle he believed that her arthritis and her eye problems were related to her inflammatory bowel disease?

A Yes.

Q And did Michelle subsequently start this anti-TNF therapy?

A Yes, she did.

Q Does it have a particular name?

A Humira. Humira injections.

Q And you said it was injections?

A Yes.

Q Who administers the injections?

A I had to be trained to administer them myself.

Q And did you learn how to administer these injections?

A I did, yes.

Q Where did that occur?

A That occurred at UCLA Medical Center.

Q And when did you go to learn how to administer this?

A That was about three weeks ago. I'd have to look at a calendar to give you the exact date, but approximately three weeks ago.

Q And at that time did Michelle receive her anti-TNF therapy?

A Yes, she did.

Q So she received her first dose at UCLA?

A She received her first dose. It's called the Crohn's starter pack.

Q And when they told you that they wanted to start her on Humira did they tell you what the potential side effects of Humira could be?

A Yes, they did.

Q And what did they tell you?

A Well, the one they talked about the most is there is a potential to develop cancer, and if I'm saying it right I think it's lymphoma. In the studies it was seen in adolescent girls.

However, Dr. Ziring said that the children that were more likely to get it were also on another immunosuppressant, so to try to offset that risk at the time we decided to make sure that she was only on the one immunosuppressant, which would be Humira.

Q Is she taking any other bowel medications right now?

A Yes, she is.

Q And what else is she taking?

A She's taking Prevacid for GERD and then Sulfasalazine.

Q For her bowels?

A For the bowels.

Q How many treatments has Michelle undergone?

A How many treatments?

Q Treatments of Humira.

A Okay. She's had two. They're every two weeks.

Q And is there a set schedule that you administer the Humira? Is that it?

A Yes. It's every two weeks. You began with the higher dose. Then the second dose is half of the first, and then the subsequent doses are half of that one.

Q And at some point in time do they believe

that this therapy is going to end?

A I've not been told an ending point. I think it depends on the response time. I'm sorry. It depends on her response, and then if she continues to show a positive response or if she plateaus. I mean, it could be indefinitely or unless she were to have a side effect.

Q And have you spoken or seen Dr. Ziring since you began the Humira?

A Yes, I have.

Q And did he indicate anything about the treatment at all?

A Yes, he did.

Q What did he say to you?

A I'm quoting from memory. It may not be the exact words, but he said something like that he was amazed by her response to the Humira from her most recent labs, which were taken a week after she had started it, compared that to previous labwork that was taken three weeks prior to that, and he hoped that she would continue to respond in this manner.

Q Now, you indicated that he was happy with the improvement in her labwork.

A Yes.

Q Did you notice any change in Michelle's

clinical condition?

A Yes. At home she began making very formed stools, as opposed to loose or loosely formed stools, and that was the first.

She also seemed to walk with a little more ease, but that's something we need to gauge with a little more observance.

Q Okay. Now, Dr. Ziring is Michelle's current GI physician, correct?

A Yes, he is.

Q Who is Michelle's current rheumatology person, the person who sees her for her arthritis?

A The last one that she saw is Dr. Ilona Szer at San Diego Children's Hospital.

We were thinking of doing a consult with the one that works with Dr. Ziring because it's easier with two doctors that work together, but that was her previous rheumatologist or last seen. I guess she's still current. I don't know how you put that.

Q Now, when did you first start seeing Dr. -- I'm sorry. I missed the name.

A Dr. Szer or which?

Q The current rheumatologist.

SPECIAL MASTER HASTINGS: Both counsel and the witness, speak up a little bit more.

THE WITNESS: Even more? Okay. Okay.

BY MS. CHIN-CAPLAN:

Q The current rheumatologist. When did you begin to see him?

A Okay. We saw her in I believe it was March of 2006 for the current one.

Q And at the time that you saw her, what was Michelle's arthritis like?

A I mean, to me it was moderate. I would say moderate to moderate-severe.

Q And when you say moderate to moderate-severe, what do you mean by that?

A Okay. She still had trouble. Her left ankle, I don't know the right medical term, but it was kind of like locked in place. She couldn't flex it down. It was still that way. She had some slight swelling in her ankle, the last one.

She was sore to move or lift her back, and I believe at that point, or it might have been at a previous doctor's appointment, they said they felt that her hands, the joints in her hands, were affected.

I'm just talking from memory. It was close to that timeframe. If it wasn't her, it was another doctor that had mentioned about her hands.

Q And was any treatment ordered for the arthritis at all?

A She deferred to the GI doctor to order. She thought she should be put back immediately on Remicade.

Q So she had been on Remicade?

A She had been on Remicade previously before she broke her leg.

Q And is Remicade also an anti-TNF agent?

A Yes, it is.

Q When was she on the Remicade?

A She began in June of 2004.

Q And who started her on the Remicade?

A It was two doctors consulted about it. It was Dr. Robert Sheets, who works with Dr. Szer at San Diego Children's Hospital, and Dr. Arthur Krigsman.

Q And at the time that they ordered the Remicade, what was Michelle's response to the Remicade?

A She responded very well. She was steroid dependent prior to the Remicade. Without the steroids, she had chronic diarrhea and could not -- well, she was to the point of having to crawl instead of walk with the arthritis part of it.

Q To get a clear picture of the treatment for

her inflammatory bowel disease still, I'm going to ask you to go back to when she first began treatment for her inflammatory bowel disease.

A Okay.

Q Who was the first person who ordered treatment for her inflammatory bowel disease?

A Okay. Not counting the GERD?

Q Well, let's start with the GERD. Could you just tell the Court what GERD is?

A I'm sorry. It's gastroesophageal reflux disease.

Q And when was that first noticed?

A That was first noticed in June of 2000.

Q And who noticed that?

A That was Dr. Ramon Montes.

Q And was that when Dr. Montes did one of his endoscopies?

A Yes, the upper endoscopy.

Q And do you recall what that endoscopy revealed?

A Yes, I do. That showed an ulcerated esophagus, a Grade III ulcerated esophagus, which is the worst grade. There's Grade I, II and III, according to what I understand.

Q And you said it was ulcerated?

A Yes.
Q Was it ulcerated in a particular area?
A I believe it was the entire or close to the entire esophagus.
Q And earlier you had mentioned that Michelle would hit herself in the chest.
Did anybody tell you whether there was any correlation between striking herself in the chest and the ulcerations that were seen in her esophagus?
A Yes.
Q Who made that correlation for you?
A Dr. Montes did.
Q And after Dr. Montes did this endoscopy he ordered some medication for Michelle, didn't he?
A Yes, he did.
Q What medication did he order?
A He ordered Prilosec.
Q And did the Prilosec help Michelle's symptoms?
A Yes, it did.
Q How did it help?
A The hitting on the chest disappeared. She seemed happier. She vomited less frequently.
Q And did it affect her stools at all?
A Not really. She still continued to have

diarrhea.

Q And after that Dr. Montes continued in her care? Was that it?

A He did continue for probably about a year and a half after that.

Q And after the Prilosec what did Dr. Montes do next?

A The next procedure was an upper and lower endoscopy.

Q And when did that occur?

A That was in January of 2002.

Q And do you know what the results of that endoscopy was?

A Yes. She was diagnosed with lymphoid nodular hyperplasia and I believe colitis. I'm not for certain if that was written on the actual diagnosis, but in other subsequent paperwork it listed colitis.

Q And did Dr. Montes order any treatment for Michelle at that time?

A He did. He ordered Pentasa.

Q And were you able to administer the Pentasa to Michelle?

A We tried pulling the capsules apart, but it was very difficult. She required a large number of

capsules per day, so it was hard to get the tiny beads in the amount of food she was eating three times a day.

Q At some point in time did you stop the Pentasa?

A Yes, we did.

Q Was any other medication ordered for Michelle at that time?

A I believe there was a four-day course of Solumedrol or a similar injectable form of Prednisone, but I can't remember the date. I think that was the final medication. I mean, no further medication after that.

Q You indicated Solumedrol, and then Michelle went on Prednisone? Was that it?

A No. Just the injections.

Q Just the injections. So after the injections that would still be in roughly 2002?

A I believe it was prior to that. Well, let me see. No, it would be 2002. Right, because that was the year of the colonoscopy. Right.

Q So from that period of time after the Solumedrol, was Michelle's inflammatory bowel disease treated?

A No, not other than the Prilosec.

Q And when was the next time somebody ordered an anti-inflammatory agent for Michelle's bowel disease?

A That would be in 2003.

Q And so how long between the administration of the Solumedrol and the next time somebody ordered anti-inflammatory medication for Michelle was she not receiving anything for her bowel disease?

A That would be probably close to a 12-month period. I'm guessing that the Solumedrol was in May or am approximating was in May of 2002, and I believe it was all the way until July of 2003 before she began receiving anti-inflammatory medications for the bowel.

Q Okay. And during that approximately one year what were Michelle's GI symptoms like?

A They worsened to a great degree. She had very severe problems.

Q Can you describe to the Court what those severe problems were?

A She had chronic loose stools, chronic diarrhea, many, many bowel movements, up to sometimes 12 in one day.

She was drinking a lot of fluids and not wanting to eat. Then it began like a progression where she was able to eat and drink a little bit, but

then she quit eating and then just started drinking more fluids, which is what led her to have to be in the hospital later.

She got to the point where she would not drink either, and then she was no longer able to stay awake. She wasn't getting anything in her, and she did not have a feeding tube at this point.

Q What did you do when Michelle stopped eating and drinking?

A I took her to the ER in I think it was in late May of 2003, and she was admitted for dehydration, and she actually had a urinary tract infection at that point.

Q And did they tell you what the cause of the urinary tract infection was?

A It related to dehydration. She was not taking enough fluids in.

Q When they discharged her from the hospital, what did they tell you to do?

A Well, she was on antibiotics. She had received IV antibiotics I think at that point, and I believe when we took her home -- she was in probably five to seven days -- we had a few more antibiotics, but given via an injection because I knew she wouldn't take it by mouth.

I think it was about five to seven days in the hospital and then maybe three more days after that with injections at the pediatrician's office, and then I was supposed to increase her fluids, you know, which I tried to, fluids by mouth.

Q And that was solely for her urinary tract infection?

A At that point, it was. Well, at that point, they tried to get her transferred to Phoenix Children's Hospital to have her bowel disease treated.

Q You say they tried. Were they unsuccessful?

A Yes, the ER doctor was unsuccessful.

Q How was the ER doctor unable to transfer Michelle?

A She called her gastroenterologist at the time and asked. She said she believed that the child needed GI treatment, so she asked that she be transferred from our Yuma hospital, which is a small, nonpediatric hospital, to the Phoenix Children's Hospital, but the treating GI doctor at that time did not want to, I don't know what the term is, accept her or have her admitted there. I don't know the medical term.

Q And did anybody indicate to you what the reason was that the GI doctor would not accept the

transfer?

A It's not in writing, but he told me that he felt that he was a specialist, he was very busy and that this was a general pediatrics problem. He was busy.

Q So Yuma admitted Michelle and they treated her dehydration. Is that it?

A That's correct.

Q And they ordered antibiotics for her urinary tract infection?

A Yes.

Q And did they treat her bowel disease at all?

A They might have given her IV Zantac, but I don't believe there was any other. I'd have to look. I don't think there was any other bowel treatment given.

Q Okay. And after she was discharged you took her on three consecutive days for IM antibiotics? Is that it? For shots?

A Yes, approximately three. Seven, eight, nine, 10. I'm thinking it was a 10-day course.

Q And did you discuss this fact with your pediatrician that Michelle had bowel disease and it wasn't being treated?

A I did loosely, but they're not GI

specialists. Michelle is a very complicated patient, and they deal mostly in general pediatrics. They had offered if I needed help with any referrals, but their knowledge in her particular GI problems I would say is limited.

I don't mean that as an insult because they've worked very well with me and with Michelle, but they were just telling the truth; that they were not equipped to deal with her bowel disease. They felt it was too complicated.

Q So what did you do then?

A After that I remembered that I had seen Dr. Krigsman, met him at a DAN! conference, so I contacted him regarding treatment because I knew it was a serious problem.

Q And did you have a conversation with Dr. Krigsman?

A I did, yes.

Q And did he agree to consult with you?

A Yes, he did.

Q Prior to your visit with Dr. Krigsman did he order a workup at all?

A Yes, he did.

Q And now we're in roughly May of 2003?

A Probably late May/early June. Probably

early June now.

Q When did you see Dr. Krigsman?

A We were unable to see him until September of 2003.

Q And how was Michelle between May 2003 and -- 2003?

A Yes.

Q And the time that you visited Dr. Krigsman in September.

A September 2003. During that time her health actually declined greatly. We were planning to go earlier. We were unable to because she had to be hospitalized for 18 days.

Q And when was that hospitalization?

A That was July 26 through approximately August 8.

Q And you said she was hospitalized for 18 days?

A Yes. Maybe I didn't count right. It was late July -- it was 18 days; I'd have to look at a calendar -- to August.

Q What did they do during this hospitalization?

A Michelle was very sick. She was malnourished. She was dehydrated again. She was

unable to stay awake. This is when she had the eye problem that I referred to yesterday.

During that time she had a nasogastric tube placed for nutrition. She was so sick that 25 ccs, which is a very small amount, she could barely tolerate, a 25 cc drip of nutrition, of formula into her stomach. She started to vomit, so they had to back off and start at five ccs at a time.

Once she had some strength to her, which actually was I think about a two-week period, maybe was a little bit less, they placed a jejunal feeding tube, and then from there we started with the -- that's how they started to treat her to get her nutritional status back to a more stable state.

She was treated with I think IV Zantac and Prednisone or Prednisolone, and then I believe she might have been on another anti-inflammatory for the bowel, but I can't recall. It might have been something like Azulfidine. I'm not sure.

Q So at this hospitalization the doctors who admitted her started treatment for her inflammatory bowel disease, as well as tried to feed her? Was that it?

A That's correct.

Q Now, Michelle was in there for 18 days you

indicated?

A Yes.

Q So at the end of the 18 days that brings us to roughly mid September? Is that it?

A It would be from July 26 to 18 days later, so it was like probably the middle of August.

Q How soon after that did you go see Dr. Krigsman?

A Approximately a month later.

Q When you travel with Michelle, how do you travel with her?

A For her own comfort, we have to kind of replicate her room or what is a comfortable setting for her, so we either ship ahead or at that time we traveled with her favorite toys. At that point she was not in a hospital bed, so we didn't have to worry about getting that set up.

We travel with her favorite things. We had to take her feeding pump, her nutrition, all her medications because the nutrition has to be mixed fresh every day. It's only good for 24 hours, so we had to travel with cans of this nutrition, her feeding pump, the bags, diapers, pads, wipes and everything, the syringes for her feeding tube to give her the medication.

For her sake so that it's not so hard for her we usually lightly sedate her as recommended by a physician. At that time it was a general pediatrician. Now we go by the recommendation of her neurologist.

Q So when you flew to New York, because that's where Dr. Krigsman is located?

A Yes.

Q You packed up everything that you needed to care for her?

A Yes.

Q And you shipped it to New York first?

A Yes.

Q And then you brought all the things that would resemble her room with you?

A Yes.

Q And you had to medicate her?

A Yes.

Q How was she on the flight?

A She was okay on that one. She slept. She slept most of it.

Q Now, you saw Dr. Krigsman at the end of September?

A Yes.

Q What did Dr. Krigsman do?

A He did an upper and lower endoscopy, colonoscopy.

Q And did he tell you what the results of those procedures were?

A Yes, he did.

Q And what did he say?

A He said that she had lymphoid nodular hyperplasia. He saw ulcers. I can't remember the exact place where. I just can't remember. I know he told me where, but I can't remember at the moment.

He said she was very, very sick and was very sick with inflammatory bowel disease.

Q And did Dr. Krigsman order some treatment for her?

A Yes, he did.

Q What treatment did Dr. Krigsman order?

A He ordered anti-inflammatories for the bowel, 6-MP, 6-Mercaptopurine called for short 6-MP, and Azulfidine and Prednisolone.

Q And how was Michelle after the treatment began?

A After the treatment began, I would say maybe a two to three week period after she began having formed stools again, and the arthritis was I guess you could say less noticeable.

Let me say it was easier for her to get around. It was still noticeable, but easier for her to move around.

Q Michelle didn't stay permanently on the Prednisone?

A No. We tried several times to wean her off of the Prednisone.

Q And were you successful?

A No, we were not.

Q So when you were unable to wean Michelle off the Prednisone, what happened then?

A Well, we weaned her off. I mean, like say she was on like a two-week course, for example, and then when we got it down to where we could stop it completely probably within a week's time she was limping, it was very difficult for her to walk, and then she had the chronic diarrhea again.

Q So after she was weaned off the Prednisone was other medicine, other anti-inflammatory medication, ordered for her?

A The same. I think we tried Pentasa, but we couldn't get the beads in the feeding tube and you can't crush it, so we were back with Azulfidine and 6-MP.

Q And all this went into Michelle's tube?

A Yes. Even today all her medications except for the injection are given in the tube.

Q You didn't have a hard time crushing it fine enough to get through the tube?

A Well, we had to find the right pill pressure and kind of work with it, figure out how to dissolve it and learn. I was trained on how to flush the tube properly and how much water to give, that kind of thing.

Q And were there problems with the feeding tube at all?

A There was a few problems. A couple of times it became clogged and one time it became dislodged and a different kind had to be placed, but for the most part especially after it gets clogged you kind of learn how to be diligent about how to keep it from doing that because that requires a trip to the ER, which is something we try to avoid.

Q You say that when it gets clogged it requires a trip to the ER. What does the ER do?

A Well, if they can't open the tube like if it's clogged say with medication then they would have to replace it, which it's not a surgery, but it's still a procedure, which would be very uncomfortable for her.

Q And did Michelle have to have her tube replaced at some time?

A The one that became dislodged. She had to have that one replaced, and she has to now have it replaced every six months.

Q When she has the tube replaced, you indicated that it's a procedure.

A Yes, it is.

Q What type of procedure is it? Where is it done?

A It's done in the Interventional Radiology Department at our hospital.

Q And is Michelle able to cooperate with this procedure?

A She's sedated with Versed and I believe it's Fentanyl so that it's easier for her, not as traumatic and so she can be completely still.

Q So there's an anesthesiologist present for these feeding tube changes as well?

A Yes.

Q And how many times has she had it changed to date?

A To date? Let's see. It's every six months. I have to count. It's September 2003, 2004, 2005, 2006, 2007. That's four years. It's twice a year.

She's probably had it changed eight times.

A And each time she has it changed anesthesia has to give her Versed and Fentanyl?

A Yes.

Q And then somebody has to watch her while she comes out of anesthesia?

A Yes.

Q So a tube change for you would be the better part of a day?

A Oh, yes. Yes, it would.

Q Mrs. Cedillo, after you saw Dr. Krigsman and he ordered the Prednisone you indicated that you tried to wean her off and her symptoms would recur.

A Yes.

Q When you said that her symptoms recurred, you noticed it first by the fact that she had more difficulty walking?

A Yes, and diarrhea.

Q And diarrhea.

A The diarrhea would come first. I mean, that would be immediate, and then the walking would be a little bit -- you know, the limping would return.

Q So did Michelle have to go on Prednisone repeatedly?

A Yes, she did.

Q At some point in time did she develop any side effects associated with the Prednisone?

A She had a lot of weight gain.

Q And did they decide at some point that she could not remain on the Prednisone?

A Yes.

Q When was that decision made?

A It was made in early to mid 2004.

Q In mid 2004, what happened then?

A Then she began taking Remicade, which is an IV infusion.

Q You said it was an IV infusion. Was that done at home?

A No. That's done at the hospital at the outpatient center.

Q At the hospital you said?

A Yes.

Q And how often does she receive Remicade?

A It was given at the beginning -- you have to start, and you get the first dose in week zero, and then two weeks later you get another dose.

Remicade is a little bit different than Humira. I'm trying to remember. I think it's zero, two, four and then every four weeks after that.

Q So in the beginning you were in the hospital

quite frequently for the Remicade infusion?

A Yes.

Q How was Michelle after the Remicade began?

A She responded quite well.

Q And when you say that, what do you mean?

A She was able to move around a lot better without as many symptoms from the arthritis. She was able to eat and drink better. Her stools were formed and eventually of a normal frequency instead of so many a day, just maybe, you know, one to two per day.

Q And were you able to continue on the Remicade?

A We were up until October of 2005.

Q What happened in October 2005?

A She had a grand mal seizure and fell and broke her leg.

Q And when she broke her leg what was the reason for stopping the Remicade?

A Because Remicade and any anti-inflammatory medication, even Ibuprofen, interferes with the healing process.

Q And was there a problem with Michelle's fracture healing?

A There was. Initially a rheumatologist in town consulted with the orthopaedist in town, and he

was afraid for her to be taken off of all her anti-inflammatory medications. His quote was, "You'll have a great bone, but she'll be a complete mess." This doctor only knew Michelle -- he didn't see her as a patient, but he did the consult knowing what her background was.

She stayed on some of the anti-inflammatory medications, but not the Remicade. After I believe it was an eight-week period she had no signs of healing. The bone showed no signs of healing.

Q And at that point was that when the Remicade was stopped?

A It was stopped. Well, what happened was they never restarted. She had a dose in September 2005, and then she didn't have any more doses because the bone wasn't healing.

You know, I guess you could say it was stopped. We just never restarted it for that reason.

Q So after the eight weeks and the bone hadn't healed, what happened then?

A Then I made the decision, because to me that was pretty scary because then you can get into a lot of other problems, so I made the decision for them to stop the anti-inflammatory medication at that time for a short period.

Q And what anti-inflammatory medications was she on at that time?

A I'll have to look because they started her on different ones at Phoenix Children's Hospital. I think she might have still been on 6-MP. I think it was Colazal instead of Azulfidine, and she was in Imuran for a short period for arthritis. There might have been one other.

I'd have to look at her records to tell you for sure, but they more or less left it up to me to say yes or no for the medications. I had to decide to go with the orthopaedic recommendation or the other doctors.

Q So Michelle had to come off all her bowel medications?

A Yes.

Q And did her bone eventually heal?

A Yes, it did.

Q When Michelle came off all her bowel medication, did her symptoms come back?

A Yes, they did.

Q So her diarrhea returned?

A Yes.

Q And how was the arthritis?

A Well, she was in bed, but she was very sore.

She looked like she couldn't lift her back like if we changed the underpads or her bedding.

At that point we couldn't get her on her foot because she couldn't put any pressure on her foot, so we had to change her bed with her in the bed so we had to teach her to roll to one side and roll back to the other side the way you learn to change a hospital bed.

It was very hard for her some days to roll back and forth, and she would kind of moan and make sounds. You knew it was hurting her. I couldn't give her Ibuprofen, you know, for a while for the pain.

I'm sorry. Now I got sidetracked. Your original question? How was she?

Q How were her symptoms?

A How were her symptoms? Okay. As far as the arthritis and she had the diarrhea, and unknown to us at the time she was beginning to have the optic nerve damage from the chronic inflammation, but at that time we didn't know. We wouldn't know until a little bit later.

Q Now, you and your husband were still caring for Michelle by yourselves?

A Yes.

Q At some point in time did you require

additional help?

A Well, my parents were helping, you know, so the four of us.

Q The four of you would take care of Michelle?

A Yes.

Q Around the clock?

A Yes.

Q How old are your parents?

A Now they're 77 and 78.

Q At some point in time after Michelle's bone healed did she resume her bowel medication?

A Yes, she did. Yes, she did.

Q And when did that happen?

A I'll have to look. I can't remember exactly. I think it was close to eight months after the break.

It took eight months after the break. I think the bone was almost completely healed, and it may have been sooner than that that the orthopaedic said it was okay to resume because it was almost healed. I think it took almost a full year for it to completely heal.

If I could add, during that time she also had trouble tolerating the tube feedings, so it took longer to heal because her bowels were unable to

absorb the tube feeding formula which was given in a drip. I don't know what they call it. By drip feeding.

So she was not getting her full nutrition even though we had the feeding tube, so that also contributed to it.

Q You said she was unable to tolerate her tube feeding. What do you mean by that?

A As we raised the ccs per hour, you know, like you have 60, 80 or 100, which she was previously at 100 ccs per hour. She was having trouble tolerating I think it was like 50 or 60 ccs an hour.

The way we knew she was not tolerating it was because you'd be doing the drip feed, and she would have profuse, explosive, watery stools, uncontainable even with a diaper and pads.

That was at the hospital. All the aids were always in her room and were always changing her back and forth. That's when she was at Children's Phoenix Hospital.

Q And when she was at home and you'd taken her off all the bowel medication you indicated she was unable to tolerate her tube feeding at that time. What do you mean by she was unable to tolerate it?

A It was the same. Her bowels couldn't absorb

it, so she would have diarrhea. It was the same.

Q So it was the explosive diarrhea?

A Exactly.

Q And how many times a day did you have to change her?

A It was continuously. It could be every couple of hours because sometimes some would kind of like leak out on its own. Of course, we don't want her laying in stools.

It would depend. Sometimes it was just an all day thing, you know, changing and making her roll back and forth, that kind of thing.

Q And this continues for a year after the break almost?

A It wasn't for a full year. Once we resumed some of the medication, and I have to look at my notes or the medical records to tell you exactly when, but when we resumed the bowel medication then, you know, she was able to begin tolerating and actually keep the nutrition in.

Q Michelle's not toilet trained, is she?

A No, she's not.

Q She has to wear diapers?

A Yes, she does.

Q So when she was off her bowel medication you

had to continually change her diapers?

A Yes.

Q Once she restarted her bowel medication you said that the diarrhea stopped and she was able to tolerate her tube feedings better?

A Yes.

Q What bowel medicines did she resume?

A I believe at that time it was Azulfidine and 6-MP.

Q And by that time had you started to see Dr. Ziring?

A It was close to that time. It was November 2006. Let's see. The bone would have been healed. The bone had already been healed, so, yes, it was around that time we had resumed.

Q And when you first saw Dr. Ziring, what did he tell you about Michelle's bowel disease?

A The first thing practically that he said was that she needed to be on Humira.

Q And did you have some discussions about Humira?

A Yes, we did.

Q That was in 2006, and you indicate that she just started Humira this past few weeks?

A Yes.

Q Is there any particular reason for why you did not begin it in 2006?

A I was afraid to begin it. I was afraid that with everything she has going on that there was the strong risk for her to get cancer. I had many discussions with family.

There's other many side effects to it, and since she's nonverbal I wouldn't know whether she's getting tingling in her hands and feet. Some of these say report it to your doctor immediately. I would never know if she's getting tingling. What if she had visual changes or vision changes I should say? I wouldn't know that either.

I don't know if you feel different if you're beginning to get the cancer. I would never know. We wouldn't know until we had some other sign like in a lab report or something.

After many discussions with family, I had to come to terms with, you know, what we were going to do. I hesitated for that, and they were very respectful of my decision or of my waiting, you know.

Q So you had to make the decision whether to treat Michelle's bowel disease or to put her at risk for developing cancer?

A Yes.

Q And what tipped it in favor of the bowel disease?

A I was hoping that we were able to keep it controlled with the current medication, which was the 6-MP and the Sulfasalazine. I think she had been on Colazal again, and we switched to Sulfasalazine. Like I said, I'd have to look at the records to be sure.

She went to what they call a quiet stage where her eye problems were stable. She still had them, but they were I guess controlled is a better word. She had like loosely formed stools, so they were almost formed, and the frequency was within a normal range, maybe three times a day versus eight times a day or something.

I was hoping maybe this quiet stage would maybe go into an area where she wouldn't require Humira, but she just didn't respond like she should have, and I felt that we could not take the risk to her eyes because if she were to have a very severe bowel flareup the chronic inflammation could lead to inflammation in the optic nerve.

She only has 10 percent optic nerve that's healthy. To me, you have very little room to play with. Her markers of inflammation that I've been taught to look at on her lab readings had kind of

maintained for a short period of time, but then they started to go up. When that happened then I knew it was no longer controlled by the medication.

Q So you made the decision to treat Michelle with Humira to try and save the vision that she had left?

A The vision, yes, and to keep the bowel under control and arthritis. Right. Yes.

Q Now, we discussed this very briefly yesterday. You indicated that in the admission of July 2003 --

A Yes.

Q -- that's when you noticed that Michelle did not appear to be able to see.

A Yes.

Q Could you describe for the Court again what made you think that she could not see?

A Yes. She did not respond to people in the room, where previously she would at least kind of halfway look your way if you came in. We tried where you put the hand in front of the eyes or like make the motion like you're going to touch the person in the face, and she didn't do anything. She didn't respond.

She would put her hands in the air like she was feeling the air, you know, trying to find

something and didn't want to run into it with her hands, and she would let her VCR play to where it reached like a snowy part, which that's something she would never do. At that point I was afraid that she had completely lost her vision.

Q And it was you who noticed this, not the health care professionals?

A That's correct.

Q Who you brought this to the attention of the staff at the hospital?

A To the pediatrician and the staff as well.

Q And what did they do?

A They called in a consultation with an adult ophthalmologist.

Q And what did that adult ophthalmologist say to you?

A He said that he did not have the proper equipment to evaluate her in the hospital. We would probably have to make a trip to his office. There was no portable equipment available to him at the hospital, but we couldn't leave the hospital at that time. That was before she had the feeding tube.

I mean, it was at that visit she had the feeding tube, but she didn't have it placed yet. She was still too sick to leave.

Q So what did they do to treat Michelle's loss of vision?

A Nobody could determine. I mean, they saw what she was doing, what I was explaining, but since she was nonverbal we couldn't ask her can you see this or does it look different or anything like that.

She also had a very dry look to her eyes and redness all around them, so he thought the antibiotic drops were not helping her, and then he went back and tried to research what he thought could be similar symptoms.

Anyway, he stopped those drops and he began with rewetting drops. I think we had to give them every four hours, something like that. It was very frequent.

Q They're rewetting drops?

A Yes.

Q For dry eyes?

A For dry eyes. It's not a medicated product or medicinal product.

Q So during this hospitalization did Michelle receive any other treatment for her loss of vision?

A Not for the loss of vision.

Q And did that loss of vision persist during that hospitalization?

A No. Actually, she began to get better.
Q And after she was discharged did you follow up on the loss of vision?
A Yes, I did.
Q And what did you do next after the discharge for the loss of vision?
A For the loss of vision we saw a pediatric ophthalmologist. A pediatric neuroophthalmologist.
Q And where was this pediatric neuroophthalmologist located?
A At San Diego Children's Hospital.
Q So you had to make a three hour trip to see a pediatric neuroophthalmologist?
A Yes.
Q And when you saw this pediatric neuroophthalmologist what did he tell you?
A At that point in 2003 she had some paling, which shows optic nerve damage, but it was slight at that point. It's not what it is today, but at that point. He thought she had a good potential for her vision.
Q And that was roughly in 2003?
A Yes. That was December 2003.
Q And did you go back to see this doctor?
A We did in early 2004.

Q And was there any particular reason why you went back to see him?

A As a follow-up.

Q And at this follow-up was there any change in Michelle's vision?

A No. Well, I mean, it was the same as the previous one.

Q At what point in time did you learn that Michelle had developed significant optic atrophy?

A It was in February of 2006.

Q And would that be in that timeframe when her bowel disease was untreated?

A Yes, it would.

Q And how did you learn that she had optic nerve atrophy?

A They had to do an eye exam under anesthesia and examined her eyes.

Q And where was that done?

A That was done at San Diego Children's Hospital.

Q Was that as a routine follow-up?

A No. That was as a referral that I needed to have her eyes checked.

Q Did something happen that made you think that Michelle was losing her vision again?

A This time I didn't have the signs like before so, no, it didn't, but it looked like she was starting to get pink eye, but she never developed pink eye. Another doctor recommended that I take her to be seen by an ophthalmologist.

Q So it was simply because she was developing some symptoms and you wanted to check out the symptoms?

A Yes.

Q At this evaluation under anesthesia what did the doctor tell you he discovered?

A He told me he discovered that she had approximately 90 percent damage to the optic nerve, and he discussed briefly low vision products.

He said that we should keep her room and everything in the house exactly the same so that she could find it because she would probably be able to recognize things, but not really understand what new things were because he had suspected more of a loss of vision or low vision, which is not completely blindness, but it's still not being able to see like you and I see.

Q So he was recommending essentially that you do the same type of things that you would do for a blind person?

A Yes. He said don't change anything in the house because she'll need to know where it's at.

Q Did he order any treatment for Michelle's eye problem?

A Yes, he did.

Q What did he order?

A He ordered Pred Mild eye drops.

Q And is there something in this eye drop that would help Michelle retain the vision that she had?

A I believe it's Prednisone-based. I'm going by the name Pred Mild. I don't remember what's on the box, but it is a steroid eye drop.

Q An anti-inflammatory eye drop for her eyes?

A Yes. It's steroid-based. I know that though.

Q Has Michelle's vision stabilized?

A In a subsequent visit, which was by another ophthalmologist in the practice because the first one we saw was gone for a couple of months, it was discovered that she had open angle glaucoma, so her vision stabilized, but not until the uveitis and the glaucoma were treated, so she was being treated with two eye drops at that point.

Q Did anybody tell you that the glaucoma was related to existing eye problems?

A Yes, to the inflammation in the body and, as they put it, "everything she has going on."

Q Does Michelle continue on those eye drops to this present day?

A Yes, she does.

Q Now, we've discussed Michelle's bowel problems. We've discussed her eye problems. When did you first notice that she had arthritic type problems?

A Okay. That would be probably in 2002, shortly after the time period where she was unable to eat very much, but she was still drinking a lot of fluids, so that would be around late 2002.

Q Would that be before the hospitalization?

A Yes.

Q What did you notice?

A She was limping. We thought she had twisted her ankle, but it continued forever.

Q And what made you seek treatment for that?

A It wasn't until after -- well, I did seek treatment, but nobody knew what it was. They thought she was favoring the leg. We had her x-rayed. There was no bone break, no -- what do they call it -- green stick fracture.

I can't remember what it's called. It's when a child fractures a bone, but their bones are

still in the developing stage. I can't remember the exact term, but all that was ruled out so we thought okay, she favors that leg, but we didn't really know why until much later.

Q So she was limping for a while before the hospitalization?

A Yes.

Q When was the arthritis diagnosed?

A In December of 2003.

Q And how did it come to be diagnosed?

A I was asked to take her to be evaluated by a pediatric rheumatologist.

Q And who asked you to do that?

A Dr. Arthur Krigsman.

Q And it was Dr. Krigsman in New York who thought that Michelle should see a pediatric rheumatologist?

A Yes.

Q None of your local doctors suggested this?

A They didn't suggest a follow-up, but they suggested she might have arthritis when they saw the swelling in the leg. That was about three days before we went to see Dr. Krigsman.

Q So they told you that she potentially had arthritis?

A Yes.

Q And they suggested follow-up for the arthritis?

A Yes, Dr. Krigsman did.

Q Your local doctors now.

A Oh.

Q They suggested that she have follow-up for her arthritis?

A They said maybe it's arthritis, but they didn't really suggest any follow-up. I took it to mean that if it continued.

They knew we were going on this big trip, and I just took it to mean that, you know, if it continues they can refer us. It was unspoken, but, you know, like that.

Q And you told us that it was Dr. Krigsman who suggested this?

A He said you need to get her in to a pediatric rheumatologist right away.

Q And was this after your visit with him?

A During the visit. Right.

Q During the visit. And that was roughly September of 2003?

A September 25, more or less, 2003.

Q So who did you see?

A We saw Dr. Robert Sheets at San Diego Children's Hospital.

Q So another three hour ride?

A Yes.

Q And when you first saw Dr. Sheets what did he tell you?

A He examined her for arthritis, checked her hands, her arm movements, her hips, her ankles, her legs, and he said she had he thought it was mostly in her subtalar joints and mostly in the left leg.

Q And did he tell you what he thought was the cause of this arthritis?

A He said I believe it's secondary to the bowel disease.

Q Did he order any treatment?

A No. He said that he could if she was not responding enough to the bowel medication, but he said by treating the bowel disease, since her arthritis is secondary to the bowel disease, by treating the bowel disease and getting it under control, the arthritis symptoms should disappear.

Q And did you continue to see Dr. Sheets?

A Yes, we did.

Q And in the course of your treatment with Dr. Sheets, did he make any other recommendations, other

than to treat the bowel disease?

A He recommended that she be put on Remicade, but that was in conjunction with the GI, with Dr. Krigsman.

Q Okay. So he concurred with Dr. Krigsman when Dr. Krigsman recommended the Remicade?

A Yes, he did.

Q And you've indicated that when she went on the Remicade, her bowel symptoms improved and her arthritis improved?

A Yes, it did.

Q And do you continue to follow up with Dr. Sheets?

A No. Well, with his partner.

Q And has Michelle's arthritis changed at all in the last few years?

A Some of it is about the same. She still has difficulty moving the ankle, but I think because she's not as swollen because she's in bed more, but she's very sore. When she walks, some days she's very sore like she can't get up. So maybe it's changed, how it appears, but I would say it might have improved slightly.

Q Okay. So we've discussed the bowel disease, her eye problems and her arthritis, which your

treating physicians indicate are related, all related, is that true?

A Yes.

Q Now, at some point in time, Michelle developed seizures, is that true?

A Yes.

Q Could you describe to the Court the circumstances under which these seizures began?

A The first seizure, that would have been around July of 2004 after the administration of Demerol, and we thought at that time that it was a one-time episode. Probably about an eight-month period passed with no seizures and then she began to have them again.

Q And you said that she began to have them again. How frequently was she having the seizures?

A At that point, eight months after the first one, she had a grand mal seizure and then it was probably a couple of months before she had another one, but then they began to increase in strength and frequency both, to the point where -- well, actually, that was right before the time when she broke her leg. Over that period of time, they began to increase, but it was slowly, but then right around the time she broke her leg was when we were like, oh my gosh, she

just had one and now she's having another one, and then that's when she broke her leg.

Q So when these seizures began, did you seek treatment for them?

A Yes, we did.

Q Who did you see?

A Well, she was seen in the hospital by an adult -- not rheumatologist -- neurologist.

Q An adult neurologist, you said?

A Yes.

Q And what was the reason she was seen by an adult neurologist?

A He was called in as a favor to the pediatrician because we don't have any local pediatric neurologists.

Q And what did he recommend for Michelle?

A He recommended treatment with Topomax.

Q And did Michelle go on Topomax?

A Yes, she did.

Q Did she continue on the Topomax?

A She did for a period of time.

Q So at some point in time she came off the Topomax?

A Yes.

Q And what was the reason she came off the

Topomax?

A Because we were unsure, the doctor was unsure if -- I mean, the pediatric ophthalmologist was unsure whether or not Topomax was contributing to the optic neuropathy -- or optic atrophy, sorry.

Q So that's why she had to come off the Topomax?

A Yes.

Q There was fear that it was contributing to her eye problems?

A Yes.

Q And when she came off the Topomax, did she go on any other anticonvulsants?

A Not at that time.

Q How long was Michelle off anticonvulsants?

A I'd need to look at my notes or my calendar, but I would say it would probably be about a six-week period, maybe an eight-week period at the most.

Q And during this period of time, did Michelle have any seizures?

A Yes, she did.

Q What type of seizures was she having?

A She was having the grand mal seizures, that type.

Q And did you seek treatment for her grand mal

seizures since she was no longer on anticonvulsants?

A Yes, we did.

Q Who did you see then?

A We saw Dr. Michelle Sahagian at San Diego Children's Hospital.

Q And how did you find Dr. Sahagian?

A I called the neurology department and asked who was the -- who could -- well, just to make an appointment, the soonest available, so she was the one that was available.

Q Okay, and when did you see Dr. Sahagian?

A I can't remember the month. I think it was June or July of 2006, I guess around that time.

Q And at that time, Dr. Sahagian evaluated Michelle?

A Yes, she did.

Q And what did she tell you after her evaluation?

A She diagnosed her with epilepsy.

Q Epilepsy?

A Yes.

Q And did Dr. Sahagian explain to you how she could have epilepsy in such a brief period of time?

A She said that with everything, she's so involved medically and she had so much going on that

everything together combined to put her body in a state to where she had developed epilepsy.

Q And is Michelle on medication for her epilepsy now?

A Yes, she is.

Q And what medication is she on?

A She is on Keppra.

Q Did Dr. Sahagian start the Keppra?

A Yes, she did.

Q What dose did she start the Keppra at?

A We started at a small dose. I'll have to look. I think it was 500 milligrams a day. It was a low dose.

Q And at that dose, did Michelle remain seizure-free?

A Only for a short period.

Q So she started having seizures again?

A Yes, she did.

Q What did you do then?

A I called Dr. Sahagian's office.

Q And what was Dr. Sahagian's recommendation?

A She outlined for me, she basically said to do it this way, you increase it by this many milligrams per day. If she stays seizure-free, you can leave it at that dose. If she has one or so I

think they call them breakthrough seizures and doesn't have any more, you can still keep it at that dose, but then if she starts having more, then you increase it to the next, you know, add I think it was by 250 milligrams each time per day until you get to a point where she seems to be seizure-free.

I mean, I was free to call her anytime if I had any questions, but her concern, she was very fair about the side effects of the medications so she said, as you increase the medication, you will also begin to see probably increased side effects, which can be different neurological manifestations. OCD, some kind of extraneous hand movements, not like a palsy but I don't know what else to call it, that's kind of what I consider it, and maybe obsessions with certain things.

You know, that those things I would have to look for, but sometimes after a two-week period, the body will adjust, but, you know, so as I increased it I was trying to be real careful because she also agreed that we didn't need to keep putting a lot of medication into her system. So that was her treatment plan.

Q So on your own, you were told that if Michelle suffered breakthrough seizures, you were told to gradually increase her medication, is that true?

A Yes, yes.

Q And as you gradually increased the medications, you were told that she might suffer some side effects?

A Yes.

Q And you were told to watch for those side effects?

A Yes, I was.

Q How far have you increased Michelle's Keppra?

A We are up to 2000 milligrams a day.

Q And does she remain seizure-free?

A No, she does not.

Q Are you continuing to increase the Keppra?

A I stopped at 2000 milligrams a day. We are allowed to go up just a little -- she's almost at the maximum, so I stopped, I have not increased it past the 2000 milligrams a day.

Q What do you do when Michelle has breakthrough seizures?

A We try to make sure that she's safe and we give her oxygen to help her recover quicker from the seizure, and then if she looks like she's going to have a seizure, we are allowed to give her a 2 milligram dose of Valium.

Q And have you had to give her Valium?
A Yes.
Q Are there any plans to add additional seizure medications at all for Michelle?
A Not at this point, but it's, I mean, it is an option later.
Q And when was the last time you saw Dr. Sahagian?
A Probably in 2006. I think it was late 2006. I have to check. I know that was the year but I don't remember the month.
Q And at that last visit, what was Dr. Sahagian's recommendations to you?
A It was the same, with the Keppra.
Q Did Dr. Sahagian indicate to you whether Michelle's seizure disorder could be controlled?
A She said that sometimes you don't get what you call tight control of the seizure, is the term she used, "tight control." There's a possibility that they will not be completely controlled, so, you know, that was -- you mean like a prognosis? That's what she told me.
Q So essentially, you were being told that this may be the best that you can do for her seizures?
A Unless we wanted to put her on, or try, I

guess, several -- if I wanted to go the route where she's taking a lot of medication at one time. But then at that point you are probably going to see a lot of other side effects.

Q So Mrs. Cedillo, who currently cares for Michelle's inflammatory bowel disease?

A Dr. David Ziring as well as Dr. Arthur Krigsman.

Q Dr. Krigsman is where?

A He's in New York.

Q And Dr. Ziring is where?

A At UCLA in Los Angeles.

Q And who cares for Michelle's arthritis?

A Right now, Dr. Szer at San Diego Children's Hospital.

Q And her eye problems?

A Dr. Scher, spelled a different way, and Dr. O'Halloran at San Diego Children's Hospital.

Q And her seizures are being cared for by Dr. Sahagian also --

A Yes.

Q -- at San Diego Children's Hospital?

A Yes.

Q And they are all three hours away from you?

A Three hours one way for San Diego and about

a five-hour drive one way for UCLA.

Q What do you do in emergencies?

A Well, I call and see if it's something I can handle at home. I usually try to handle it myself with a phone call with the doctor, which over the years I've learned to do. Before I would try to get her into the ER. But for an emergency like if she were to not be responding or look unresponsive then we cal 911.

MS. CHIN-CAPLAN: The video is ready now, Special Master. I'd like to go through it with the Court and Mrs. Cedillo.

SPECIAL MASTER HASTINGS: All right.

MS. CHIN-CAPLAN: Special Master, we are going to be showing some "before" home videos, and they are dated from 6-95 through 12-95, and then we are going to be showing some videos also dated from 12-25-95 to approximately 8-30-00. We may not show them all, but if the Court wants to see anything in the middle, we will certainly be glad to run through them for you.

SPECIAL MASTER HASTINGS: All right. So are you, Ms. Chin-Caplan, you're going to run through them with Mrs. Cedillo on the stand and not with an expert witness, or?

MS. CHIN-CAPLAN: Yes, that's correct.

SPECIAL MASTER HASTINGS: Okay.

MS. CHIN-CAPLAN: And at some point in time we might go through the points that the Respondent had raised, and I would go through it with Dr. Kinsbourne. I hadn't quite decided that one yet.

SPECIAL MASTER HASTINGS: All right.

THE WITNESS: Special Master Hastings?

SPECIAL MASTER HASTINGS: Yes?

THE WITNESS: Am I speaking loud enough?

SPECIAL MASTER HASTINGS: I think so, I can hear you.

THE WITNESS: Okay.

SPECIAL MASTER HASTINGS: Yes.

THE WITNESS: Do I need to move?

SPECIAL MASTER HASTINGS: Is it possible for you to move a bit to your right?

THE WITNESS: Yes, okay.

SPECIAL MASTER HASTINGS: Great. It's easier for us to see you.

THE WITNESS: This way?

SPECIAL MASTER HASTINGS: Great.

THE WITNESS: Okay.

SPECIAL MASTER HASTINGS: Thank you.

THE WITNESS: Sure.

SPECIAL MASTER HASTINGS: You may have to slide the microphone.

THE WITNESS: Sure. Is this better?

SPECIAL MASTER HASTINGS: For those at home, we are having a bit of technical difficulty here. Bear with us. Nothing is going on right now.

(Whereupon, a video was played.)

BY MS. CHIN-CAPLAN:

Q Now, Mrs. Cedillo, could you just generally describe what you see here?

A Okay, this is Michelle playing with her jungle gym and I believe my niece Jennifer is doing the videotape.

SPECIAL MASTER HASTINGS: Can you stop for a minute, Mr. Shoemaker? Is the audio of the video important?

MS. CHIN-CAPLAN: Yes, it is.

SPECIAL MASTER HASTINGS: It is.

MS. CHIN-CAPLAN: Perhaps what we could do is have the scene come up and Mrs. Cedillo could describe it, and then we will run that segment.

SPECIAL MASTER HASTINGS: All right, and what am I looking for here? What's the purpose up here, so we have a better chance to understand what you are showing here, and the purpose of it?

MS. CHIN-CAPLAN: These are the videos that we have of Michelle before she became symptomatic, and we would like to show the difference between the before and the after.

SPECIAL MASTER HASTINGS: All right, go ahead.

MR. MATANOSKI: First, Special Master, could the Petitioners' counsel identify which segments these are from the video files they provided?

SPECIAL MASTER HASTINGS: Is that possible?

MS. CHIN-CAPLAN: I'm not certain.

MR. SHOEMAKER: I'm not sure what you mean by what "segment." There are three DVDs. You want to know which one they are on, or?

MR. MATANOSKI: What we did in responding to the Court's order, designating what parts of the videotapes we were looking at, we gave specific cites to the videotape. There are separate files, and we gave cites to those files, and that is what we are asking for now.

SPECIAL MASTER HASTINGS: Did any of you ever see the designations the Respondent gave you?

MR. HOMER: We did, sir.

SPECIAL MASTER HASTINGS: Did you understand what they were cited to?

MR. HOMER: I did, but our approach is different. We are not exactly doing what the government is doing. Our approach is that we are giving a span, we are giving dates, as Ms. Chin-Caplan just stated on the record, from June '95 through 12-95, and that's what we're showing the Court. Now, the government went a little further and I guess decided upon their own to divide it up into segments, but that's simply not our approach here. But we are giving the dates.

SPECIAL MASTER HASTINGS: You are giving the dates?

MR. HOMER: And the witness will go through from June through 12-95 and describe what the Court is seeing. That is our approach.

SPECIAL MASTER HASTINGS: All right. Go ahead.

MR. MATANOSKI: So you're not --

SPECIAL MASTER HASTINGS: They are going to give us dates.

MR. MATANOSKI: They're not designating -- but you are giving a six-month period, in other words.

MR. HOMER: This will -- exactly.

SPECIAL MASTER HASTINGS: Are you going to give us a date, not just a six-month, but June 6, are

you going to give us that for each segment?

MR. HOMER: Yes.

SPECIAL MASTER HASTINGS: Okay. All right, go ahead.

MS. CHIN-CAPLAN: Some of these are dated at the bottom. There are others that, for some reason, there's not a date, but we are going to ask Mrs. Cedillo to identify this and when it occurred.

SPECIAL MASTER HASTINGS: All right.

BY MS. CHIN-CAPLAN:

Q Mrs. Cedillo, do you recognize this scene?

A Yes, I do.

Q Can you just generally tell the Court how old Michelle was and what she was doing and who else was present in the room?

A Okay. What's the start date on this? Because I think it ran past the start date.

Q The date that we have on the DVD was June '95.

A Okay. Depending on the day of the month, I think this was probably June 9 if I'm remembering, so she was still 9 months old.

Q And what was she doing here?

A She was playing, and my niece Jennifer was doing the videotape and Michelle loved Jennifer. Q

Was anybody else in the room at the time?

A I think my dad would be over to the right side, and I think he was laying there on the side, so, and my mom might have been in the background but Jennifer was the one holding the camera.

Q And is this you in the photo as well?

A Yes, that's me.

MS. CHIN-CAPLAN: Okay.

(Whereupon, the video was continued.)

BY MS. CHIN-CAPLAN:

Q Mrs. Cedillo, there's a person on the right of the screen?

A That's Michelle's grandfather.

(Whereupon, the video was continued.)

BY MS. CHIN-CAPLAN:

Q Mrs. Cedillo, when was this scene?

A This is 6-10-95, so Michelle was 9 months old. She was taking a bath in the kitchen sink. That's my mom, or her grandmother, to the left over here, and then I'm filming it.

(Whereupon, the video was continued.)

SPECIAL MASTER HASTINGS: For those listening at home, the Petitioners are presenting home video of Michelle as an infant and we're sorry you can't see what's going on, but the sounds you are

hearing are mainly sounds coming from the videotapes themselves.

Go ahead, Ms. Chin-Caplan.

MS. CHIN-CAPLAN: Thank you, Special Master.

BY MS. CHIN-CAPLAN:

Q Mrs. Cedillo, this portion of the video is dated 6-12-1995. How old was Michelle at that time?

A She was 9 months old.

Q And can you identify who the individual is here in the camera shot?

A That's her father.

Q And was there anybody else in this scene that is not reflected on this video?

A I'm not sure if it's this one. I think eventually I get into the scene and either my mother or my niece Jennifer takes over the filming.

Q Okay.

A So there might be another similar one, so I'm not sure if it's this one or the next one.

MS. CHIN-CAPLAN: Okay.

(Whereupon, the video was continued.)

THE WITNESS: I'm telling my mom how to work the camcorder, so that's my mom recording now.

(Whereupon, the video was continued.)

BY MS. CHIN-CAPLAN:

Q And this one is dated 6-20-95. Can you describe the scene to us?

A She is 9 months old, and she loved Big Bird and Bert, and so she would get real excited when the opening song for Sesame Street came on when they would show all the characters, and she's trying to say "Big Bird." She said "Bert" but in here it kind of sounds like a scream. She's trying to say "Big Bird," and that's her dad with her. And then I'm to the side. I think we are the only two. I'm the one recording. I think it's just the two of us and Michelle here.

Q I noticed in the last few photos that she was sitting up by herself.

A Yes.

Q So she was 9 months old at this time?

A Yes.

Q And she was sitting up by herself at 9 months old?

A Yes.

(Whereupon, the video was continued.)

THE WITNESS: Our dog.

(Whereupon, the video was continued.)

THE WITNESS: It's the same date. Her father is doing that same motion to her. She is imitating him.

(Whereupon, the video was continued.)

THE WITNESS: So she's still 9 months old. It's her first time in the swimming pool in our backyard, and she's with her dad, I'm filming, and I think my mom is to the left or right of me, I can't remember. The dog is there, and I think my dad might be there.

(Whereupon, the video was continued.)

THE WITNESS: Okay, 8-22, so she's just shy of one year old. August 30 she would have been -- I mean she would be one year old, so she's 11 months here. That's my dad, her grandpa, playing with her over here. And I'm recording, and other than the dog, I think we are the only ones in the room.

(Whereupon, the video was continued.)

BY MS. CHIN-CAPLAN:

Q When was this scene taken?

A This was taken on her -- it might have been a couple days -- it's either on her birthday day or it's a couple days later. I think my brother bought her a Big Bird -- I mean, a Sesame Street birthday cake. So if it's not exactly on 8-30-95 then it's within a couple of days. So I'm taping, my husband is there behind Michelle, my brother Philip and his daughter Jennifer are to the left on another sofa.

(Whereupon, the video was continued.)

THE WITNESS: My brother's making her laugh to the side, but you can't see him.

(Whereupon, the video was continued.)

SPECIAL MASTER HASTINGS: At the end of this segment, can we stop it now? Let's take our morning break now, fifteen-minute break. I've got 10:46, so let's convene back just after 11. So let's go off the record.

(Whereupon, a short recess was taken.)

SPECIAL MASTER HASTINGS: To those at home, we had a longer break than we anticipated but we are going to be starting up again right now. All right, Ms. Chin-Caplan, if you want to go ahead with whatever you're going to do next here, please go ahead. Mrs. Cedillo is back in the witness chair.

MS. CHIN-CAPLAN: Special Master, we're going to move on to December of 1995 and show a few of the clips after the MMR in December of '95.

SPECIAL MASTER HASTINGS: Okay, fine.

MS. CHIN-CAPLAN: We just need a little time to get to that frame.

SPECIAL MASTER HASTINGS: All right.

THE WITNESS: Do you want, Sylvia, right prior? Do you want 12-25-95 or do you want 12-17?

MS. CHIN-CAPLAN: That's the next scene after it, isn't it? 12-25?

THE WITNESS: I think it's after this one.

MS. CHIN-CAPLAN: Okay, why don't we start with 12-17-95.

THE WITNESS: Okay.

SPECIAL MASTER HASTINGS: Okay, do speak up.

THE WITNESS: Okay, I'm sorry, I was -- okay, so we're at 12-17-95, so Michelle is -- sorry -- 12, 13, 14, 15 -- she's 15 months here. And this is a ball pit that my mom and dad bought for her and we gave it to her as an early Christmas present.

(Whereupon, the video was continued.)

THE WITNESS: This is Christmas Day and that's her grandmother giving her a Christmas present, and I think we are all in the general area. I think we come in and out, so it would be her father, her grandfather, I'm filming, my mother and Michelle. And she's 15 months old.

(Whereupon, the video was continued.)

SPECIAL MASTER HASTINGS: Ms. Chin-Caplan, what next?

MS. CHIN-CAPLAN: The next scene will be post-MMR.

SPECIAL MASTER HASTINGS: Okay.

(Pause.)

SPECIAL MASTER HASTINGS: So for those at home, the Petitioners are going to be showing a few more videos here, so bear with us. What you will be listening to is the --

THE WITNESS: This is still pre-MMR.

SPECIAL MASTER HASTINGS: What you'll be listening to is there will be audio of the video and with Mrs. Cedillo testifying today telling us something about those videos.

Go ahead.

THE WITNESS: Okay, this is December 25, '95, so Michelle is still 15 months old, and this is pre-fever -- okay, well, it skipped. Sorry. Okay, this is, I believe, the same day, 12-25-95, so the same. She's 15 months old and I think it's just a brief clip. And this is pre-fever. The same, the same scene.

(Whereupon, the video was continued.)

BY MS. CHIN-CAPLAN:

Q Could you identify this scene for the Court?

A This is February 16, '96, so Michelle is -- let's see, 16, 17, she's 17 months still. And this is post-fever, following MMR, and my dad's in the room and I am recording her. Actually, we are trying to

get her attention, but --

(Whereupon, the video was continued.)

MS. CHIN-CAPLAN: We're going to stop here, Special Master.

SPECIAL MASTER HASTINGS: All right.

BY MS. CHIN-CAPLAN:

Q Mrs. Cedillo, on that last scene, did Michelle make any sound at all?

A No, she did not.

MS. CHIN-CAPLAN: I have no further questions.

SPECIAL MASTER HASTINGS: All right. Thank you.

MS. CHIN-CAPLAN: Oh, one other thing, Special Master. There seems to be a gentleman sitting next to Ms. Ricciardella that -- I'm not aware of his identity, so I was wondering if he could just identify himself.

SPECIAL MASTER HASTINGS: Can you identify yourself, sir? I'm sorry? You're Dr. Fombonne? Okay. Thank you.

I guess next we'll have cross-examination of Mrs. Cedillo. I will note for all who might be interested at home or in the room now, I'm told that the audio download of yesterday's hearing is now

available on our website, and the transcript of yesterday's hearing is now available on our website.

So with that, Ms. Ricciardella, you have some questions for Mrs. Cedillo?

MS. RICCIARDELLA: Just a few. Thank you.

SPECIAL MASTER HASTINGS: Please go ahead.

CROSS EXAMINATION

BY MS. RICCIARDELLA:

Q Good morning, or I should say, yes, it's still morning. Good morning, Mrs. Cedillo.

A Good morning.

Q I want to state at the outset that it is very clear, from the medical records, from the home videos that we just watched, and really from every piece of evidence that is specific to Michelle that has been submitted in this case, that both you and your husband are very loving and dedicated parents to Michelle.

A Thank you.

Q And the same holds true for Michelle's grandparents.

A Thank you.

Q She's very fortunate to have you all as her family.

A And we're fortunate to have her. Thank you.

Q And because you all are such dedicated caregivers, you take her to the doctor when she is sick, correct?

A That's correct.

Q I mean, you've done that throughout her life, isn't that true?

A Yes.

Q Now, Mrs. Cedillo, you testified yesterday about the behaviors that you noticed following the febrile episode in December of '95, in January of '96. Do you recall that testimony?

A Yes, I do.

Q When did you first have concerns about Michelle's development and her behavior?

A It would be following the fever, after the fever had stopped the second time.

Q So sometime in mid-January of 1996?

A Around that time.

Q And what was your first concern?

A That she no longer spoke.

Q Did anybody else in your family share your concerns?

A Yes.

Q Who? Your husband?

A My husband and my parents.

Q Your parents. Now, yesterday, you testified about some of the behaviors that were concerning to you, and I think you said that she, as you just said now, she stopped talking, that she didn't want to play with toys, is that correct?

A She played differently --

Q Played differently with toys?

A -- with toys.

Q How did she play differently?

A Before she would play with the toy appropriately, like if it was the stacking rings, she would stack them and maybe now she would just look at them or touch the stacking ring or line -- I don't think at that point she was lining them up yet, but she didn't seem to -- I guess the easiest way is to say she didn't seem to have the same kind of interest in the toys she had been playing with that she did before.

Q I believe you said she was withdrawn, you noticed she was withdrawn?

A Yes.

Q And quiet?

A Yes.

Q And I believe you said too that she would push or lean away from you, is that correct?

A Yes.

Q All right. Now, in an affidavit that you filed in this case, you also -- you said that Michelle would cry inconsolably unless you played a Sesame Street video during this time, is that correct?

A Yes, a video.

Q When do you recall that she first became -- that she would first display this behavior unless you played a Sesame Street video?

A To the best of my knowledge, which is an approximate --

Q I'm sorry, I didn't hear.

A To the best of my knowledge, as an approximate, I would say one to two days into the fever, so that would be December 27 or December 28, 1995.

Q And could you describe how she would react to a Sesame Street video?

A It would calm her.

Q Did she stop interacting with people during this time?

A It began declining, yes. It stopped, yes.

Q With you and your husband as well?

A Yes.

Q Did she stop pointing at objects during this

time?

A Yes.

Q Did you notice any problems with her motor skills during this time?

A Not with her motor skills. You mean as in walking, picking up an object?

Q As walking or crawling, correct.

A No.

Q Okay. Did you observe any hand flapping during this time? Do you know what I mean by "hand flapping"?

A Yes, I do.

Q Did you observe that?

A I observed it. My recollection most notably would be probably around February --

Q Of which year?

A -- of '96.

Q '96, okay.

A So, and I truly can't recall if it started immediately or if it was, you know, around -- I recall at that time from a video.

Q From the video that we just saw?

A Yes.

Q Okay, and that was, I believe it was, February 16 of '96, is that the date?

A There is a -- it's either February 16 or 17.
Q Okay, is it the video where she's sitting by a clothes basket?
A No it's -- she's in a little caboose train, but it's very dark, the picture was very dark, but she's flapping this way.
MS. RICCIARDELLA: Okay, and for the record, Mrs. Cedillo is flapping her hands back and forth.
THE WITNESS: Flapping my hands, right.
BY MS. RICCIARDELLA:
Q Now, Mrs. Cedillo, you've just described the behaviors that you began observing in Michelle shortly after her febrile episode in 1996, correct?
A Yes.
Q All right. Now, I'd like to discuss the behavior you observed in Michelle in the 6 to 12 months following that. What behaviors was she displaying that you now think were autistic behaviors?
A So 6 to 12 months from February, or --
Q Correct.
A Okay.
Q Six to 12 months from the febrile episode.
A Oh, from the -- okay, so that would put us about June of '96. At that time, I would say that she -- we're talking behavior strictly?

Q We can start with behavior, yes.

A Okay. She, at that point, I believe is, and I'm, again, estimating, that we could no longer take her with us to church, to restaurants, to shopping malls. We attempted to, and it might have been during that period that we were still trying to attempt to take her out to public places that we could take her before, but it was, for lack of a better word, it was overwhelming for her. She would cry and withdraw and, you know, she was, I guess you could say, unmanageable.

She had -- began to develop repetitive behaviors or showed, if you want to call it abnormal interest in maybe lining up or stacking toys or books, children's, like, board books.

Q When you say repetitive behaviors, what do you mean?

A She would do the hand flapping. By "repetitive," I mean like maybe she would, for example, line up some toys and then leave them that way and then, you know, distribute them a different way and then line them up again. Those kind of things.

Q Would you describe how Michelle's socialization was with you or your husband was with

you and your husband in the 6 to 12 months following --

A Six to 12 following?

Q Following your initial observation of these behaviors.

A Of the fever, okay. Socially, she was withdrawn. She did not respond to her name. It was hard to interact with her. When we tried to do the things that we could do prior to then with her, you know, we couldn't do them or she was resistant, I guess is the best way to phrase it.

Q Did she show any interest in interacting with other people, notwithstanding you and your husband?

A Very little, not really.

Q Did you observe her making more eye contact with the television than with human beings?

A At that point, yes.

Q And during this time, how would she react to the video of Sesame Street?

A She was engrossed in it.

Q What do you mean by "engrossed in it"?

A She would watch it and, I guess you could say, tune everything else around her out.

Q Would you please describe any motor

behaviors that you witnessed during this time period that you now attribute to the autistic behaviors?

A The hand flapping, and I don't know if lack of eye contact would be considered a -- is that a motor behavior? If it is, I don't know what that falls under, but I would say lack of eye contact and hand flapping.

Q Do you know what hand regard is?

A Yes, I do.

Q And is it studying one's hand in front of one's face and trying to study it?

A Yes, it is.

Q Did Michelle display hand regard?

A Yes, she did.

Q Did Michelle have shaking of her legs during this time period?

A Uncontrollable shaking of her legs, or?

Q Any shaking of her legs that you attributed to any abnormality?

A No, I'm not sure. You mean like did she shake her legs --

Q Was she shaking -- were you -- did she shake her legs that you felt was any kind of behavior that was unusual with regard to her legs?

A Not that I recall.

SPECIAL MASTER HASTINGS: Ms. Ricciardella, let me interrupt you for just one second here to make sure I understand what the time period we're talking about is. Let me ask Mrs. Cedillo.

Are you understanding that you are now talking about the 12-month period after the MMR vaccination or which period do you think you are being asked about?

THE WITNESS: I think I am being asked about the period from the -- since the fever was on December 27, 1995, I think she means until December 27, '96.

SPECIAL MASTER HASTINGS: So the one year after the fever?

THE WITNESS: For the full year, is that correct?

MS. RICCIARDELLA: Correct, the full year, and also -- and really into 1997. Up until her diagnosis of autism.

THE WITNESS: Oh, okay, so we're -- okay, because there were more behaviors starting in -- I mean, I know exactly when they started, but --

MS. RICCIARDELLA: Okay, well, I was going to go back, but --

SPECIAL MASTER HASTINGS: But the questions you've asked thus far, I just wanted to make sure you

were both -- you were asking about anything in the year after the fevers and Mrs. Cedillo was answering about anything in the year after. Okay, so we're on the same wavelength. Very good. Go ahead.

MS. RICCIARDELLA: Thanks for the clarification, sir.

THE WITNESS: Okay.

BY MS. RICCIARDELLA:

Q Now, you just testified that you were answering in response to my question that you -- the behaviors that you witnessed in Michelle until December of 1996. What autistic behaviors did you start to notice in Michelle from December '96 up until her diagnosis of autism in 1997?

A Okay, probably most prominent was her lack of vocalization or speech. Her withdrawn state, or I guess you could say her lack of socialization, interaction with her family, which is my mother and my father and my husband and myself. And inability to take her to public places. The hand flapping, and if I didn't say, lack of eye contact. I'm sorry if I'm repeating. Lack of eye contact. At that point.

Q And would you please describe Michelle's language in the 6 to 12-month period following the --

A Following?

Q Following the febrile episode, correct.
A Okay, 6 to 12 months following 12-27-95 --
Q Yes.
A -- there was no language.
Q No language at all?
A No.
Q Okay. What about in the period between December of '96 to her diagnosis of autism in 1997?
A No.
Q And would you please describe Michelle's play in that 6 to 12-month period following December 27, 1995?
A Her play was much the same. It was, well, it's not really play, but it was watching Sesame Street, recorded videos only, as opposed to the show that, you know, that it would just come on on PBS. It had to be certain recorded videotapes of Sesame Street. So that was unusual. I'm sorry, so --
Q Let me interrupt you. So, if I'm understanding, she would really only respond to DVDs of Sesame Street rather than if it was on live on the television, correct?
A That's correct. At that time, it was what was recorded is what she preferred to watch.
Q Okay. Did you have certain DVDs of Sesame

Street that she would watch all the time? The same show?

A Yes. In the -- we're talking about the after period, right?

Q Yes.

A Up to diagnosis?

Q Up to diagnosis.

A Okay.

Q Would she play with any toys?

A Very limited. She wouldn't play like, again, the stacking ring, the shape sorter, those kind of things, she wouldn't -- she might put the shape sorter here and then line up the rings and line up books, but nothing was actually played with like she would before.

Q Now, Mrs. Cedillo, when did you first come to think that the MMR vaccine may have caused her autism?

A May have caused her autism?

Q Yes.

A Okay. That would be close to the time of diagnosis. Actually, following diagnosis. So that would be around August of 1997.

Q Now, you testified yesterday that you met Dr. Andrew Wakefield at a 2001 Defeat Autism Now

conference, is that correct?

A Yes.

Q And the acronym for Defeat Autism Now is D-A-N, or DAN, is that correct?

A DAN, yes.

Q Okay. Had you heard of Dr. Wakefield before that conference?

A Yes, I had.

Q How did you hear of him?

A On the internet and from other parents. I guess I should say websites and other parents.

Q Was the 2001 DAN conference the first time you had met Dr. Wakefield?

A I believe so.

Q Was it the first time you had ever talked to him?

A I believe so.

Q Did you actually talk to him at that conference?

A Yes, I did.

Q What did you tell him?

A I told him that I had a child that was very ill, and that she had the same symptoms and manifested the same way as what I had read online and the children that he had treated -- well, I guess he

didn't treat them, but that he had examined.

Q And what did he tell you?

A I -- excuse me, let me take a drink of water. Okay. I asked him if there was anything we could do because at this point she was having -- she was already manifesting with the bowel problems, with the diarrhea, and she was very sick. And I asked him if there was anything that could be done. So he suggested that I contact a pediatric gastroenterologist, and he gave me the information that I need to -- medically speaking, what I needed to tell the gastroenterologist to see if he was willing to do that.

Q Did he recommend a pediatric gastroenterologist?

A Not a name, no.

Q Have you ever exchanged e-mails with Dr. Wakefield?

A Yes, I have.

Q Approximately how many?

A Boy, I don't have a number.

Q More than 10?

A Yes, more than 10.

Q More than 50?

A Probably more than 100 but less than 150.

I'm guessing.

Q More than 100 but less than 150?

A I'm guessing.

Q Are you still in contact with Dr. Wakefield?

A Yes, I am.

Q Has he ever seen Michelle?

A He has physically seen her, yes.

Q Yes, he has?

A I mean, he has -- right.

Q How many times?

A Oh, how many times, I think just once.

Q Did you take her to Thoughtful House in Austin, Texas?

A Yes, I did.

Q Is that where he saw her?

A Yes, it is.

Q Now, other than recommending that Michelle see a pediatric gastroenterologist when you met him at the DAN conference in 2001, has Dr. Wakefield ever recommended any other treatment for Michelle?

A No, he did not.

Q Has he ever provided treatment for Michelle?

A No.

Q How many times has Michelle gone to Thoughtful House?

A Just one time.

Q And when was that?

A That was in November of 2006.

Q Now, why did you decide to contact Dr. Arthur Krigsman?

A Because Michelle's bowel problems persisted, continued to get worse, and I was not satisfied with the care from the current at that time pediatric GI.

Q How did you hear of Dr. Krigsman?

A At a DAN conference and from another parent.

Q When did you first contact him?

A In, I believe, other than when I introduced myself at the conference, if that counts at the first contact, that would have been -- that probably would have been October of 2002. Beyond that, the next contact would have been January 2003 or somewhere within a month's time to that.

Q So you heard Dr. Krigsman speak at a DAN conference in San Diego in October 2002, is that correct?

A Yes.

Q And did you speak with him after that conference?

A Yes, I did.

Q Okay, what did you tell him?

A I told him that I had a child that was very ill and that she, again, was manifesting the problems that he spoke of during his presentation.

Q What did he tell you?

A He asked me if we had a current gastroenterologist, and I said, yes, we did, and he told me that if I wanted he could call him, because I asked him can you tell him what you found in the children that you're seeing because I think Michelle is very similar to the children that you've seen.

Q So if I'm understanding correctly, you met him in October 2002, but your next contact with him was January of 2003? Is that correct?

A Yes.

Q And what type of contact was that?

A By phone.

Q By phone. Okay. And if I understand your testimony today, Dr. Krigsman is still treating Michelle?

A He's still involved in her treatment.

Q Along with Dr. Ziring at UCLA as well?

A That's correct. Dr. Ziring is the primary treating doctor. Dr. Krigsman is overseeing -- well, I don't know. Yes, they're both involved in her care.

Q Now, Mrs. Cedillo, what is your

understanding as to why Michelle's tissue samples from her January 2002 endoscopy were sent to a laboratory called Unigenetics in Dublin, Ireland?

A What is my understanding as to why?

Q As to why they were sent there.

A To determine if she had measles RNA in her colon tissue.

Q Do you know how the samples were sent there?

A They were shipped.

Q Directly from the hospital?

A Yes. They were frozen and shipped. Well, they were frozen when they were taken and then shipped.

Q At the time did you know that the tissue samples were being sent there?

A Yes, I did.

Q And what is your understanding of what Unigenetics Laboratory is?

A It's a laboratory. I mean, it's a laboratory. I don't know beyond that.

Q Fair enough. And who suggested to you that you should send Michelle's tissue samples to Unigenetics?

A It was actually my desire, my husband and myself.

Q And how did you hear of Unigenetics?

A How did I hear? I think I found it on-line or from another parent.

Q When you say you found it on-line, what do you mean?

A Probably from maybe a posting from another parent. I can't remember where I very first heard of Unigenetics, but I did hear directly from another parent to send it there.

Q Okay. And approximately what time period did you first hear of Unigenetics?

A Oh, that's hard. Let's see. Probably not until around late 2001, maybe between that timeframe and early 2002.

Q And do you know to whom the Unigenetics results were sent?

A Do I know who? Oh, who received them?

Q Who received the results?

A Okay. The results or do you mean the biopsies?

Q Once Unigenetics tested the tissue samples and wrote a report, to whom did they send that report or send the results?

A To Dr. Montes.

Q Okay. Did you ever see those results?

A Yes, I did. I think I might have been faxed a copy. Maybe it was U.S. mail. I can't remember for sure. I did. We both got our copies around the same time.

Q And did someone explain to you what the results meant?

A Yes.

Q Who explained to you what the results meant?

A I believe it was -- well, Dr. Montes did. Oh, I can't remember. I think -- no, I don't think that's right. Dr. Montes did.

Q What did he say that they meant?

A He said it meant that she tested positive for measles virus in her colon tissue, and he said he would try to determine how he could treat her.

Q Now, Mrs. Cedillo, yesterday when you were talking about the results received from Unigenetics you stated, "It was information confirming to us what we thought we had seen in her." What did you mean by that?

A A normal developing, healthy child that regresses and goes on to develop severe bowel symptoms and, of course, autism.

Q Now, Michelle has had five endoscopies. Is that correct?

A Right. Some are upper only, and some are lower and upper.

Q And the last one was in June of 2006?

A That's correct.

Q She's not had another one since?

A That's correct.

Q Is she scheduled to have another one any time in the future?

A No.

Q Do you know? Has her cerebral spinal fluid ever been tested?

A No, it has not.

Q And to your knowledge has Michelle ever been treated with any antivirals?

A Does Tamiflu count? Is that an antiviral?

Q I don't know. I'm not sure.

A Okay. I don't know. Well, since the flu is a virus, she was treated by her pediatrician with Tamiflu with I think it's a five-day or three-day dose, but I don't know if it's technically termed an antiviral. I'm guessing that it might be.

MS. RICCIARDELLA: I have no further questions.

THE WITNESS: Okay.

MS. RICCIARDELLA: Thank you.

THE WITNESS: Thank you.

SPECIAL MASTER HASTINGS: Ms. Cedillo, I know we've kept you here --

THE WITNESS: That's okay.

SPECIAL MASTER HASTINGS: -- a long time yesterday and today. I just have a very few questions.

THE WITNESS: Okay.

SPECIAL MASTER HASTINGS: I wanted to clarify a couple items with you.

First just help me. The doctor, Dr. David -- how do you spell his last name?

THE WITNESS: Ziring. It's Z-I-R-I-N-G.

SPECIAL MASTER HASTINGS: All right. And what's his specialty?

THE WITNESS: Pediatric gastroenterology.

SPECIAL MASTER HASTINGS: Okay. Thank you. And then I wanted to ask you about the testimony you gave in response to Ms. Ricciardella's questions here.

THE WITNESS: Okay.

SPECIAL MASTER HASTINGS: She asked you about the period first the year after the fever incident and then extended that on into the next year, and you talked about some symptoms that occurred during that whole period.

Now, did the symptoms change throughout that period? Did they start low and get worse?

THE WITNESS: Yes, they did. Exactly what you said. They started I would say on a low level and continued to progress, or new symptoms came into the scene.

SPECIAL MASTER HASTINGS: All right. You also said in response to one of Ms. Ricciardella's questions that you said in August of 1997, which was just after the diagnosis of autism, August of 1997, you first began to suspect that there was a connection to the MMR vaccine. Is that correct?

THE WITNESS: For the autism part, not for the change in her. I want to clarify.

I had suspected the change in her had something to do with the fever. I suspected that the fever had something to do with the MMR, but as far as the autism part, since we didn't have the diagnosis until 1997 then that's when I started searching further in a different format.

SPECIAL MASTER HASTINGS: So you began to look for causes of autism at that time?

THE WITNESS: Autism and bowel disease and related to a fever or MMR.

SPECIAL MASTER HASTINGS: Who told you or

where did you find some indication that an MMR could be connected to these?

THE WITNESS: I read on-line, and that could have been in 1998 because I can't remember the dates of the papers when they came out, but Dr. Andrew Wakefield had published around that time. It might have been published in 1997.

I believe it was his very first paper and maybe a subsequent follow-up describing the children, and it was describing Michelle. In my mind, you know, that was the first time. That's where I read it, I mean.

SPECIAL MASTER HASTINGS: The first inkling then was through your own on-line research?

THE WITNESS: That's correct.

SPECIAL MASTER HASTINGS: All right.

THE WITNESS: And then other parents following that.

SPECIAL MASTER HASTINGS: And how did you get in contact with other parents?

THE WITNESS: Through the internet, through friends that I had already made who said, you know, you should talk to this mom or dad. They have a child just like your daughter. Maybe they can help you. You know, that's how.

SPECIAL MASTER HASTINGS: And tell us what is DAN! that stands for Defeat Autism Now! Tell us about that organization.

THE WITNESS: Okay. That's through the Autism Research Institute, and they hold a conference twice a year. At that time they were all in San Diego. Now they move around the country.

That is looking at alternative views and treatments for children with autism. I guess not alternative medicine, but differing -- it's kind of everyone coming together that has anything to do with autism -- behavioral, medical, nutritional if you want to try special foods.

It's all together in one, so it's kind of like a one stop shop, so to speak. You can go and listen to whatever speakers you want. If maybe your child has more issues with behavior you could concentrate on the behavioral speakers.

For me it was always with the gastrointestinal part with Michelle, so that was the focus at that point.

SPECIAL MASTER HASTINGS: All right. And then the last question I have, again a follow-up to one of Ms. Ricciardella's questions, is she asked if it was you and your husband who decided to send the

tissue samples to the Unigenetics Lab.

I guess I'm curious. I know from what you've said I doubt that there's a good lab in Yuma, Arizona.

THE WITNESS: Right. Okay.

SPECIAL MASTER HASTINGS: But I guess the natural question is is there a lab in Phoenix, San Diego or LA? How did you end up picking Unigenetics in Dublin, Ireland?

THE WITNESS: Right. Yes, that would seem very unusual, especially from Yuma, Arizona.

It was because of another mother that I had met on-line and spoken to on the phone. I never asked for an alternate lab, to tell you the truth. She said if you want to get that done you need to get them to ship it to this lab. Here's the address. Here's the contact. I guess you could say I never looked for an alternate lab.

SPECIAL MASTER HASTINGS: I'm not sure I understood that answer.

THE WITNESS: Okay. How did I --

SPECIAL MASTER HASTINGS: What do you mean by an alternate lab?

THE WITNESS: When she gave me the information of where I could have the samples tested

for the measles virus I said okay, I'll send it there, you know.

SPECIAL MASTER HASTINGS: I see.

THE WITNESS: I didn't say --

SPECIAL MASTER HASTINGS: You weren't looking for something closer?

THE WITNESS: Exactly. I didn't go say well, let me see if there's one in Phoenix.

SPECIAL MASTER HASTINGS: Right.

THE WITNESS: Or let's see if there's one in San Diego. I just said okay, we'll send it here. These are the people doing this test.

SPECIAL MASTER HASTINGS: And were they testing it for anything or for some particular? Were they looking for something particular in your understanding?

THE WITNESS: To my understanding they were looking for the measles virus RNA.

SPECIAL MASTER HASTINGS: All right. Thank you.

THE WITNESS: Okay.

SPECIAL MASTER HASTINGS: That's all that I have. Thank you very much.

THE WITNESS: Okay.

SPECIAL MASTER HASTINGS: Ms. Chin-Caplan,

anything more for this witness?

MS. CHIN-CAPLAN: No, Special Master.

SPECIAL MASTER HASTINGS: Okay. Mrs. Cedillo, thank you again.

THE WITNESS: Okay.

SPECIAL MASTER HASTINGS: We put you through a lot here.

THE WITNESS: That's okay.

SPECIAL MASTER HASTINGS: We really appreciate your testimony.

THE WITNESS: You're welcome.

SPECIAL MASTER HASTINGS: You may step down now.

(Witness excused.)

SPECIAL MASTER HASTINGS: Counsel, I understand Dr. Krigsman is going to be testifying. Do you want to start with him?

MS. CHIN-CAPLAN: It would be better if we could just break for lunch and then go straight through. Would that be all right with the Court?

SPECIAL MASTER HASTINGS: Is that all right with the Respondent?

MR. MATANOSKI: That's fine for us, sir.

SPECIAL MASTER HASTINGS: Okay. Let's go ahead and do that. It's high noon right now, so we'll

reconvene at 1:00 p.m.

Again for you folks at home, we're going to take a one hour break now and reconvene at 1:00 p.m.

(Whereupon, at 12:00 p.m. the hearing in the above-entitled matter was recessed, to reconvene at 1:00 p.m. this same day, Tuesday, June 12, 2007.)

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

(1:05 p.m.)

SPECIAL MASTER HASTINGS: We're ready to go back on the record here.

Dr. Krigsman has taken the witness stand. Dr. Krigsman, would you raise your right hand for me?

Whereupon,

ARTHUR KRIGSMAN

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

SPECIAL MASTER HASTINGS: Both of you please speak up. Go ahead, Ms. Chin Caplan.

MS. CHIN-CAPLAN: Thank you, Special Master.

DIRECT EXAMINATION

BY MS. CHIN-CAPLAN:

Q Could you kindly state your name for the record, please? I should wait until you pour your water.

A Sorry about that. My name is Arthur Krigsman.

Q Dr. Krigsman, what is your current business address?

A 290 Central Avenue, Suite 204, Lawrence, New York 11559.

Q Are you a physician?

A I am.

Q Do you have a specialty that you practice?

A Pediatrics and pediatric gastroenterology.

Q Could you kindly give a brief description of your educational background for the Court?

A Starting from undergrad?

Q From undergrad.

A I received a Bachelor of Science graduating with honors at Johns Hopkins University. I went on to medical school at SUNY-Downstate in Brooklyn. I was there four years.

I did a three year general pediatric residency at SUNY-Downstate/Kings County -- it's a combined program -- and I did a three year fellowship in pediatric gastroenterology after that at Mount Sinai Hospital in Manhattan.

Q Since that time, have you practiced either pediatrics or gastroenterology?

A Yes. Since that time I practiced general pediatrics up until 2004. Actually 2005, early 2005.

At the same time as doing general pediatrics I practiced pediatric gastroenterology from completion of my fellowship until the present.

Q And do you have any board certifications?

A I'm board certified in general pediatrics

and pediatric gastroenterology.

Q Doctor, you indicated that you practiced pediatric gastroenterology concurrently with pediatrics.

A Correct.

Q Can you tell us generally where you practice pediatric gastroenterology?

A Well, upon finishing my fellowship at Mount Sinai I practiced pediatric gastroenterology at Beth Israel Hospital in New York, and I was there from 1995 until 2000. My title there was Director of the Department of Pediatric Gastroenterology. It was actually a department of one, and that was myself.

I did all the clinic work. I did all the in-house referrals. I oversaw resident teaching. Residents made rounds with me on the pediatric floors and also were with me in the clinic. As well as teaching pediatric residents, the adult GI fellows were also routinely part of the pediatric gastroenterology clinic services there at Beth Israel.

After 2000 the medical merger wave hit New York, and a number of large hospitals banded together, my understanding is in an effort to have greater negotiating leverage with reimbursement, but because of that all the part-time physicians at Beth Israel,

those who were not full-time, were released, and they only kept the full-timers. I was a part-time salaried physician at Beth Israel, so at that point I left Beth Israel.

Lenox Hill Hospital recruited me. Lenox Hill Hospital in Manhattan recruited me. They called me. Heard you're available. Would you come and join us?

I was very happy to do that, and I assumed the same type of position at Lenox Hill Hospital as I had had at Beth Israel where I oversaw their entire pediatric GI clinic and I did all their in-house pediatric GI consultations.

Q How did you become interested in autistic children and enterocolitis that they exhibit?

A The first patient I saw with autism and gastrointestinal problems was sometime late in 2000. I was a member of a pediatric practice, a general pediatric practice in Woodbury, New York, with a number of associates in the practice.

One of them is an allergist. He's a board certified allergist, as well as a pediatrician, and he had a number of children with autism that he followed within our pediatric practice because he viewed them as having an allergic disorder, and he would do

allergy testing and allergy desensitization techniques, either shots or nasal sprays to desensitize them.

He referred me a few of his patients because he was concerned that the parents all said that those kids had this ongoing nasty diarrhea and seemed to have abdominal pain, something he saw in a number of patients, and he wondered if him and I working together as associates within the same pediatric practice, if I would be interested in evaluating them from a gastrointestinal standpoint.

I told him that I would. I told him that I did not think I would find anything wrong with them, but I'd be happy to do the evaluation, which I did. Those were my first patients.

Q And what were the clinical indications for a referral to a GI doctor?

A Well, the gastrointestinal indications were chronic diarrhea and abdominal pain. That seemed to be going on for many years in these patients that he initially referred to me.

Q Doctor, can you just generally describe the workup that you did on this initial group of children?

A Well, it's a standard diarrhea workup. You know, it's sort of the bread and butter of pediatric

gastroenterologists.

You know, you look for cause for the diarrhea. You look for dietary causes. You look for the possibility of toddlers diarrhea. You look for infectious diarrhea. You look for any underlying metabolic abnormalities.

Most of those, if not all of those possibilities, would be covered by some simple, routine blood tests and a careful history and careful physical examination.

Q And did you do this routine bloodwork and examination on this initial group of children?

A I did.

Q And did you find anything that would lead you to believe that it was related to this noninvasive type of evaluation that you conducted?

A No. The evaluation, the standard evaluation for diarrhea and abdominal pain type of diarrhea that these children had, was unremarkable, and I had no answer for these patients. And I told them that I just don't know and left it at that.

Q So they didn't have any infectious sources of their diarrhea?

A I'm sorry?

Q They didn't have any infectious sources of

their diarrhea that you could determine?

A No. No, their stool cultures were negative. I looked for parasites. These were the routine measures that we would do for a workup to rule out infectious diarrhea.

Q And you indicated that you took a history of these children?

A Correct.

Q And was there anything in their history that would indicate that their symptoms would be related to dietary foods?

A Some of them did. Some of the parents claimed that certain types of foods would cause worsening of the diarrhea and worsening of the abdominal pain.

Most, if not all, of the patients that initially came to me, those first bunch of patients, had already enacted some sort of restrictive diet that they had heard about from their friends or heard about at meetings or conferences.

But despite a variety of dietary intervention, both those that were circulating amongst the autism community at the time and also the more standard dietary changes that a pediatric gastroenterologist would put in place to try and

determine if this is a toddlers diarrhea or if this was other forms of innocuous diarrhea, those were all done or attempted and didn't result in any improvement, so I really didn't understand why these children had diarrhea.

Q So what did you do next for these children?

A I told them goodbye.

Q And then what happened?

A And at that point -- well, probably it was sometime in 2001 is how I recall it. I may be off by a few months.

In 2001, the doctor who initially referred these patients to me, my associate, showed me an article written by Professor John Walker-Smith, amongst others, describing exactly this group of children that I had seen with identical histories, meaning that they had autism, they had chronic diarrhea, chronic abdominal pain.

They did the workup that I had essentially done, and they had also come up with no diagnosis based upon lab tests, history and physical exam. What they did different was they considered the possibility of an inflammatory bowel disease, which I had not considered.

When I initially met with these children,

the possibility of this being an inflammatory bowel disease of some type didn't enter my mind because the conventional teaching of the specific types of diarrhea that you would have, meaning bloody or microscopic or grossly visible blood, weight loss, recurring fever, those symptoms were not present in any of these children so I didn't entertain that possibility, but this Royal Free group did.

They went ahead and performed a colonoscopy, a diagnostic colonoscopy on a number of these children. Specifically I think it was 62 of 63 children. They published their results in September of 2000 in the *American Journal of Gastroenterology*.

What they demonstrated was that the majority of those children who were in fact identical in history, physical examination and laboratory presentation to the ones that I was seeing, the majority of those children there demonstrated this nonspecific inflammation of the colon and of the very end of the ileum.

I was shown that article, and I read it a number of times. I paid attention to it because I didn't know any of the authors on the article, but the final author, the senior member of the group, the senior investigator, Professor John Walker-Smith, is a

world-renown pediatric gastroenterologist who is very prominent, and it was his textbook that I had actually used in my training to learn the pediatric gastroenterology, so he was a name that I recognized.

It made an impression on me because again it was exactly what I was seeing in my own office.

Q Doctor, you indicated that this was an article that your colleague showed you?

A Correct.

Q You yourself did not see this?

A No. I did not make the effort to investigate myself.

Q And you indicated that it was published in the *American Journal of Gastroenterology*?

A That's correct.

Q Do you recall the year that it was published?

A September of 2000.

Q September of 2000. So after you reviewed this article what did you do then?

A So at that point I wondered whether some of those or all of the patients I had initially seen and didn't think I could help perhaps had this disease.

What was interesting, again just to go back to that article, is that if the diagnosis in fact is

an enterocolitis that's something that's treatable, so that was what was so attractive about this finding is that it offered something to these children that you could do for them to make their quality of life that much better.

I called these folks back and performed a diagnostic colonoscopy on them, and to my great surprise the pathologists that were reviewing the biopsies that were obtained at those initial colonoscopies were reading the same nonspecific colitis that the pathologists at the Royal Free had read and had been published. That was very interesting.

Q Doctor, at this point in time did you do colonoscopies on all the patients that you had initially turned away?

A I don't remember if it was all of them or how many, you know, were interested in pursuing that, but many of them. Many of them.

Q And do you recall of the initial group how many you actually did perform a colonoscopy on?

A I don't recall the number of the group. I want to say it was seven or eight kids that initially I said I wasn't interested and I can't help you.

I made the effort to call back all of them.

I don't remember how many of them came back, but a number of them followed through with it.

Q And did you continue to perform colonoscopies on these children?

A Yes. You know, at that point we had a very large pediatric practice, and certainly within our own practice there were many children with autism who had these same gastrointestinal symptoms.

In addition to that, this associate of mine had a separate allergy practice in which he had a lot of children with autism as well, so he would send those patients my way if they had gastrointestinal problems.

Q Doctor, how many colonoscopies did you perform before you believed that there was some connection between the child's autism and the enterocolitis?

A I remember it being after my twenty-second patient. I don't know why that's when the light went off, but I remember seeing that twenty-second pathology report.

You know, virtually all those first 22 showed identical findings, and that's when I concluded that there's probably something going on in the bowels of these kids.

Q You said that they showed similar findings. Could you describe to the Court what those findings were that you were seeing?

A Well, the findings were both endoscopic -- in other words, when you have the colonoscopy within the colon there's a certain appearance that the mucosa, the lining of the bowel, has to the endoscopist.

It's defined in terms of how red or pink it is, pink being healthy color, red being unhealthy. It's defined in terms of ulcerations in the lining of the bowel. It's defined in terms of the degree of vascularity and vascular markings in terms of the smoothness of the surface. Those are all endoscopic appearances that one can appreciate just visually looking at the mucosa, the lining of the colon.

Then beyond that there's a microscopic appearance of what the pathologist sees when they examine the thin slices of biopsies that are obtained. The biopsy findings that most of these children, the majority, had were what would be called either chronic or an active colitis or both, meaning whether the types of inflammatory cells are lymphocytes or whether they're neutrophils or whether they're eosinophils, where they're located, how they're clustered. Those

all go into determining if this would be labeled as an acute or a chronic colitis.

There are also additional findings such as cryptitis, which is highly characteristic of inflammatory bowel disease and also others. I shouldn't say just IBD, but cryptitis is a sign of advanced -- a more advanced -- invasion of the lining of the bowel and burrowing into the crypts. The colon is full of these small crypts. That's premucous primarily.

Cryptitis is a very characteristic finding of a more advanced inflammation, and we saw those as well. There were a few patients who have what's called a crypt abscess, which is even the more advanced level of colonic inflammation.

This first bunch of patients had varying combinations of these findings.

Q What did you do after you did these colonoscopies?

A After the colonoscopies were done and the biopsies were reviewed by the pathologist I decided to try treating this enterocolitis. Primarily it was a colitis.

The term colitis, by the way just to clarify, refers to inflammation of the colon. When I

use the term enterocolitis, the term entero refers to involvement of the small intestine as well, so an enteritis would be small bowel inflammation. A colitis would be colonic inflammation. An enterocolitis would be both inflammation of the small bowel and also of the colon.

When I saw these biopsies that demonstrated enterocolitis, I decided I would treat them with oral anti-inflammatory drugs, the same ones that are very commonly used in inflammatory bowel disease. That's what I was using at the very beginning.

My observations at that point where that when these patients with biopsied proven enterocolitis were started on these oral anti-inflammatory drugs their symptoms markedly improved, meaning the diarrhea markedly improved and their abdominal pain markedly improved as well.

Q You indicated that you were treating them with anti-inflammatories. The fact that they responded to the anti-inflammatories, would that be an indication that they were suffering from a form of inflammatory bowel disease?

A It indicates that they were suffering from intestinal inflammation. It doesn't prove that it was in and of itself.

Taken as an isolated observation, the response to an oral anti-inflammatory drug, a symptomatic response, an improvement in diarrhea, in and of itself doesn't prove that the diagnosis is inflammatory bowel disease.

What it does suggest is that the bowel inflammation that's there of some type that's being treated with an anti-inflammatory drug.

Q Now, at some point in time did Theresa Cedillo contact you?

A Yes. I first met Theresa, as she testified earlier today, at a conference, at a DAN! conference that I had spoken at.

I think it was the October 2002 DAN! conference -- well, I'm not sure -- in San Diego. That's where I think it was though.

Q And do you recall what she said to you?

A Well, she came over to me and introduced herself, and I remember the conversation only because, you know, the story was a very sad one, and Michelle sounded like a very sick little girl.

I remember hearing some of the details and encouraging her to work with her pediatric gastroenterologist who she was already associated with locally.

Q What was her response to that?

A She was happy to do that, and I offered to be available, you know, to input any experience that I had had in dealing with these children.

Q And did you speak to her local gastroenterologist?

A At that point, no. He did not call me. Not immediately.

A few months afterwards I did speak with him on the phone. I don't recall if it was he that called me or I that called him.

Q Okay. Do you remember what the substance of that conversation was?

A We spoke a little bit about my experience with these children and what I thought might be going on in Michelle's bowel based upon the story that Theresa had told me.

Q Okay. At some point in time did Mrs. Cedillo contact you about evaluating Michelle?

A Yes. In the middle of 2003, either late spring or summer of 2003, she called and she said that Michelle was getting worse, that she had lost about 20 pounds over the previous six months. She wasn't eating. What she was eating she was vomiting. Her diarrhea had become unmanageable. She was sick. She

was pale, and she was weak.

She was very concerned. At that point she called me to let me know that this was going on.

Q And did she inquire about whether she could come and see you?

A Yes. She indicated that she really wanted to come and see me. What I told her was that it didn't sound like it was a good idea because Michelle did not sound like someone that should be traveling across the country on an airplane in that condition.

She ended up being hospitalized locally in Yuma, which you heard about this morning. She was hospitalized for dehydration. She had evidence of malnutrition as manifested by a vitamin K deficiency.

At that hospitalization she had placed a surgical jejunostomy tube to ensure that she would be able to get the calories that she needed to reverse the malnutrition and the weight loss.

Q And did Michelle Cedillo eventually come to you for evaluation?

A After she was discharged from that hospital stay in July/August of 2003 she called and she said, you know, we've been discharged, and she really would like to come see me. That's what she did.

Q And when Michelle arrived did you conduct a

physical and an exam of her? What did you do when Michelle came for evaluation?

A Well, when she came the expectation was that she would undergo another diagnostic endoscopy and colonoscopy. The indication for that endoscopy and colonoscopy was the dramatic worsening of her condition over the previous few months.

With the previous endoscopy and colonoscopy in January of '02, that was essentially normal and didn't explain why she would have such dramatic worsening of her GI symptoms, so the hope was that now a year and a half later, a year and three-quarters later, there might be some answers that the biopsies or the colonoscopy might show.

That was the expectation. She came. History, physical exam, which the history was again as you've heard. The physical exam, she was a sickly looking girl. She did not look well at all. The next day she underwent the diagnostic endoscopy and colonoscopy.

Q And what were the results of her colonoscopy and endoscopy?

A The endoscopic appearance, the visual appearance looking through the upper endoscope, was one of this streaking lymphonodularity of the

esophagus. She had a gastritis, meaning stomach inflammation.

On the colonoscopy she had a presence of four ulcerations, which are labeled as aphthous ulcerations. I want to define that term. The slide is a bit later on.

She had four aphthous ulcerations of her sigmoid colon that were photographed. In addition to that, visually she had marked lymphoid hyperplasia of the terminal ileum. Those are her endoscopic findings.

On biopsy the only finding that was demonstrated was this lymphoid hyperplasia of the ileum.

Q And at this colonoscopy and the endoscopy did you come to a conclusion whether Michelle had a condition?

A Yes. I concluded, based upon her history, based upon the presence of arthritis, which was known at that point, and what appears to be a uveitis, although it was not yet diagnosed when I saw her, and the appearance of these aphthous lesions of the colon, taken in combination it's highly suggestive of some form of inflammatory bowel disease.

If I had to choose one particular diagnosis

at that point it would be Crohn's disease, but I was hesitant to call it Crohn's at that point because it didn't fit. It didn't have the diagnostic criteria that would allow me to label it definitely as Crohn's disease then, but I was quite sure that she had a variant of some sort of inflammatory bowel disease.

Q Doctor, you mentioned inflammatory bowel disease. Are there many inflammatory bowel diseases?

A Well, the term inflammatory bowel disease is really an umbrella term, and it encompasses a number of different diagnoses.

The two primary diagnoses that it encompasses are ulcerative colitis and Crohn's disease. There are, however, other diagnostic entities such as an indeterminant colitis or microscopic colitis that can technically fall under that category.

You know, particularly the indeterminant colitis is one where the features, the overall presentation of the physical examination, is suggestive of either Crohn's or ulcerative colitis, but you don't get the tissue diagnosis or the x-ray diagnosis that allows you to confirm with certainty which one of those two diagnoses it is.

That happens fairly frequently in

gastroenterology. When that happens, when the clinician suspects that it's inflammatory bowel disease but we are unable to label it definitely as Crohn's or ulcerative colitis, it sort of goes into the category of indeterminant colitis.

Many of those patients over the course of time, it becomes clear which diagnosis they truly have. Is it Crohn's, or is it ulcerative colitis or something else?

Q So what is the distinction between ulcerative colitis and Crohn's disease?

A A distinction. There are many. The distinction of them is primarily as follows. In ulcerative colitis you tend to get inflammation limited to the lining of the colon. It doesn't penetrate deep into the muscular layer of the bowel so it involves the lining, and it's also contiguous meaning the inflammation always begins at the anus and it extends proximately to varying lengths.

In some people it can only involve an inch or two of the rectum starting from the anus, in other people it can involve the entire colon and in other people it involves varying portions of the colon anywhere in between the entire thing and almost nothing, but it always starts distally at the anus and

extends proximally. There are no skip lesions.

You tend to have a contiguous inflammatory pattern. That's a classic definition of ulcerative colitis as opposed to Crohn's Disease which number one, can occur anywhere from the mouth into the anus, so unlike ulcerative colitis it occurs only in the colon, perhaps the last inch or so of the ileum, but nothing more proximal than that.

The Crohn's Disease can occur anywhere from the mouth to the anus, anywhere in the gastrointestinal tract. In addition, Crohn's Disease is known to involve not just the interior lining of the bowel, but even deeper layers and even perforate the bowel and form a fistula of tracts between the bowel and other organs.

In addition to that as opposed to ulcerative colitis, as we just discussed that's contiguous, Crohn's Disease tends to be patchy. You can have abnormal areas, diseased areas of bowel that are interspersed with areas that appear normal and that in fact are normal to all the ways that we are testing. So those are the three primary differences between Crohn's and ulcerative colitis.

Q And you indicated after Michelle's colonoscopy and endoscopy that her history of

diarrhea, arthritis, the uveitis and the active ulcer lesions in the colon that you find were highly suggestive of inflammatory bowel disease but you hesitated to call it Crohn's. Can you tell the Court why you did not believe you could make a definitive diagnosis of Crohn's here?

A I hesitated to call it Crohn's because Crohn's Disease, if you're a Crohn's purist you would want specific findings to label it as Crohn's. You would look for number one, a tissue diagnosis, a biopsy, that demonstrated particularly something called a granuloma.

A granuloma is a complex of inflammatory tissue that has a very characteristic appearance on a biopsy and pathologists are trained to look for that and notify the gastroenterologist when it's present. Most patients with Crohn's Disease in fact you don't find the granuloma at biopsy, but when you do and the clinical suspicion is high that is something that would lead you to conclude that there's Crohn's Disease.

In addition, a patient who has strictures or fistulas, those are the classic protean manifestations of Crohn's Disease and Michelle didn't have them, although she had many other features of inflammatory

bowel disease. From a physical exam point she had uveitis, she had an arthritis, both of which are known to accompany Crohn's Disease.

Those are well-documented, and well-established and that's beyond dispute. She had them. She had laboratory markers of inflammation such as the ESR and the erythrocyte sedimentation rate. It's a nonspecific marker of inflammation. It's not diagnostic of bowel inflammation, but it's certainly expected when you have Crohn's and ulcerative colitis.

She had elevated C-reactive protein, which again, is another inflammatory marker that's nonspecific. She had an elevated platelet count known as thrombocytosis, which is also nonspecific, but she had all of those in the presence of uveitis and arthritis and aphthous ulcerations of the bowel with a history of abdominal pain and diarrhea.

So that's what made me suspect Crohn's Disease, but I was hesitant to label it as Crohn's because I would have liked to see the absolute characteristic and diagnostic features of Crohn's, and in Michelle's case that was absent. I should add one more thing. The most impressive lab test of all was an elevated it's called OmpC, O-M-P-C, and it's outer membrane foreign *C*. This is an antibody that's found

in the blood of Crohn's patients.

The majority of Crohn's patients do not have anti-OmpC, but the presence of anti-OmpC, in other words the specificity of that lab test, in other words how many times do you have a positive OmpC and in fact don't have Crohn's Disease is very small. So on top of all the things I mentioned that made me clinically suspect that this girl had an inflammatory bowel disease she has an anti-OmpC, which is highly specific for Crohn's Disease as well.

Q And after reviewing all the findings did you decide on a course of treatment for her?

A So once we had the visual confirmation of the aphthous ulcerations I was satisfied that I was dealing with an inflammatory bowel disease, an indeterminate colitis is what I really wanted to call it, and the designation is not that important because the treatment is really the same anyway, so we don't go to extraordinary lengths to confirm a diagnosis with this sort of situation.

Those things tend to resolve and solve over time and the diagnosis ultimately becomes clear. In Michelle's case it did and we'll get to that in just a few minutes, I guess. I decided to treat her with a combination of sulfasalazine, which is an oral anti-

inflammatory drug. It acts topically on the lining of the intestine.

I treated her with a steroid, Prednisone, which of course is an anti-inflammatory drug. I also treated her with a medicine called 6-MP, 6-mercaptopurine, which is an immunosuppressant agent. I chose that combination of drugs based upon the degree of illness that Michelle had.

This dramatic weight loss, this inability to tolerate food by mouth is a necessity for a feeding jejunostomy tube, the uveitis, the arthritis, the horrendous diarrhea, the intensity of all of it, and also the fact that this family was really out in the wilderness of Yuma. All those things made me want to ensure that we got this disease under control very quickly.

Q And, doctor, you're in New York and Ms. Cedillo and her family, Michelle, were living in Arizona. That's a problem, treating her long distance.

A That's a big problem. It's a testimony to Theresa and her obvious endurance and desire to help her child. You know, I had encouraged her to find someone local that would be able to see Michelle, that would be able to understand the illness, that would be

available, that would look at Michelle as having bowel inflammation and treating it, and she made every effort to do that.

It took her a while to find the right people, but during the period of time that she was searching she really didn't have any other available gastroenterologist that was willing to prescribe these medications because they saw the disease the way that I did. So I ended up working very closely with her pediatrician who was very, very cooperative, and together we managed Michelle in the early part after I had seen her initially.

Q Now, you indicated that you ordered sulfasalazine, Prednisone and 6-MP. Are those all drugs that are standard in the use of inflammatory bowel disease?

A Yes, they are.

Q And to your knowledge did Michelle improve on this medication?

A Yeah. Her clinical symptoms improved markedly. Her stools, you know, the horrendous diarrhea which you've heard so much about, either I don't recall if it disappeared and they became normal or if the frequency went down to once a day and became almost normal, but clearly it was not the eight or

nine liquidy stools anymore. That was a dramatic quality of life improvement.

The pain, the irritability, the self-abusive behaviors and also her arthritis, the degree of swelling of the joints and her ability to ambulate at least to some extent all improved.

Q Now, doctor, Prednisone. Is that a drug that a person can remain on long-term?

A Prednisone given over the long-term will almost always if not always produce toxicities, so Prednisone is not a drug that you want to have someone on long-term unless you absolutely have no other choice.

Q And did you try to wean Michelle off her Prednisone?

A A number of times we tried to wean her off it. My hope was that because she was on 6-MP, and because she was on sulfasalazine and because we had started an elemental enteral formula, meaning a school of thought in Crohn's Disease that one way to treat it is by decreasing the antigenic stimulation to the bowel from dietary factors so that you give an elemental formula, a formula which is broken down to its elemental parts, there are no complex proteins in the formula to act as antigens, that's one way to

treat IBD and Crohn's as well, and we had that going through the J-tube at that time.

My hope was that between the enteral feedings, the elemental feedings, the 6-MP and the sulfasalazine we would be able to get her off Prednisone. We found that whenever we got her below a certain threshold dose the symptoms returned, so she was demonstrating what we call steroid dependency.

Q What did you decide to do then when it was clear that she was steroid dependent?

A Well, at that point, you know, what you normally try and do is you want to maximize the sulfasalazine that a patient gets and maximize the 6-MP. You know, maximize the nonsteroid drugs in the hope that you can eliminate the steroids. With Michelle when we tried to do that a lab test called the lipase, L-I-P-A-S-E, became elevated.

Lipase is most frequently an indicator of pancreatitis. Not exclusively, but when you see an elevated lipase the first thing you think of is the pancreatitis 6-MP. One of the known complications of 6-MP is that it can cause a pancreatitis in many people, and pancreatitis can be a nasty illness that could become chronic.

So I don't recall that we had ever obtained

a baseline lipase. In other words no one had ever drawn that particular lab test prior to her starting on 6-MP, but most clinicians once they start a patient on 6-MP will monitor the lipase at regular intervals just to make sure that there is no pancreatitis that's forming.

So when we did that we found that Michelle's lipase was markedly elevated. The immediate and recommended response to that is to discontinue the 6-MP, which is what we did. Now she's off 6-MP, and she's again stuck with the Prednisone, and the sulfasalazine and the enteral feedings all the while demonstrating some Prednisone toxicity.

Q What did you do then?

A So at that point is that it was clear that she needed to come off Prednisone yet she needed it to function. The next step in that type of patient is to go to the next class of immunosuppressive drugs. There's a newer class that was introduced about 10 years ago, and it's called anti-TNF, anti-tumor necrosis factor, drugs. TNF is a cytokine, it's a molecule, and it's a product of lymphocytes and it's a molecule that is particularly active in excess in patients with Crohn's Disease.

This drug was developed in the last 10 years

or so, maybe 11, 12 years, that acts to block the effects of TNF so that TNF is not able to stimulate an inflammatory response. And that's it. It's a new class of immunosuppressants, but it's very effective, very, very effective in those diseases that involve TNF as the mediator of inflammation.

Using an anti-TNF agent is very, very effective in bringing about clinical improvement. That was the next step for Michelle. The trade off is that along with its therapeutic efficacy because of it's potent immunosuppressive capacities therein lies the potential for side effects so that when you immunosuppress a patient too much you get a whole host of potential side effects.

That of course goes into your decision in whether to start this drug or not. Clearly, Michelle was a candidate for this drug because there was no other choice. It's a widely used drug, but this is the thinking that clinicians go through before deciding to use it. At this point she was at a state where she needed this anti-TNF drug. It's most commonly known as Remicade as a trade name.

The decision was made to institute Remicade therapy.

Q And did Michelle respond to the Remicade?

A Yeah. She did very well with that, actually. It markedly improved her diarrhea again because once the 6-MP was stopped her diarrhea really became horrendous and so did her arthritis. When Remicade was begun, I don't recall the exact date it was started, but when it was begun it produced again this marked improvement in both her diarrhea, her abdominal pain and the arthritis.

Q We've heard testimony that at some point in time the Remicade had to be stopped. Is that true?

A That's correct.

Q What was your understanding of why the Remicade had to be stopped?

A It was stopped because she had a seizure. It wasn't her first, it was one of her many seizures, but this one occurred while she was standing and she fell. She sustained a fracture to her I think it was a tibia, fibula fracture I think, and it required immobilization, and screws, and casting and you've heard the story from Theresa. There was concern from the orthopaedic surgeon who was responsible for the bone healing that the Remicade may interfere.

There's some evidence that Remicade has the potential to interfere with bone healing. In fact, in Michelle's case the bone healing took a very long

time. The concern was, well, the intent was to eliminate all the potential confounding factors that might inhibit the healing of that bone, so the Remicade was discontinued.

Q Doctor, at some point in time you had suggested earlier to Ms. Cedillo that she get a local gastroenterologist, correct?

A Correct.

Q And at some point in time did she eventually do so?

A Yeah.

Q Did you communicate with that gastroenterologist?

A Absolutely.

Q Do you know who that gastroenterologist was?

A The one that Theresa had met with that she liked was Dr. Donna Ursea at Phoenix Children's Hospital.

Q To your knowledge did Dr. Ursea conduct some additional diagnostic testing of Michelle?

A Yes. So Dr. Ursea wanted to establish a baseline, this is now 2006, of the status of Michelle's bowel disease. She performed an upper endoscopy, a colonoscopy and also a pill camera study of the small bowel.

Q You mentioned a PillCam. What is a PillCam?

A A pill camera is exactly what it sounds like. It's a camera, but it's the size of a small pill and it's designed to be swallowed.

Q When you swallow the pill, what does it do?

A What the PillCam does, it takes two photos per second as it traverses its way through the upper gastrointestinal tract so that the moment you swallow it you've begun to photograph the esophagus, the stomach and the small intestine. It has a batter life of eight hours, which is usually long enough for the pill to make its way all the way through to the small bowel and to the colon.

The PillCam is designed to image primarily the stomach but the small bowel as well. That's what was used in Michelle's case.

Q Doctor, you mentioned a few words that I'd like you to explain to the Court. You mentioned that when you did the endoscopy of Michelle she had some aphthous ulcers?

A That's correct.

Q Can you tell the Court what an aphthous ulcer is?

A Well, now would be the time to show the slide that I've prepared. Also, can I ask for a laser

pointer?

SPECIAL MASTER HASTINGS: Just for the record, Dr. Krigsman, Dr. Aposhian is going to be showing some slides, we've got the first one up on the screen, and a paper copy of the slide is going to be filed into the record by the Petitioner.

Go ahead, Ms. Chin-Caplan.

Mr. Homer, did you folks give a copy of the slide to the court reporter as well?

MR. HOMER: No. I'll give her one now.

BY MS. CHIN-CAPLAN:

Q Doctor, I had asked you what is an aphthous ulcer?

A Excuse me. Before we define an aphthous ulcer I want to first define a few other terms that I've used this afternoon, and that would give us a foundation to understand what an aphthous ulcer is. So the first slide, the definition of an ulcer in general. This is from a standard pathology textbook that is widely used in this country in medical schools.

I used it when I was in medical school. This is the definition and the photograph from the electronic version of the textbook. An ulcer is a local defect of the surface of an organ produced by

the shedding of inflammatory necrotic -- necrotic means dead -- tissue. Ulceration can occur only when tissue necrosis and the resultant inflammation exist on or near the surface.

I'm going to use the laser pointer to demonstrate on the slide on the screen behind me. This area over here is the lining of the organ, and this hole is the ulcer. So it's kind of punched out and it's a crater. An ulcer can involve either a shallow ulcer, which this is the absolute external lining of the organ, or it can go deeper and penetrate deeper layers.

Depending on the organ and what layers are there an ulcer can extend to various depths. In the case of the gastrointestinal tract if the process of ulceration goes deep enough it can perforate, it can go all the way through, and that causes all kinds of horrendous complications. That's an ulcer. This is a kind of ulcer.

The same type of process would be seen in classic acid-related diseases of the stomach where the erosive entity is stomach acid and that's causing the erosion and then ulceration. Many drugs can cause this as well, aspirin, other nonsteroidal anti-inflammatories. The reason why they can injure

stomach, which many of us are aware that it does in the corresponding case, is because for a variety of reasons it ends up ulcerating the lining of the stomach. That's what an ulcer is.

Q Now, doctor, you had also mentioned the term lymphonodular hyperplasia.

A Okay. Let's look at the next slide. This is an example of the lymphonodular hyperplasia that we talked about. On the slide on the left, this is a photograph that I took of a patient. This is a colon. The colonic mucosa is typically smooth, and here we see the presence of these small, little bumps. Can you appreciate that. There's small, little nodules that are present beneath the surface. These are submuco. They're below the muco level.

Because of their size they cause a small protrusion. I don't want to get into the issue now whether this is considered always normal, or always abnormal, or sometimes normal, sometimes abnormal. I want to avoid that issue for now. I just want to show the picture of what the entity is. This would be the microscopic appearance of lymphoid hyperplasia.

What you see here is this is lymphoid tissue. This is the collection of primarily *B* lymphocytes, and they're coalescing. They're not

encapsulated, they're kind of loosely formed and they form a nodule. This mass is what causes the pushing out or the protrusion that you see here that's evidenced as the nodule.

This lower arrow, it shows another lymphoid nodule here, and the tail portion at the center is called the germinal center. A germinal center is the area of the lymphoid nodule that's actively replicating. The function of lymphoid tissue in general but those of the intestine is to detect anything that the immune system sees as foreign.

Lymphoid nodules are part of the overall immune system of the bowel. It detects anything it sees as foreign, and that could be a virus, it could be a bacteria, it could be a fungus, it could be a food allergen.

Whatever comes its way that it sees as a threat it goes through a series of processes that initially involve the lymphoid nodule, and when it does that the lymphoid nodule is stimulated to produce and replicate *B* cells, which is the subpopulation of lymphocytes, and those *B* cells are the area of rapid replication is that germinal center. This is the normal immune response to any sort of invading pathogen.

When you have those active germinal centers that would cause even further enlargement of the lymphoid nodule. The photograph on the left would show even more prominent lymphonodularity because the underlying lymphoid nodule is now bigger because of the presence of this hyperactive germinal center.

Q Was it your testimony that you found lymphonodular hyperplasia in Michelle's colon?

A Yes. In her colon, but it was most prominent in the terminal ileum, which is an area that's most rich in lymphoid tissue.

So if you would take a look at the density of lymphoid nodules throughout the bowel the terminal ileum is the area which is most dense, has the most lymphoid activity, so that when you have lymphoid hyperplasia, when you have an allergic response, when you have a bacterial infection, you would expect that the region of the bowel that most manifests that in terms of lymphonodularity would be the terminal ileum.

Q And, doctor, the presence of the lymphonodular hyperplasia, would that be an indication that there was some process in Michelle's bowel that was causing the inflammatory bowel disease?

A Well, it suggests that the immune system is recognizing something and responding to it

appropriately.

Q Would that something be some sort of infectious agent?

A It could be.

Q Now, doctor, you included on your next three slides definitions of aphthous ulcers.

A Okay.

Q Could you kindly tell the Court the reason why you included these definitions?

A Yeah. Michelle's finding on her PillCam study was one of aphthous ulcerations, and I wanted to give the Court the definition of an aphthous ulcer. We know what an ulcer is, and we know what lymphoid hyperplasia is. The aphthous ulcer -- and this is taken from a standard gastroenterology textbook, and it's also widely used and it's accepted as authoritative.

The definition reads that the earliest characteristic lesion of Crohn's Disease is the aphthous ulcer, meaning that Crohn's Disease starts off as being an aphthous ulcer. That is the earliest lesion seen in the disease. That the horrendous manifestations of Crohn's Disease is the deep ulcers, the fissures, the fistula, the strictures, all begin as an aphthous ulcer.

These superficial ulcers are minute. They range in size from barely visible to three millimeters and they're surrounded by a halo of erythema. So this is the endoscopic appearance. The appearance to the clinician who has the scope in the colon is that you see an ulcer, a bit of a depression and there's a halo of redness -- erythema is redness -- that surrounds this ulcer.

Now, in the small intestine the aphthous ulcers arise most often over lymphoid aggregates. That is a characteristic feature of the aphthous ulcer is that it occurs specifically over a lymphoid nodule with destruction of the overlying *M* cells. The colon, the definition continues, the aphthae can occur endoscopic.

So the visual appearance in the colon you might not be able to appreciate ulceration like you can in the small bowel, but still even in the colon they occur over these lymphoepithelial complexes or lymphoid nodules, lymphoid aggregates. Okay. That's the first definition.

The second definition, which is the same definition just from another source, from a standard pathology textbook that will be used for the first slide, "a characteristic sign of early Crohn's Disease

is focal mucosal ulcers resembling canker sores, aphthous ulcers, edema and loss of the normal mucosal texture. With progressive disease mucosal ulcers coalesce into long serpentine linear ulcers which tend to be oriented along the aphthous of the bowel. Narrow fissures develop between the folds of the mucosa."

Now, that's in bold font because what I'm going to show you in a few minutes is that Michelle's pill camera demonstrates that not only does she have the appearance of aphthous ulcers on her PillCam study, but there is some excellent quality photographs of the linear orientation of these ulcers within the fold of the small bowel. So it fits the definition of the early lesions of Crohn's Disease to a *T*.

Again, in more advanced disease it penetrates deeply through the bowel wall. Now, the earliest lesion in Crohn's Disease appears to be focal neutrophilic infiltration into the epithelial layer, particularly overlying mucosal lymphoid aggregates. Again, in bold because that's what we're going to be showing you Michelle had.

The third definition, which is identical also, I've just scanned this from -- this is a very, very interesting paper published in the *Journal*. It's

not from a textbook, but I included it here because this goes back as far as 1980. So this is not new information, this is old information. This study was landmark in that it defined and described an aphthous lesion and compared it to electron microscope studies, so it proved the ultrastructural finding.

It went beyond what you see with a regular light microscope, and it correlated it with an even finer ability to see small structures. Again, the definition that they go by when they did this work was if you look at the last sentence an almost constant feature of these minute lesions is active proliferation -- I'm sorry. Go back up. The second sentence.

The lesion is typically located over an aggregate of lymphocytes and the basil portion of the lamina propria. Again, same definition. What this adds which we didn't see in the two definitions before was that an almost constant feature of these minute lesions is active proliferation of the epithelium at the ulcer margin, an apparent attempt at healing. That's another characteristic of the aphthous ulceration. That's what this is.

Q Doctor, do you have a photograph of an aphthous ulcer to show the Court?

A The next slide will demonstrate using the same slide I showed you before, we're taking it from a textbook, of a lymphoid nodule, and I'll just use my laser pointer again on the screen behind me, if this is the lymphoid nodule that's causing the protrusion of the overlying epithelium into the lumen of the bowel the aphthous ulcer would then be ulceration of the mucosal lining that overlies those lymphoid nodules and lymphoid follicles.

That would be a definition of the aphthous ulcer. So when you're looking at an aphthous ulcer you would like to be able to identify an underlying lymphoid nodule either visually with a good quality photograph or histologically from a tissue specimen under the microscope.

Q Doctor, you obtained this through what procedure?

A Obtained what?

Q You are able to determine that an aphthous ulcer exists through what procedure?

A Well, in Michelle's case the earliest indication of her having aphthous ulcers was on a colonoscopy that I did in September of 2003.

Q Okay. And, doctor, a colonoscopy again is what?

A Colonoscopy, I have a slide just to demonstrate what that is to make sure that everyone understands. This is also a classic. It's the cartoon of the intestine. The area in pink is the colon. You see the scope entering at the anus and going all the way around the colon. The tip of the scope emits a very bright light using fiber optic technology.

What is seen at one end of the scope is transmitted and displayed on the video monitor that the endoscopist looks at, so you see the images in real time. So we did a colonoscopy on Michelle in 2003, and the photograph on your right, these two photographs are from the colonoscopy that I did on Michelle in 2003.

What you see here are classic colonoscopy appearances of an aphthous ulcer. You have a central white area with a surrounding red halo of erythema. Now, one could argue using the definition of there being an underlying lymphoid nodule how do you know that this is underlying lymphoid nodule? Maybe this is just a regular depressed ulcer.

That's a good question, but other photographs here suggest, this one in particular, that there is a protrusion into the bowel lumen and

surrounding erythema. There's another one over here. This is the central area with ulceration. Now, again, you really can't appreciate the ulceration from these photographs. The colonoscopy generally does not have the resolution to allow you to see very small epithelial ulcerations.

Sometimes you can see it, but very often you can't. In these photographs there's no clear evidence that there is an ulceration going on, but there's clearly a nodule, the surrounding erythema. These I call aphthous ulcers, and there are four of them. On the photo on the left you'll see a photograph that was obtained by Dr. Ursea in 2006 of Michelle's colon and you'll see again the central either nodule or ulcer, it's hard to tell from this photo, with surrounding erythema, the redness.

I want to point out, also, that when you look at these photos when you have erythema around these inflamed ulcers/nodules, when you have that the erythema does not tend to have a sharply demarcated border. It just kind of fades out and dissipates as it moves further away from that central lesion. That would be distinct from an ulcer, which you would expect to demonstrate a very sharply demarcated border.

I make this point now because the PillCam photos will show a sharply demarcated border, and that's how I know that what the PillCam is showing in the small bowel is an ulcer which is really not appreciated in these photos.

Q Doctor, you mentioned a PillCam. What is a PillCam?

A The PillCam is a demonstrated in this slide. The photograph on the left is a close up view of it manufactured by Given Imaging in Yokneam, Israel, and it's a capsule with a clear dome lens. Those four white rectangles on top are the eye source. They flash twice per second. They take a photograph. The black circle between them is the photographic lens.

Just to give you an idea of the size and a perspective on that is a photograph of somebody holding it between their fingers.

Q Doctor, who performed the PillCam on Michelle?

A The PillCam was done in 2006 by Dr. Ursea at the same time that she performed an upper endoscopy and colonoscopy. So at that colonoscopy there was this apparent aphthous ulcer seen in her colon.

Q And did you have an opportunity to review this PillCam yourself?

A Yes. I reviewed it way back when soon after it was performed, and we'll discuss that in just a few moments.

Q Are these photos of Michelle's PillCam that was done by Dr. Ursea?

A No. This slide is just to give the Court an idea about what a PillCam photo would look like of an aphthous ulcer. These photos were taken off the Given Imaging online atlas. They provide gastroenterologists with online photographs that are demonstrative to help us clinically. These are downloaded from their website, free photos of examples.

The atlas labels it as aphthous ulcers in Crohn's Disease. What you see here, again, that central tail lesion, the surrounding halo of erythema or redness. Same thing you see over here, the central lesion. Hard to tell from these photos if there's a depressed ulcer there or if it's projecting in the lumen surrounding erythema. The same thing over here. The central lesion with surrounding erythema.

The next slide shows what Michelle's PillCam photos show, and you will notice how identical these lesions are to the lesions that the atlas identifies as aphthous lesions of Crohn's Disease. Central

lesions, surrounding erythema here as well. The blue arrows are pointing to the lesions that are of interest to us.

The upper left in each frame tells you the time that's elapsed since the beginning of the study, so we see that this is multiple locations. This is three hours and 16 minutes, this is a minute later and this is over two hours later, giving you the idea that these aphthous lesions are scattered throughout her small bowel.

Q Doctor, so the slides that you have up here, the photographs that you have, this is the passage of the PillCam through her small bowel?

A Right. Right.

Q And how rapidly does this passage take?

A It depends on a number of factors, mostly on the motility of the bowel. The way the bowel works, it has what is called peristalsis, so it propels things forward from top to bottom by a series of sequential contractions of the smooth muscle of the bowel wall. There are many diseased states that affect the peristalsis of the bowel.

Some diseased states make the transit time quicker so things move through very rapidly. Other diseased states affect it the other way, they make

transit time slower and it could take many, many hours to pass through the bowel.

Q And in Michelle's case there was a passage of almost two hours between the initial findings of aphthous ulcer and the later finding?

A More than that because her initial findings were very early on. We'll show some more slides coming up. This is another example of the central nodule, the lesion, and here you get the sense that there's erosion. There's more of a sharply demarcated border, which is different from the photograph of erythema that we saw in the picture of the pink in the colonoscopy that didn't have that sharp demarcated border. These have a distinct impression of a sharply demarcated border of an erosion.

Q You indicate that this is a picture of the colon.

A I'm sorry. This is the small bowel. The photo before it that we showed, the first photo of the aphthous ulcer of the colon, what I meant to say was that surrounding rim of erythema did not have a sharply demarcated border. So when you're dealing with erythema or redness you don't expect to see a sharply demarcated border, but when you're dealing with an ulceration you do expect to see a sharply

demarcated border, which is what this photograph shows.

There are even better examples in the slides to come. Again, these are all examples taken from Michelle's PillCam study. I want you to look at the black arrow. The four photographs, one, two, three and four, are sequential, so they're taken over a period of two seconds. Again, it's one photograph per every half second. What you're seeing over here is again the central area of -- this appears, too, to be a raised nodule with surrounding again area of erythema and erosion that is around it.

What's interesting is that in these photographs if you remember the photograph of the PillCam that we showed at the beginning to be the lens of the PillCam is a dome. As the camera is traveling through the bowel the bowel mucosa is pressed up against the lens. That's one type of photograph that the camera can take. So you have the mucosa of the bowel pressed up against the lens and you're photographing it.

Another way that the camera could photograph the mucosa is if the camera is sitting within an open lumen, so it's photographing like taking a picture of a hallway. We'll show some photos of what Michelle's

bowel is like over there. These particular photos, what we're looking at, is the bowel mucosa is pressed up against the lens.

The way we know that is because this area, the central area of the photograph, is a bit lighter color than the surrounding area and that's because it's pressed up against it, and it's pushing out the blood. This circular appearance of this mucosa here is clearly different, it's pinker, it's lighter, than the area around it.

I mention this because when you have an erosion and it's small, it's one millimeter, when you have the mucosa pressed up against the lens of the capsule you would expect that erosion area would not be pressed up against it as well because it's a bit off the lens. That's appreciated in these photos, and that's why you're able to see it. So even though the mucosa is up against the lens there's still a depression with the sharply demarcated border.

This gives you again a sequence of four photos that shows the appearance of that particular lesion as the camera is moving slowly by it.

SPECIAL MASTER HASTINGS: All right. Just for the record that was page 13 of the sequence of Dr. Krigsman's slides.

Go ahead, Ms. Chin-Caplan.

BY MS. CHIN-CAPLAN:

Q Dr. Krigsman, what does the next slide show?

A This is, again, a very similar type picture. You have the mucosa pressed up against the lens of the camera, and what you see here, this is demonstrated even better than the previous photos, is you have one nodule there, another one there, another one there. So here we're beginning to see the pattern that we referred to before in the definition of the earliest lesions of Crohn's Disease.

We have this aphthous ulcer with surrounding erythema, redness, the sharply demarcated border and the presence of this lymphoid nodule within it, three lymphoid nodules.

Q Doctor, the next slide, how does that differ from the other ones that you showed us previously?

A This slide is different because this is a photograph of that same lesion taken through air. So here, although the periphery of the photograph shows the mucosa pressed up against the lens of the PillCam, the center of the PillCam is photographing the lumen or taking a picture down the hallway. What you can see very clearly here, and these pictures are very impressive, is this distinct nodule. This does not

have the appearance of an ulcer at all.

This clearly is a protruding nodule. And there's again the sharply demarcated area of erythema around it. The same things are back over here in the back of the photograph. These lesions are contained linearly again along the fold of the small bowel.

Q Doctor, the next slide is a slide of what?

A Is again viewed through air, and it's just the same as the previous slide, just another location and again the sharply demarcated border.

Q Doctor, this slide shows that this is four hours and 34 seconds after Michelle had swallowed the PillCam?

A Well, she didn't swallow it. It was placed endoscopically. It was done during the endoscopy. So a device called a Roth net was attached to the endoscope and the pill camera was deployed in the proximal duodenum using the Roth net. But, yes, from the time the capsule was activated this is four hours later.

Q Okay. So you've shown us photos from approximately on page 15, that first PillCam photos indicate 20 minutes?

SPECIAL MASTER HASTINGS: Could you say that again, Ms. Chin-Caplan?

BY MS. CHIN-CAPLAN:

Q I was saying on page 15 that the time -- no.

A Yeah. This one is 20 minutes and 51 seconds.

Q So this is 20 minutes and 51 seconds after the PillCam had been placed by Dr. Ursea?

A Correct.

Q And, doctor, the next photo was four hours and 34 seconds after the placement of the PillCam?

A Four hours, 34 minutes and one second.

Q Okay. Is that an indication that in that period of time this PillCam is taking photos of the lymphoid nodular hyperplasia that you have described throughout her colon?

A Well, not just the LNH, but also these aphthous ulcerations. Right. And I should add that these photos are by no means all of the lesions. The bowel contained dozens and dozens of these lesions.

Q Were there some additional photos that you wanted to show this Court?

A Yes. This one also demonstrates again the mucosa is pressed up against the lens of the capsule and the lumen is actually down this way, but this area clearly is unable to be pressed up against the lens of the capsule because there contains a small erosion,

central lymphoid nodule, surrounding erythema, sharp demarkation of the border.

Throughout this whole area you can see a whole bunch of those small nodules there with surrounding erythema again lined up in folds along the fold of the small bowel. You can even see it through here as well.

SPECIAL MASTER HASTINGS: That was Slide 17. Ms. Chin-Caplan, if you mention that you're going to the next slide if you give the page number that will make a little better record on this.

MS. CHIN-CAPLAN: Okay.

BY MS. CHIN-CAPLAN:

Q Dr. Krigsman, we're moving on to page 18 now.

A Okay. This slide on the left taken at 31 minutes and 54 seconds after activation of the capsule shows again more of the same. It's the tissue of the bowel mucosa pressed up against the lens of the capsule, and you have a central nodule over there, surrounding erythema, sharply demarcated border.

What's interesting about this photograph is that as you recall, the third definition that we gave of aphthous ulcer included the finding of this heaping up at the rim of the ulcer as an indication of the

aphthous ulcer entity, and that's the sero with epi attempt at healing, and that epithelial regeneration and that you can see and appreciate the thickening around the rim. You can see it over here also.

In my mind this is a more impressive picture. Here you certainly see again this area where the tissue is otherwise pressed up against the lens of the capsule, this area is not, it's in central nodule, surrounding erythema.

Q Doctor, on page 19 of this PillCam --

A Okay. This photograph, these two show more of the same. Here again it's just these same central nodules, surrounding erythema, heaped up rim and it's pushed off the lens of the scope. The reason why I'm repeating these photos, it may seem repetitive, but the point I want to make is that these were present throughout Michelle's bowel, not just in one or two locations. I don't want to show all of them. That will take all day.

Q And, Doctor, if we just briefly run through the next few PillCam slides?

A Skipping to the last slide or maybe it's the next to last slide, and this is a very nice demonstration of the linear aspect of these lesions. You see here central nodule, erythema around it,

sharply demarcated border and you see it again over here as well, the nodule, erythema, nodule along the fold of the small bowel, exactly as described to be the earliest lesion of Crohn's Disease.

SPECIAL MASTER HASTINGS: So that was Slide 20. Go ahead.

BY MS. CHIN-CAPLAN:

Q I'm sorry. Twenty-one, doctor?

A This is the last I believe of Michelle's PillCam photos which shows more of the same taken at 44 minutes, 29 seconds, and it shows where the three black arrows are three distinct lymphoid nodules, surrounding erythema and mucosa ulceration within the fold of the small bowel, exactly as described.

Q The photos that you took on pages 22 through 24, can you describe for the Court what the significance of these photos are?

A Yes. This photo I had forgotten about. I included this to demonstrate --

SPECIAL MASTER HASTINGS: Which one are you talking about?

THE WITNESS: This is the photograph taken after one hour, 42 minutes and 32 seconds --

SPECIAL MASTER HASTINGS: Okay. Page 22. Go ahead.

THE WITNESS: And what the black arrows are again pointing to the rim of this ulcer, the small mucosal ulceration. If you look of course you see the central nodule that is evident over here, but the area around it is not homogeneous, it's actually heterogeneous. This area is darker than the surrounding area even though they're all within the rim of the ulcer. What this suggests is that the ulcer is varying depths.

I thought that was just something that illustrated, and I wanted to include that.

BY MS. CHIN-CAPLAN:

Q And what is present on page 23?

A This is a demonstration of an ulcer without erythema which I found very interesting. These photographs show again the same pattern of mucosa standing away from the lens of the capsule despite everything else being pushed up against it around it.

Within that area that's off of the lens you have those lymphoid nodules that are there and you see a very sharply demarcated border, but you don't really appreciate the presence of redness or inflammation, and I wanted to include that as something that I thought was interesting as well. This is more of the same. We're taking a look at slides now taken at 31

minutes and 46 seconds.

These are two sequential photos. Again, central lymphoid nodules, surrounding erosion with minimal erythema or inflammation.

Q Doctor, what is page 25 a picture of?

A Page 25 for those of you who don't know what this is is a photograph of Michelle's diaper and her diarrhea. This is as recently as July of 2006. I included this slide because I thought that it was important for the Court to see firsthand what the diarrhea was. We're talking about liquidy stool.

If there's any question in anyone's mind whether this diarrhea was real, or not real, or semisoft, or otherwise, other various degrees of being formed, this is Michelle's typical stool. To be any more formed than this is unusual for her and is almost always a result of being on either Prednisone, or 6-MP, or Remicade, or Humira.

Q You indicated that Michelle had also had arthritis. Is this a picture of what you saw when you first saw Michelle? This is page 26.

A I don't recall when this was taken, but at some point clearly. This is Michelle taken by Theresa sent to me by mail, and it shows actually, both ankles are swollen but there's clear asymmetry between the

left leg and the right leg. Theresa had mentioned earlier in her testimony that the swelling had gone all the way up to the knee.

This is a photo demonstration of exactly that. The ankle is deformed, it's swollen, the foot is turned out and the swelling does indeed extend up to the knee.

Q Doctor, on page 27 what was the reason for including this photo?

A I included this photo to show you what Michelle looked like right before I saw her. This is at around the time she was hospitalized, in July-August of '03, and one of the things that resulted in that hospitalization from the investigations was the diagnosis of a Vitamin K deficiency. Vitamin K is needed for clotting.

When Theresa had called me, before the hospitalization, saying that Michelle, who is self-abusive when she is in pain, which always improves when the diarrhea and arthritis improves, during this period when things were really bad, she was self-abusive, but she was causing severe black and blue marks, or ecchymoses.

This is a photograph of that, and the reason why they were more severe than usual was (a) her pain

was worse, so she probably was hitting herself harder, but, more importantly, she had a clotting disorder that was diagnosed in the hospital from Vitamin K deficiency, which is a result of malnutrition. Because of her anorexia and inability to tolerate anything by mouth, she became deficient in Vitamin K. When she was banging, it tended to bruise more than it normally would have.

Q Doctor, with the history that you took, the physical exam that you conducted, the information that you obtained from Mrs. Cedillo about Michelle's early years, the laboratory findings, and the endoscopic procedure that you performed, did you come to a conclusion about whether or not Michelle Cedillo suffered from an enterocolitis?

A No. In my mind, there was no doubt, even going back to 2003, that she had an enterocolitis of some sort. In my mind, I was calling it an indeterminate colitis at that point.

After looking at the PillCam study of 2006, I have no hesitation in labeling this as Crohn's disease, based upon the characteristic features of those aphthous lesions within the small bowel, as just described in the series of slides that we saw, but it's not just the presence of those lesions. The

aphthous lesions of the bowel, in isolation, even if they have the characteristic features described as early Crohn's disease, if that was the only finding, I would be hesitant to label it as Crohn's disease.

But when you have those dramatic photos and the presence of a history of diarrhea and abdominal pain, in the presence of a physical exam that shows extra intestinal manifestations of arthritis, uveitis, and iritis, with marked irritability and self-abusive behaviors, when you have growth data when she was at her worst, when she had the worst flare of her bowel issues and her arthritis that coincided with the 20-pound weight loss over six months, coinciding with laboratory findings of thrombocytosis, an elevated OmpC, which is, as you recall, highly specific, up to 95 percent specificity, for Crohn's disease.

An elevated ESR, and elevated C active protein, in the presence of two colonoscopies done three years apart or two years apart by two different endoscopists showing aphthous ulcerations of the colon in different areas of the colon, in the presence of a PillCam study showing widespread aphtha ulcerations in the characteristic pattern that you would expect, based upon all previous descriptions of Crohn's disease, and in the presence of aphthous ulcerations,

which all agree are the earliest sign of Crohn's disease, meaning, whether every aphthous ulceration is Crohn's disease, the answer is no. Every aphthous ulcer is not Crohn's disease, but all bowel lesions of Crohn's disease do begin as aphthous lesions.

So when you have all of this taken together, and, in addition to that, what is not on the slide is her clinical response to anti-inflammatories and immunosuppressants, the predicted response of improvement in all of her organs that are inflamed, to anti-inflammatories, to prednisone, to sulfasalazine, to 6 MP, to remicade, and now to unero. All of those together form an undeniable diagnosis of Crohn's disease.

Q Doctor, at some point in time, did you become aware that Michelle had had a bowel biopsy done earlier by Dr. Montes?

A Yes.

Q Did you, at some time, become aware that that gut biopsy result returned with measles RNA in the biopsy sample?

A Yes.

Q Do you know approximately when you learned that information?

A I don't remember when Theresa mentioned it

to me.

Q And, at some point in time, did you come to a conclusion that there was a relationship between the presence of the measles RNA that was found in the gut biopsy done in 2002 and the enterocolitis that Michelle suffered?

A I was very interested in that because once I realized that these children do, in fact, have bowel disease and that this is going on in so many of the kids with autism and GI symptoms, because of their reports or clinical association or observed association, I should say, by so many parents, that the onset of their bowel disease and their autism occurred shortly after MMR, it's a reasonable question to say, is there, in fact, an association?

So that question did interest me, and, in fact, we have an RB-approved study to look exactly at that, among other issues of bowel disease, but one of the features of the bowels that we're looking at is that, to see whether we can find any evidence of measles RNA.

Personally, I didn't want to believe it until the specimens that I took and I processed and I preserved and I sent, done by lab personnel that I'm familiar with, if we could find that, then I would be

very much convinced of that.

So we embarked on this project in 2003, at the end of 2003, and we presented our preliminary findings at the IMFAR conference -- IMFAR is the acronym for International Meeting for Autism Research -- in June 2006, exactly a year ago, and it was held in Montreal.

We had a poster at that meeting, "we" meaning myself and Steve Walker from Wake Forest University and Karen Hepner and Jeff Segal, and on that poster we displayed our preliminary findings of measles virus in the biopsies that I had obtained from the terminal ilium of a number of our patients with autism and bowel disease.

Q You indicated that you presented this information at IMFAR.

A That's correct.

Q What is "IMFAR"?

A IMFAR is the International Meeting for Autism Research. It's a very prestigious annual meeting where researchers from all around the world gather to present the abstracts, and sometimes even longer, speaking presentations of their findings. It incorporates medical issues of autism, behavioral issues of autism, diagnostic issues, psychiatric

issues. It's just a very comprehensive meeting.

Q Doctor, you indicated that you presented this information on a poster.

A That's correct.

Q Is it literally a poster on an easel?

A It was exactly what you imagine. It's a big poster on an easel, yeah.

MS. CHIN-CAPLAN: Special Master, could I just refresh the witness about that?

(Pause.)

MS. CHIN-CAPLAN: Special Master, we're going to be passing around a document which is the poster that was presented at this meeting.

SPECIAL MASTER HASTINGS: I take it, this is not something that's already in the record.

MS. CHIN-CAPLAN: No, Special Master.

(Pause.)

SPECIAL MASTER HASTINGS: And why wasn't this particular document already in the record?

MS. CHIN-CAPLAN: The abstract is in the record. This is what was posted, I guess, outside the door.

SPECIAL MASTER HASTINGS: The abstract is in the record where?

MS. CHIN-CAPLAN: The abstract is contained

in Dr. Krigsman Exhibit Number -- if you give me a moment, I'll tell you exactly where.

SPECIAL MASTER HASTINGS: Okay.

MS. CHIN-CAPLAN: Tab K, I was told.

SPECIAL MASTER HASTINGS: I'm sorry?

MS. CHIN-CAPLAN: Tab K.

SPECIAL MASTER HASTINGS: Tab K. All right.

(Pause.)

MS. CHIN-CAPLAN: Special Master, would this perhaps be a good time to just break for the afternoon so I can locate my own file?

SPECIAL MASTER HASTINGS: All right. Let's take our 15-minute break for the afternoon right now.

(Whereupon, a short recess was taken.)

MR. MATANOSKI: We were planning to take a brief break between Dr. Krigsman's testimony and the beginning of cross, particularly in light of the fact that we were just handed this document that he is apparently going to be testifying to now.

SPECIAL MASTER HASTINGS: Okay. If you need another break. Where do you stand right here? Why do we need a break right now?

MS. CHIN-CAPLAN: Just to locate the abstracts. I could tell the Court where it is.

SPECIAL MASTER HASTINGS: I've got it.

MS. CHIN-CAPLAN: Oh.

SPECIAL MASTER HASTINGS: I've got in front of me.

MS. CHIN-CAPLAN: Okay.

SPECIAL MASTER HASTINGS: You said Tab K.

MS. CHIN-CAPLAN: We can continue.

SPECIAL MASTER HASTINGS: For the record, this is Tab K, I think, to Dr. Krigsman's, which is at Exhibit 59.

(Pause.)

SPECIAL MASTER HASTINGS: Ms. Chin-Caplan, to get a handle on the stuff that's being produced at trial here, let's try to do that right now. You filed a group of exhibits that were the copies of Dr. Aposhian's slides yesterday. You didn't file it, but you gave us copies, and I want you to file that. Let's call that Petitioner's Trial Exhibit 1.

MS. CHIN-CAPLAN: Dr. Aposhian?

SPECIAL MASTER HASTINGS: Dr. Aposhian. And then the one that we just went through of Dr. Krigsman, let's call that Petitioner's Trial Exhibit 2. And then the document you just gave us now --

MS. CHIN-CAPLAN: We can call that "2A"?

SPECIAL MASTER HASTINGS: Well, let's go to No. 3. Let's just go to No. 3.

Actually, there was something else filed, they just called to my attention, which is the calendar. You're going to file that afterward. Let's call the calendar Trial Exhibit 4, then.

So this one you just gave us will be Trial Exhibit No. 3.

(The documents referred to were marked for identification as Krigsman Exhibit Nos. 1 through 4.)

SPECIAL MASTER HASTINGS: Why don't we number? The pages of this particular document aren't numbered, so let's number them as we go through. Go ahead, Ms. Chin-Caplan.

MS. CHIN-CAPLAN: Thank you, Special Master.

(Pause.)

BY MS. CHIN-CAPLAN:

Q Doctor, you indicated that this was a poster presentation.

A Correct.

Q And on the poster presentation, what does a poster presentation do? What is it for?

A Well, it's presented at a conference, and the intention of these conferences are for researchers to share what they have learned with their colleagues

because no one can know one can know everything about everything.

So they tend to be lined up, and the people that attend the conference walk around from poster to poster, and they read the data. It's in abstract form, meaning that you don't have lengthy descriptions of methodology or of technique. It's preliminary, and it's understood to be preliminary. This is not a peer-review presentation, by any means.

It has to be accepted by the organizers of the conference, so it does pass some sort of elementary screening test, but certainly it's not considered peer reviewed. Typically, there are specific galleries where one or more of the researchers are physically present at their poster to answer questions that people passing by may have when they read it.

Q So would it be fair to call it a "snapshot" of your presentation?

A I would say it's snapshots of preliminary data.

Q Fair enough. Doctor, this handout, which has been labeled as Krigsman Trial Exhibit 3; do you have a copy?

A No, I don't have a copy.

(Pause.)

BY MS. CHIN-CAPLAN:

Q So, Doctor, I'm just going to ask you to run very briefly through this poster presentation. This is Krigsman Trial Exhibit No. 3. In the introduction, what information were you relating to the participant?

A Just as a bit of background, autism is very common. The frequency has been increasing over the years. There is a gastrointestinal involvement that has been published and documented, and there is a previous publication that found the presence of measles virus RNA within the inflamed intestinal tissue, and we made the point that that's only one publication. No one, to date, has ever tried to replicate that information from that particular source, specimen source. We attempted to do so. That's the first page.

Q And, Doctor, what does the second page represent?

A The second page are a variety of photographs. Photograph A is a child leaning against a table, which we have come to learn, in our experience, these children with autism and bowel symptom, meaning diarrhea, when having abdominal pain, what they tend to do, in an effort to make their

bellies feel better, is to apply pressure on the lower abdomen, sometimes upper but usually lower abdomen, and they assume all sorts of interesting positions and spend a good deal of their time doing that, and Photograph A is an example of that. Photograph B is a little girl laying on a floor, pressing her hands onto her lower abdomen.

This is Figure 1. Figure 1 has four photographs, labeled A through D. We just reviewed A and B.

Photograph C of Figure 1 is a photograph of this marked abdominal distention that so many of the children with autism and bowel symptoms have as an accompanying finding to their diarrhea and their pain.

And Photograph D in Figure is another example of the abdominal distention, and the child clearly is very thin, very thin.

In Figure 2, Photograph A is a photograph of an endoscopy that I have done with a patient with typical lymphonodular hypoplasia, demonstrating the excessive nature of the lymphoid nodularity and the magnitude of it.

Photograph B -- in black and white, you really can't appreciate it -- Photograph B is a photograph of numerous aphthous ulcerations of the

colon, very similar to the aphthous lesions that you've seen just a moment ago on the PillCam study.

Photograph C of Figure 2 demonstrates a typical biopsy, a microscopic appearance of the colon that's inflamed with colitis, and it shows a lymphocytic infiltration of the mucosa and submucosa with something called "crypt branching." At the very center of Photograph C, you'll see a crypt that branches off and forks into two. Crypt branching is an undisputed histologic or histopathologic hallmark of chronic and ongoing infiltration. This biopsy is typical of biopsies that we see in this group of children.

Photograph D of Figure 2 are the PillCam photos or similar photos that you've just seen. These photos were the two photographs taken at PillCam, and Photograph D of Figure 2 were taken by Dr. Frederico Balzola in Turin, Italy, on his patients, and he has described PillCam findings also showing aphthous ulcerations of the small bowel and presented it. I believe it's a letter that has been published in one of the gastroenterology journals in letter form. That's Photograph B.

Q And, Doctor, on page 3?

A Three, I'll just read it. This is a section

labeled "Objectives of the Poster." "The primary objective of the study was to determine whether measles virus RNA could be identified in total RNA extracted from ileal tissue of children with chronic GI symptoms, autistic enterocolitis, and regressive autism and to compare this to neurotypical controls. An additional objective was to determine whether the measles virus sequence generated from RTCPR products corresponded to the wild-type form or a vaccine-strain-specific form of the virus."

Q And on page 4, what is that?

A Page 4 is a brief description of the materials and methods. Would you like for me to read it?

Q Certainly.

A "Materials and Methods. Patients who had a diagnosis of ASD and who were referred to a pediatric gastroenterologist, myself, for evaluation of chronic gastrointestinal symptoms were eligible to participate in this RB-approved study. For each patient, medical histories, vaccination records, histopathology reports, and ileocolonoscopy biopsy tissue were available for evaluation. Gastrointestinal symptoms consisted of abdominal pain, diarrhea, constipation, abdominal distension, and growth failure.

Representative endoscopic, gross pathologic findings included marked lymphonodular hyperplasia and aphthous ulcerations. Representative histopathology is shown above and consisted of a mild, patchy, nonspecific, inflammatory, infiltrative mucosal layer. The findings at wireless capsule endoscopy of the small bowel revealed similar aphthoid lesions. Biopsies of the lymphonodular tissue were tested for the presence of measles virus by RT and PCR."

Q Doctor, to the right of this page, Exhibit 3; what is that?

A Figure 3 was just a little schematic showing, in schematic form, what we did. First of all, the graph shows a cartoon of the intestine with an arrow pointing downwards towards the photograph of two small vials, indicating that the biopsy was taken from the terminal ilium and placed in those small vials of RNAlater, which is an RNA preservative, and then there is another arrow pointing down to RNA extraction. So the RNA was extracted from the specimens contained in those vials.

RT and PCR was done on the specimens after the RNA extraction, and then another arrow going down to sequencing, indicating that, on a number of specimens, we performed sequencing.

I should mention also, since I'm mentioning sequencing, is that, at the time of presentation of this abstract, we had not yet performed all of the assays on all of the specimens or attempted to sequence them. So we reported the findings that we have, which is part of why this is preliminary.

So whatever findings we have from what we'll be discussing in a moment don't reflect the fact that we tested all of the specimens using a number of different primers and came up with those results. That's not what it indicates.

Q So this was a partial report of --

A It's partial. It's quite preliminary.

Q Doctor, what is page 5?

A Page 5 are two photographs of panels of gel, and the PCR technology, which Dr. Hepner and Dr. Kennedy will speak about in greater detail tomorrow. These are photographs of the PCR products.

Q And, Doctor, page 6; what is page 6?

A This is a detailed base pair sequences of the Edmonston vaccine virus, and, again, Dr. Hepner and Dr. Kennedy would be able to elucidate more on the details of Figure 5.

Q And, Doctor, what is page 7?

A A description of the primers that we used,

and, again, I would defer the description of this to Dr. Hepner and Dr. Kennedy.

Q And on page 8, Doctor?

A Page 8 is a summary of the results showing the results of initial PCR, PCR runs using five different primer strategies and whether they were positive or negative and what percentage were positive and how many, both enumerators and denominators of specimens that were tested using particular primer strategies, and how many of those tested using that particular primer strategy were a positive or negative for either PCR, measles virus sequencing, meaning sequencing of measles virus that would not be specific for a vaccine strain, but it could be either vaccine or wild-type measles.

Then, lastly, there I designed a primer that would look specifically for the base pair sequence of the vaccine strain measles virus, and that last row, lightly shaded, shows how many of the specimens are positive as of the date of this poster presentation for a vaccine-strain-specific measles virus.

Q These were your preliminary findings.

A Correct.

Q This was on a poster for anybody to see as they walked into the meeting.

A Correct.

Q Doctor, you indicate that you were the endoscopist doing this work.

A Right. My role in this was, as the gastroenterologist, was to identify the patients who met the clinical criteria for an indication for a diagnostic colonoscopy in whom there was a strong suspicion, based upon their presenting GI symptoms of diarrhea and pain, that an inflammatory lesion is present. Those were the patients who were colonoscoped, biopsied, and entered into the data shown on this poster.

Q Doctor, your preliminary findings revealed what?

A The preliminary findings, as far as the presence of measles virus, and, again, I'm not going to give a percentage because that would suggest that we tested all of them, and X percent were positive or negative. All we could say at the time of this poster is that, as far as vaccine-strain-specific sequencing positivity, a total of six specimens that were positive for vaccine-strain-specific RNA, the RNA gene.

So genetic material that was specific for vaccine-strain measles virus was positive in six. I

can't give you a denominator out of how many that was because, again, some were tested just using one strategy, some were tested using multiple strategies, and, again, Dr. Kennedy and Dr. Hepner actually would be able to shed more light on that.

We also found that if you, putting aside the issue of vaccine-strain specificity, if you just looked at how many were positive on base-pair sequencing for measles virus, that could either be vaccine or wild type. There was a total of 35. Thirty-five specimens were positive, with sequencing of the base pairs, for measles virus.

Q Doctor, based on your education, training, and experience, your treatment of Michelle Cedillo, her history, the findings that you saw on her diagnostic procedures, the laboratory findings that you obtained in your care and treatment of her, the treatment regimen that you ordered for her, as well as her response to that treatment regimen, in your conversations with her subsequent treating doctors, do you have an opinion, more probably than not, that Michelle's enterolitis was caused by measles virus?

A In my opinion, in all likelihood, the measles virus genome that we're finding in the ileo specimens of these patients is the cause of the bowel

inflammation that they have, and, in all likelihood, in Michelle's case, as well, the finding of measles virus in the inflamed, abnormal, enterocolitic bowel that we know she has, in all likelihood, that inflammation is the result, in my opinion, of the presence of the measles virus genome.

Q Could you tell the Court the basis for that opinion, the facts that you relied upon when you formulated that opinion?

A Basically, it's spelled out in my report, and it's that, based upon the previous publication by the group in Dublin, Ireland, of the presence of measles virus genome in the inflamed guts of autistic children who had bowel symptoms identical to the population that we're looking at here in this poster presentation, that's based upon that combination of factors, the same patients, the same presentations, the same bowel findings, and the same findings of measles virus genome, and, again, the likelihood that this genome is causing what appears to be what's consistent with viral inflammation.

The pattern of inflammation that I was seeing in these children that's been published and that we've seen in our large series of children is consistent with the viral infection. So the pattern

of nonspecific, patchy, mild, chronic active inflammation with lymphoid hyperplasia is something that you would expect to see with a viral infection.

So all of these factors, taken together, make me think that, in all likelihood, the inflammation that we're seeing in the bowel and the enterocolitis is a result of the presence of the virus in the bowel.

MS. CHIN-CAPLAN: Thank you, Doctor.

SPECIAL MASTER HASTINGS: All right. Let's take a 15-minute break at this point. Mr. Matanoski, is that good? Did you have a point?

MR. MATANOSKI: That would be fine, sir.

SPECIAL MASTER HASTINGS: Okay. All right. To the folks at home, I apologize. We did not take our break earlier. We are taking a 15-minute break now at 3:12. We'll be starting again at about 3:27.

(Whereupon, a short recess was taken.)

SPECIAL MASTER HASTINGS: All right. We're ready to go back onto the record here.

First, I want to note for counsel that I just passed on an item of information. This applies to today only, but, today, we are definitely going to need to end at 6 p.m. because the power in the building is going off at that time.

So, on other days, that will not be the case. Today, we need to get done by six, so plan accordingly. We can go from now until then.

For the Respondent, do you have any cross-examination for this witness?

MS. RICCIARDELLA: Yes, I do.

SPECIAL MASTER HASTINGS: Ms. Ricciardella, please go ahead.

CROSS-EXAMINATION

BY MS. RICCIARDELLA:

Q Dr. Krigsman, you're a partner with Andrew Wakefield at Thoughtful House Center for Children in Austin, Texas. Is that correct?

A I'm not a partner there, no.

Q What do you do there?

A I'm the director of gastroenterology services at Thoughtful House.

Q So you're Dr. Wakefield's employee.

A No. He is not an employer.

Q Is that a partnership?

A No.

Q What is it?

A It's a working association. I don't own any share of Thoughtful House, nor am I employed by them.

Q Would you consider yourself a colleague of

Dr. Wakefield at Thoughtful House?

A Yes.

Q And you're the director of gastroenterology services at Thoughtful House. Is that correct?

A That's correct.

Q Now, Doctor, Thoughtful House posted on its Web site a page entitled "Treatment at Thoughtful House." Are you familiar with that page? We'll put it on the screen.

A I'm sorry. I didn't hear the question.

Q Thoughtful House posts on its Web site a page called "Treatment at Thoughtful House."

A Okay.

Q Are you familiar with this page of Thoughtful House's Web site?

A Not offhand, but I would be happy to look at it.

Q Do you know who wrote this page?

A I would not know who authored it, no.

Q You do not?

MR. HOMER: Excuse me, Your Honor.

SPECIAL MASTER HASTINGS: Yes.

MR. HOMER: Is this filed in evidence?

MS. RICCIARDELLA: No, it's not.

MR. HOMER: Could we have a copy of it,

please?

MS. RICCIARDELLA: Sure.

(Pause.)

BY MS. RICCIARDELLA:

Q Doctor, if you look on the screen, there is a section entitled "Medical Treatment." Do you see that section? We'll blow it up for you.

A Okay. Thank you.

Q The first sentence begins with the sentence: "Children with childhood developmental disorders have disregulated immune systems." Do you, in your opinion, believe that all children with developmental disorders have disregulated immune systems?

A All children? It's unlikely that every single child with autism would have that.

Q I didn't hear the first part.

A It's unlikely that every child with autism would have a disregulated immune system, but that's the case in all of them.

Q Do you think that the majority of children with developmental disorders have disregulated immune systems?

A It's my understanding that a number of studies have demonstrated immune disregulation in children with autism that differs statistically from

those without autism.

Q And what studies are those?

A I can't cite them, but there is a good review on this by Dr. Paul Ashwood that might be cited in my report. He has a very excellent review article, in the last two years, of the immunologic disregulations of autism, a review of all previous publications.

Q And what about childhood developmental disorders other than autism? Do you believe that the majority of those are caused by disregulated immune systems?

A I'm sorry. I didn't hear the question.

Q Childhood developmental disorders other than autism; do you believe that those, too, are caused by disregulated immune systems?

A I have no knowledge of that.

Q Doctor, there is another phrase, under the section, "Medical Treatment," that states: "Treatment directed at correcting immune system abnormalities is imperative." In your opinion, should all children with developmental disorders, or, particularly, autism, receive treatment directed at their immune system?

A I think that it's appropriate to focus on

the immune system of these children. Direct knowledge of that comes from my own experience. The bowel disease that I described this afternoon is an example of a disregulated immune system.

So, certainly, to have a theory that you want a direct treatment at immune disregulation is not without foundation or support.

Q But do you believe that the majority of children with autism should receive treatments for a disregulated immune system?

A I think that a workup needs to be done to determine if there is an immune disregulation, or if a clinical observation warrants it, that's where I would have to start.

Q And, Doctor, when you say "workup needs to be done to determine if there is an immune disregulation," how would a workup determine an immune disregulation? What do you mean?

A Those questions are best referred to immunologists to determine the specific immunologic aberrations that one might want to look for, but, again, there are a number of studies that have demonstrated that this exists in these children.

Q Now, Doctor, on this same page there is a section entitled "Gastrointestinal Diagnosis and

Treatment." Do you see that, what we've just blown up?

A Yes.

Q Did you write this section?

A I either wrote it or was consulted on it.

Q As director of gastrointestinal services there, you endorse this section of the Web site.

A I would. This particular part that you're blowing up now, I endorse.

Q Okay. Now, Doctor, there is a sentence in this section that says: "Many children with CDDs have GI symptoms that precede, coincide with, or appear after the onset of neurological symptoms or regression. A child should produce one formed stool per day. Anything else merits attention."

Doctor, in your opinion, is failure to form one stool a day a significant GI symptom in an autistic child?

A No. What this paragraph says is that it merits attention. What that means is that when you have, being that we know that these children so frequently have GI symptoms that are intense, and they have findings, both laboratory findings and on biopsy, when you have something that might deviate from a simple, one stool per day, you need to direct

attention to that and get a more thorough history.

This paragraph does not suggest that if you don't have one bowel movement a day, there is something pathologically wrong with your bowel. That's a misreading of this paragraph.

Q And, Doctor, this section ends with the sentence: "There is also a subgroup of autistic children that appear to lack GI symptoms, but without endoscopy evaluation, the question of an occult or hidden GI inflammation remains unanswered."

A That's correct.

Q Now, does that mean that for proper diagnosis and treatment of this subgroup of autistic children who do not have GI symptoms, that they should undergo endoscopy evaluation to evaluate --

A No. It does not mean that.

Q What does it mean?

A It means that it is our suspicion that there is a bowel disease that is occult, meaning that it may not produce overt symptoms, particularly in this group of children who can't manifest or demonstrate pain.

For example, the presentation of the bowel inflammation that I spoke about earlier could be just abdominal pain. In Crohn's disease, the most frequent presenting symptom is abdominal pain. Even in the

absence of any other symptom, abdominal pain is known to be a presenting symptom by itself, in isolation of Crohn's disease.

This particular group of patients represents a very unique problem in interpreting conventional symptoms because, whereas, as pediatricians, we are trained to observe certain behavior patterns or relying on what a child says, in these children, we haven't got the ability to do that because they don't manifest pain. They don't say it, they often don't talk, and when they do have pain, they often manifest it in strange ways like putting pressure on their belly instead of just putting their hand on it. For some reason, this is a behavior that some of them do. They lean over tables. Why would they do that? I don't know.

Q So, Doctor, you're saying, in this phrase, that autistic children who do not have GI symptoms may nevertheless have inflammation, but there is no way to know that unless the inflammation is confirmed by endoscopy.

A Right, but that does not suggest that they, therefore, should undergo -- what the sentence that you're highlighting is saying is that there are a subgroup of patients who would not manifest overt

symptoms, but overt symptoms are obvious, for example, of abdominal pain, like I just said, and the only way to do that is to have a high index of suspicion so that if you would see a child who is excessively irritable, for example, and that's the only symptom that you can tell that's relatable to the GI tract, even though he may be irritable for a whole variety of reasons, one must take that seriously because that may be the only indication of an underlying bowel pathology.

Q Now, Doctor, you were an attending physician at Lenox Hill Hospital from September 2000 through December 2004. Correct?

A That's correct.

Q And is it true that before you resigned your position, the hospital restricted your privileges to conduct endoscopies?

Q What's incorrect about that statement?

A I didn't resign my position, number one.

Q Why did you leave?

A I did not renew my application for appointment there. Every two years, you need to renew it, and I chose not to renew it at the end of 2004.

Q During your tenure at Lenox Hill, is it true that the hospital, at one point, did restrict your

privileges to conduct endoscopies?

A That's not the hospital's position. The hospital maintains that they did not, in any way, curtail my privileges.

Q Well, you sued the hospital, didn't you?

A I did.

Q One of the reasons that you sued the hospital was because you thought that they had illegally restricted your privileges to conduct endoscopies.

A Right. That's correct. My claim was that they curtailed my privileges, and the hospital's position was that they did not.

Q Regardless, they were concerned that you were conducting endoscopies on children, particularly autistic children, without medical necessity. Isn't that correct?

A That is correct. They were concerned that the colonoscopies that were being performed on these children did not have proper indications of colonoscopy.

Q And, Doctor, you are licensed to practice medicine in Texas as well as New York and Florida. Correct?

A That's correct.

Q And in August 2005, is it true that you were fined $5,000 by the Texas State Board of Medical Examiners for misconduct?

A That's not correct.

Q What's incorrect about that?

A There was no misconduct.

Q Did you pay a $5,000 fine?

A We did.

Q What was it for?

A The fine was levied -- the reason for the fine was because the Thoughtful House Web site, before I was licensed, stated that Thoughtful House was open, and patients can call. That's what the substance of the Web site said. It gave no suggestion that I was seeing patients because I wasn't. I wasn't licensed. We didn't even know when the license would be coming because it was a very long process to get licensed in Texas.

But because Thoughtful House, on their Web site, represented that they were open, the understanding of the Texas Medical Board was that I was Thoughtful House and that I was open, and that indicated that I was available to see patients, and that, they considered to be misrepresentation since I was not yet licensed. So they levied a fine of

$5,000, which we chose to pay.

Q Doctor, was your fine in Texas also due to the fact that you did not report the Lenox Hill disciplinary action against you?

A That is not correct.

MS. RICCIARDELLA: Doctor, the minutes from your August 25, 2005, application to obtain a license in Texas are public, and we have a copy, which we will put on the screen, and we'll hand to counsel.

(Pause.)

BY MS. RICCIARDELLA:

Q Now, what we've just put on the screen reflects that a motion was made to allow your licensure in Texas if you would pay a $5,000 fine due to disciplinary action by Lenox Hill Hospital: "Falsification of Application Regarding Nondisciplinary Citation by Florida and to Misrepresentation Regarding Entitlement To Practice Medicine." That was the motion that eventually passed to allow to obtain your license to practice medicine in Texas. Is that not correct?

A No. This did not pass, number one. Number two: This was not the way it ended up. I did not have to withdraw my application. The application was never withdrawn. The initial one was submitted, and

it went through.

The other thing you asked before that was incorrect. The question you asked me was, isn't it true that this Web site demonstrates that I did not disclose the Lenox Hill dispute to Texas Medical Board? That was the content of your question, and my answer is that that is completely incorrect. I disclosed that in its entirety on my application and made no effort, in any way, to avoid dealing with this issue in my application for Texas medical licensure.

Q Doctor, your C.V. states that you're a clinical assistant professor at New York University. Is that correct?

A Correct.

Q Are you currently on staff there?

A Correct.

Q When was the last time you taught a class at NYU?

A I haven't taught there.

Q You've never taught a class at NYU.

A I'm on staff there.

Q Are you salaried?

A From NYU?

Q Yes.

A No.

Q Have you ever been salaried at NYU?

A No.

Q Now, Doctor, on page 3 of your C.V., you have an entry entitled "Publications," and you have four listings, and, for the record, I'm referring to Petitioners' Exhibit 60. Under the first listing is entitled "Suction Rectal Biopsy in the Diagnosis of Hirschsprung's disease and Comparison of Two Biopsy Devices."

A Right.

Q And you state that you submitted this paper to the American Board of Pediatrics on April 20, 1995, about 12 years ago. Is that correct?

A That's correct.

Q What do you mean by you submitted the paper to the American Board of Pediatrics?

A By "submitted," it means that, back in 1995, the requirement for completion and certification of pediatric gastroenterology training was that you had to submit a research paper to the American Board of Pediatrics. It actually is a misnomer to label it under "Publications" since, in fact, it did not end up being published. But what it was was a review and a paper and a discussion describing exactly what the title says that was submitted to them for their review

to determine if this met the criteria to grant me certification in pediatric gastroenterology.

Q You said it has not been published.

A No.

Q The second listing is a paper that you have published, you co-authored, entitled "Laryngeal Dysfunction: A Common Cause of Respiratory Distress Often Misdiagnosed as Asthma and Responsive to Anti-reflux Therapy." That has been published in 2002. Correct?

A That is correct.

Q And the third listing, you term a "slide presentation" that you presented at IMFAR, the International Meeting for Autism Research, in 2004. Now, Doctor, I note, though, that this slide presentation you also have listed under "Speaking Engagements" on page 4 of your C.V.

A That's correct.

Q Was this a speaking engagement or a publication?

A A speaking engagement. This is not a publication. You are correct.

Q And the fourth listing, you term a "poster presentation at IMFAR in 2006," and I believe this is what you were just testifying to during your direct

examination. Is that correct?

A Correct.

Q And that's a poster that describes the preliminary results of a study you're doing with Dr. Stephen Walker and Dr. Karen Hepner.

A That's correct.

Q And this has not been published, has it, Doctor?

A That's correct.

Q So, among your four listings under "Publications," it's only the second listing that is a true publication. Is that correct?

A That's correct.

Q Doctor, you served as an expert witness for the claimants in the MMR litigation in the United Kingdom. Is that correct?

A Yes.

Q And were you offered as an expert in that litigation as someone who is able to confirm intestinal inflammation in autistic children?

A Yes.

Q Did you perform any endoscopies on those children?

A On which children?

Q Any of the children that were the claimants

in the United Kingdom litigation.

A I don't know if any of my patients were claimants. I don't know that.

Q Now, in addition to your practice at Thoughtful House, you have a medical practice in New York. Is that correct?

A Correct.

Q It was unclear during your direct testimony. Are you still practicing general pediatrics?

A No. I stopped that two years ago.

Q You first met Michelle Cedillo in September 2003, when her parents brought her to New York to see you. Is that correct?

A Correct.

Q Now, Doctor, you wrote a report in this case, dated February 4, 2007, which has been filed as Petitioner's Exhibit 59. I'll go ahead and hand you a copy of your report for you to refer to. Do you recall writing this report?

A I do.

Q And on page 2 of your report, you state that, about Michelle, "Her gross motor, fine motor, behavioral and emotional development proceeded in an age-appropriate manner during the first year, as evident by the pediatrician's notes and home videos."

Doctor, what enables you to assess whether or not Michelle was developing in an age-appropriate manner during her first year of life?

A This is the history that I obtained, so this information is from the history that one usually gets when encountering a patient for the first time.

Q What type of history did you get? Let me rephrase that. A history from whom?

A This came from Mrs. Cedillo.

Q Did you review all of the medical records in this case?

A I don't think I reviewed all of them. I reviewed my entire medical chart and perhaps some of the hospital records when she was hospitalized in Yuma, but, in general, my charts, Theresa and I have an ongoing relationship, and she pretty much sends me everything that --

Q Now, Doctor, is it your understanding, after reviewing the medical records, that Michelle's GI symptoms that developed following her second bout of fever continued to worsen over the ensuing months?

A That's my understanding. That's correct.

Q Do you have an understanding of how long those GI symptoms lasted?

A It was really, the vomiting lasted for,

like, 10 weeks or 11 weeks or 12 weeks or thereabout. It sort of tapered off. This is, again, by the history that I got. I didn't know Michelle at that point. The history that I obtained was that the diarrhea lasted for a good year or two and then became constipation, primarily constipation, difficulty stooling. That lasted for about another year or two -- - again, I would have to look at the exact records -- and then the diarrhea started again, and it's persisted since then, so it's been many years now where the only symptom has been diarrhea.

Q Now, Doctor, you first met Theresa Cedillo at a DAN, Defeat Autism Now, conference in October 2002. Is that correct?

A Yes.

Q Do you remember speaking with her about Michelle at that time?

A Yes, I do.

Q Was that the first time that you had a discussion with Mrs. Cedillo about Michelle?

A Yeah. I hadn't met her before that.

Q That was the first time you met her.

A Yeah.

Q Now, sometime, Doctor, before January 15th of 2003, you told Mrs. Cedillo that it was your

recommendation that Michelle undergo another endoscopy. Is that correct?

A That's correct.

Q What was your recommendation based on?

A I stated before that, in the six months preceding the time that I met Michelle, in September of '03, her condition considerably worsened. Specifically, she had lost 20 pounds in the preceding six months. She had worsening of her diarrhea in terms of the number of stools per day and also the consistency of the stool. Her degree of abdominal pain worsened, so she was much more irritable and much more self-abusive, and her arthritis had worsened as well.

So the overall downturn in her clinical condition, coupled with the fact that the January of '02 colonoscopy was normal, made me want to search for an inflammatory origin of her symptoms, and that would require getting a biopsy.

Q Doctor, do you recall that Michelle was hospitalized for dehydration on May 17th of 2003?

A I hadn't met her yet, but that's the history that I got.

Q And, Doctor, at this time, Michelle's treating gastroenterologist, Dr. -- I'm not sure of

the pronunciation -- Montes, did not want to perform another endoscopy on Michelle. Isn't that correct?

A I don't know.

Q Well, referring to Petitioners' Exhibit 28 at 51, which we'll put on the screen, Mrs. Cedillo sent you an e-mail, and she told you that Dr. Montes told her that Michelle's problem of not eating and drinking, in his opinion, was behavioral in nature and not a gastro one. Correct? Do you recall receiving this e-mail?

A I don't recall it, but, obviously, I received this. I'll be happy to read it now. Can you magnify it again? Thanks.

(Pause.)

THE WITNESS: Okay. I've read it.

BY MS. RICCIARDELLA:

Q Okay. But you didn't agree with that, Doctor, did you, because, on May 19th of 2003, you responded to Mrs. Cedillo, and we'll put that up: "If you can't find a GI to explore her for GI problems, then you could find a DAN doc near you who could treat her empirically for suspected enterocolitis with anti-inflammatories or steroids." Do you recall writing that e-mail?

A I do.

Q And, Doctor, by "DAN doc," you mean a doctor who is part of the Defeat Autism Now?

A Well, it's not quite part of it. What I would mean by that is a physician who embraces the notion that autistic children with GI symptoms very frequently have a medical condition that's responsible for those conditions.

Q And what did you mean by recommending that she find someone to treat Michelle empirically with anti-inflammatories?

A Well, what happens is the story that Theresa told me was my experience because I had already seen so many of these children by this time. It was entirely consistent with well over 100 children that I had seen an endoscope and biopsy until then.

So, in my mind, there is very little doubt that, even then, even never having seen her, just from the story, the presentation, there was very little doubt in my mind, coupled with her labs, that she had an enterocolitis. The best way to approach that would be to get a biopsy. There is no question about it.

But in the absence of that, if you just can't do it, if no one seems to see it that way in Yuma, or if she physically can't get to one because of other medical reasons, the biopsy could not be done to

confirm the diagnosis, at that point, it becomes appropriate to treat empirically. "Empirically" means you make the assumption, based upon your knowledge and experience, that this diagnosis is the most likely one, and we treat accordingly.

Good physicians tend to avoid treating empirically because that tends to obscure some of the findings that you otherwise could get, and it would leave questions that potentially could be answered unanswerable. So you really avoid doing that whenever possible, but if the situation doesn't allow for any alternative, then empiric therapy is accepted.

Q Doctor, further in this same e-mail, you state that you would be available to be a sounding board to another physician so long as that person was responsible and a prescribing physician. Do you recall writing that?

A Yes.

Q Now, Doctor, the next day, on May 20th --

A I didn't quite say "as long as they were responsible." That's a misquote from what I wrote.

Q "[S]o long as the responsible and prescribing physician --"

A No. So long as they are the responsible physician, not that their character is responsible.

In other words, they are responsible for the care of the patient.

Q Okay. Now, on the next day, on May 20th of 2003, Mrs. Cedillo wrote you back an e-mail, and I'm referring to Petitioners' Exhibit 28 at 107.

MS. CHIN-CAPLAN: What number?

MS. RICCIARDELLA: Twenty-eight at 107.

MS. CHIN-CAPLAN: Thank you.

BY MS. RICCIARDELLA:

Q She stated that she had been talking to Dr. Cindy Schneider in Phoenix, who, herself, was a parent of two autistic children. She says, I quote: "She is not a gastro, so unable to scope, but very willing to prescribe help in any way."

Doctor, did you ever have a conversation with Dr. Schneider about Michelle?

A I don't recall ever speaking with Dr. Schneider about Michelle.

Q At that time, Doctor, in May of 2003, did you ever recommend to another physician that he or she prescribe anti-inflammatories or steroids to Michelle?

A I don't think so. I don't recall telling any physician or speaking with any of her physicians at that point.

Q Doctor, on July 10th of 2003, you wrote a

letter addressed "To Whom It May Concern," and I'm referring to Petitioners' Exhibit 28 at 84. In the letter you state, "Over the past six months, her --" meaning Michelle "-- inflammatory bowel condition has worsened to the point of requiring hospitalization for severe dehydration and malnutrition." Do you recall writing this letter?

A Yes, I do.

Q And in the letter, you further state, "I'm only one of three pediatric gastroenterologists in the United States with significant experience in diagnosing and providing appropriate treatment for children with autism and this particular form of inflammatory bowel disease that is somehow associated with autism."

Now, you made this statement about Michelle having inflammatory bowel disease to such an extent that it required hospitalization before you had even met her. Correct?

A That's correct.

Q And, Doctor, when you refer to this particular form of inflammatory bowel disease, are you referring to autistic enterocolitis?

A I am.

Q Doctor, you wrote another letter, on August

5th of 2005, addressed "To Whom It May Concern," and I'm referring to Petitioners' Exhibit 28 at 73, and you state in the letter that Michelle needs a colonoscopy and upper endoscopy, and you further state that only two individuals in this country have any experience in the colonoscopic findings in children with autism.

A That's correct.

Q Now, Doctor, on July 10th, you were one of three people who had the requisite experience, but now, on August 5th, you're one of two. Who is the third, and what happened to him?

A That may have been a mistake. Tell me the years again of these letters.

Q 2003.

A In 2003. I know that the other person with experience with these children and scoped a large number of them is Dr. Tim Buie at Mass. General in Boston.

Q Whose name was that?

A Timothy Buie, B-U-I-E. He is another pediatric enterologist who has a specific interest in the bowel disease of these children.

Q He was at Mass. General?

A He is at Mass. General. The only other

physician in the country -- I don't know why I wrote three and then two, but either are, at least at the time of writing this letter, the only other person who had expressed an interest, and I had spoken to in looking into these children, is Dr. Michael Hart, who I spoke to on the phone.

I'm pretty sure I had spoken with him by then, and he had expressed interest in looking at these kids and taking symptoms seriously as a sign of potential bowel disease and having a lower threshold perhaps to make a diagnostic biopsy, to have a high index of suspicion of an underlying bowel inflammation.

He expressed also a desire to do formal research in this area.

Q And where does Dr. Hart practice?

A He is in Virginia. I don't recall the name of the hospital.

Q Now, Doctor, you first saw Michelle, I believe you testified, in New York.

A I should also mention that Dr. Hart has collaborated with Dr. Wakefield in gathering data on these patients, and the work has not yet been published, but I know that the data has been gathered.

Q Are Dr. Hart and Dr. Wakefield working on a

study?

A Yes, yes.

Q Do you know, have they submitted it for publication?

A I do not know if it's been submitted. I was not part of that study.

Q Now, Doctor, you first saw Michelle in New York in September 2003. I believe that's been your testimony. Correct?

A That's correct.

Q And on September 25th of 2003, you performed an upper and lower endoscopy on her. Correct?

A That's correct.

Q And in the results of the endoscopy, you found lymphonodularity and aphthous ulcerations. Correct?

A That's correct.

Q And that, you believe, is evidence of inflammation of her bowel, specifically, inflammatory bowel disease.

A That is partial evidence. That's correct.

Q And following the September 25, 2003, endoscopy, you described two anti-inflammatories. One was prednisone. Is that correct?

A Correct.

Q What is the other one? I didn't catch that.
A There were three, actually, not two.
Q What are the three anti-inflammatories you prescribed?
A Prednisone, as you mentioned; Sixth MP; and sulfasalazine.
Q Now, Doctor, following the September 25, 2003, endoscopy, did you believe Michelle had Crohn's disease?
A No. I did not think it was Crohn's disease. If they asked to label it, I sort of refrained from giving it a label because I didn't know what label to give it. It was bowel. It was a nonspecific enterocolitis of the kind that we see in autistic children. That's the most specific I can be, autistic enterocolitis.

At that point, I didn't feel that I had evidence of the characteristic features that would enable me to label it as Crohn's disease.

Q Well, Doctor, on November 23rd of 2003, you wrote another letter, "To Whom It May Concern," and I'm referring to Petitioners' Exhibit 28 at 424, and you state, "As part of Michelle's Crohn's disease, she appears to have uveitis."

Why did you think, on November 23 of 2003,

that she had Crohn's disease?

A I don't know. I may have been nonspecific in my terminology.

Q But it's your opinion, Doctor, that she has Crohn's disease today.

A Yeah, yeah. What convinced me of that, beyond any question, was the PillCam study. Again, beforehand, I would be hesitant to label it as Crohn's disease for the reasons I said. So whether, in my mind, whether you call it an indeterminate colitis or Crohn's disease or autistic enterocolitis, from a treatment standpoint, it makes no difference because the treatment approach would be the same.

Q I believe, actually, you wrote about that in a letter, dated May 4th of 2005. I'm referring to Petitioners' Exhibit 28 at 679, and you state, "There are many clinical similarities between autistic enterocolitis and Crohn's disease, but they clearly seem to be two separate entities, at this point; however, the treatment options are the same for both."

A That's correct.

Q How are the treatment options the same for both?

A Well, really, what you want to do is you want to decrease the level of inflammation by using

anti-inflammatories. That's one large conceptual approach. The choices of drugs are many, but to reduce bowel inflammation using drugs that are described to do that is one approach, and the second approach is nutritional, giving enteral feedings.

So the approach to treating Crohn's disease encompasses both of those, and the approach to treating autistic enterocolitis involves both of those as well.

SPECIAL MASTER HASTINGS: Can I just say for the record, apparently the quotation you just read from is on page 680 rather than 679.

MS. RICCIARDELLA: Oh. Thank you for that.

SPECIAL MASTER HASTINGS: Is that correct?

MS. RICCIARDELLA: Yes.

SPECIAL MASTER HASTINGS: Okay. All right. Go ahead.

BY MS. RICCIARDELLA:

Q Now, in May of 2005, were you treating Michelle as if she had Crohn's Disease?

A Again, from a treatment standpoint, it makes no difference in my mind what you call it, because whether it's Crohn's Disease or intermittent colitis or autistic enterocolitis, the treatment would be the same. My approach would be the same.

Q The same medications?

A The same medications, and I didn't mention before, the third approach you have in treating both of these diseases would be the use of drugs that affect the microbial flora content of the bowel. That's the third large category, the intervention approach to treating both Crohn's Disease and also, in our experience, autistic enterocolitis.

Q Was she receiving the same dosage as she would, had she had at that time a diagnosis of Crohn's Disease?

A It would be the same dose, yes.

Q Doctor, during your direct testimony, and I believe it's in one of your slides, you talk about the Feldman, Sleisenger, and Forottran's gastro, intestinal, and liver disease textbook. Is that correct?

A Correct.

Q You called it authoritative. Is that correct?

A Correct.

Q You also refer to a textbook called Kumar, Robbins, and Cotran?

A Correct.

Q I hope I'm pronouncing those right. Would

you consider that authoritative?

A Absolutely.

Q Doctor, you say on page seven of your report that Michelle is an undisputed case of ASD-GI.

A That's correct.

Q What is ASD-GI?

A ASD-GI is a term that we use -- "we" meaning the people that treat children with autism and bowel disease medically -- to designate her as an ASD patient with GI problems.

Not all ASD patients have GI symptoms. Not all ASD patients have enterocolitis. But there is a large subset of children with ASD and, you know, we can argue from here until tomorrow how many they are; whether it's 20 percent or 70 percent or whatever. Different papers cite different numbers. But it's clearly a substantial portion of children with ASD who have enterocolitis GI symptoms, biopsy-proven enterocolitis.

ASD-GI is a designation that we give to those patients to indicate that they're autistic. But they're the sub-population of autistic children with gastrointestinal disease.

Q Is ASD-GI the same thing as autistic enterocolitis?

A No, I don't think it is.

Q What is the difference?

A In our experience, again, we have autistic enterocolitis that really describes bowel disease of the small intestine and of the colon. But ASD-GI would suggest that the disease doesn't just involve the small bowel and the colon. It may involve the stomach as well, and the esophagus as well; and there are very predictable abnormalities of both the esophagus and the stomach that we see routinely and very frequently.

Q If a child just had a disease of the stomach and nothing else and had autism, would that be a case of ASD-GI?

A Correct.

Q And if the child had a disease of the esophagus and nothing else, would that be a case of ASD-GI?

A Correct, it's more of a nomenclature. It tends to put in your mind the notion that there are gastrointestinal manifestations in this child with autism, without relation to the specific organ that that disease is.

Q Now Doctor, in the two text books -- the Sleisenger/Foroltran's gastrointestinal liver disease

and the Kumar, Robbins, and Cotran that you agreed were authorization -- does the term ASD-GI appear anywhere?

A No, it does not.

Q Does the term autistic enterocolitis appear anywhere?

A No, it does not.

Q Now in the last paragraph of your report on page eight, you state the following opinion. "The measles-mumps-rubella vaccine Michelle received contributed significantly to her subsequent development of enterocolitis, and it is the persistence of the virus in the lymphoid tissue of the bowel that is causing the ongoing enterocolitis."

So there are two premises to your opinion, and correct me if I'm wrong. The first is, you believe she suffers from enterocolitis, correct?

A I do. That's correct.

Q The second, you believe that the enterocolitis is caused by the persistence of measles virus from the MMR vaccine in the lymphoid tissue of her bowel, correct?

A I do. That's correct.

Q Let's look at the first premises of your opinion and why you think she has enterocolitis, and I

know that you went through this in your direct. First of all, what does "itis" mean?

A Itis means inflammation.

Q And enterocolitis is inflammation of the small bowel?

A That's correct.

Q And colitis is inflammation of the colon?

A Correct.

Q So enterocolitis is inflammation of the large and small intestine?

A That's correct.

Q Now for evidence that she has inflammation of the large intestine, in fact, on page six you state, "That Michelle has colitis is beyond question."

A That's correct.

Q And for evidence that she has colitis, you cite to the January 2002 endoscopy, the September 2003 endoscopy, and the June 2006 endoscopy. Is that correct?

A Could you say that again? What page would that be on?

Q Page six of your report.

A Okay, I'm sorry, what were you quoting?

Q You say, "That Michelle has colitis is beyond question, as evidenced by colonic aphthous

ulcerations seen on two separate occasions by two different gastroenterologists."

A Here we go -- correct, and in the question before, you mentioned --

Q I just want to make sure I'm understanding exactly what evidence you're relying upon for your diagnosis of colitis. Is it the report of the 2002 endoscopy?

A No, no, it's not.

Q Okay.

A I'm relying on my colonoscopy in September of 2003, and the colonoscopy in 2006.

Q Okay, and you state on page six of your report that Michelle's diagnosis of enteritis is also beyond question as evidence by the presence of small bowel aphthous lesions. For that, Doctor, you were relying on the findings from the PillCam, from the June 2006 caps imaging?

A That's correct.

Q Based on these finds of colitis and enteritis, that's the basis of your opinion that she has enterocolitis. Is that correct?

A That's not correct.

Q What is the basis of your opinion that she has enterocolitis?

A That is a portion of my opinion.

Q What else?

A My opinion is based upon the presence of aphthous ulcerations in the small bowel in the colon, in a manner and fashion which has been described to exist in Crohn's Disease and in the small bowel, in particular, in the presence of a history of abdominal pain and vomiting; in the presence of a physical exam that shows UV-itis and arthritis; in the presence of elevated sedimentation rates, CV-active protein, thrombocytosis, and elevated OmpC test; and with the clinical response to anti-inflammatory medications that you would expect for someone who has enterocolitis.

So that constellation of those observations leads me to conclude beyond any doubt that this is her diagnosis.

Q Doctor, if the facts were different and there's no UV-itis and no arthritis, would your opinion be the same?

A That's a hypothetical question, and I'm not sure. It depends on the overall scenario.

Q The overall scenario is exactly the same. I'm just taking out the UV-itis and the arthritis. Would your opinion that she has enterocolitis be the

same?

A That's a difficult question to answer.

Q So you don't know?

A I don't know, right. The diagnosis of Crohn's Disease is often based on a combination of clinical criteria. Unless you're fortunate enough to have the specific finding like a stenosis of the small bowel or a fistula or a granuloma, unless you have that, it's often difficult to be certain that Crohn's Disease is the diagnosis.

That's why the utility of the serologic marker, this obsida (phonetic) I referred to, was such a great advance in helping us diagnosis Crohn's Disease and also distinguish it from ulcerative colitis, which has different markers that are associated with it.

So really, the diagnosis does not rest on one or two findings. It's really a constellation of presenting some symptoms in labs. To chop off one and say we just don't feel the same way is really hypothetical.

Q Just so I'm clear, can one have enterocolitis and not have Crohn's or ulcerative colitis?

A Absolutely.

Q Now Doctor, let's look at the second premise of your opinion, that measles virus from the MMR vaccine Michelle received is persisting in the lymphoid tissue of her bowel and causing enterocolitis. Doctor, do you have an opinion as to why the measle's virus is persisting the lymphoid tissue of her bowel?

A I don't have an opinion. I have suspicions based upon published reports. That's not my area of expertise. I haven't formed an opinion, yet. But I suspect that it's due, and the weight of the literature as reviewed by Ashood and I mentioned that before, suggests that there's a skewed inflammatory response in favor of pro-inflammatory cytokines versus cytokines that are counter-inflammatory. That seems to be the overall pattern in looking at a number of publications.

That seems to be a consistent finding. The exact levels of cytokines and which ones may differ from study to study. But that seems to be overall pattern. So I suspect, and if you ask me to suspect, it has to do with a patient's immune activity.

Q Doctor, you're not an immunologist, correct?

A I am not.

Q Doctor, are you saying that you suspect that

she had a disregulated immune system at the time she received her MMR vaccine?

A In response to your question, that's my suspicion, what I believe.

Q And do you have an opinion as to why she had a disregulated immune system at the time of her MMR vaccine?

A That I don't know.

Q Okay, now in support of your opinion that Michelle has persistent measles virus in the lymphoid tissue of her bowel, you cite to the positive finding in 2002 by the Unigenetics in Dublin, Ireland of measles RNA in the tissue sample tested in Michelle, correct?

A By the published report, correct, of their findings.

Q But from Unigenetics, specific to Michelle.

A Right.

Q Doctor, if these tests from Unigenetics were shown to not be reliable, would your opinion still be the same?

A If they were shown, demonstrated not to be reliable, my opinion today still would be the same. Because we seem to be mounting our own evidence with the specimens that I've obtained.

We've shown in at least six patients with autism, with bowel symptoms, who underwent a diagnostic endoscopy, looking for enterocolitis, most of whom had diagnosed enterocolitis on biopsy -- we've found, using a different lab and different investigators in at least six of them that there's vaccine strain, measles virus genome.

So in my mind, there has been at least preliminary confirmation of that report. So even if you were to tell with absolute certainty that the findings of the lab in Dublin were erroneous, I still would tend to believe in our own experience and preliminary evidence anywhere that there is a virus there. We know it's there in at least some of the kids.

Q So then I take it from your opinion that if no test had been done at all, so we don't have evidence either way, would that have affect your opinion?

A If there's no evidence either way, that would definitely affect my opinion.

Q And how would that affect your opinion?

A If there's no evidence, then I might tend to avoid making an opinion.

Q So if Michelle's tissue had never been sent

to any laboratory, your opinion that she has persistent measles virus in her bowel would be different?

A I wouldn't know with certainty, you know, just to respond to your question, if I knew that the published reports describing measles virus were accurate; and in response to your question, Michelle never had a biopsy or tested for measles virus.

I could reasonably hypothesize, well, the other clinical characteristics of this patient are identical to those patients who were subsequently confirmed to have measles virus. So I would certainly be open to that possibility.

Q Doctor, assume the facts are the exactly the same as this case, but Michelle was shown not to have inflammation in her bowl -- no inflammation, but she has GI symptoms. Would you still be of the opinion that she has ASD-GI?

A If she has inflammation, so if every test that we know of to do failed to demonstrate inflammation -- that's the question?

Q Yes, it's the question.

A Then I would consider giving her a trial of an anti-inflammatory; and if she responded the way you'd expect a patient would respond, with

inflammation to an anti-inflammatory, then I could reasonably conclude that it is there. I just haven't seen it.

Q What if the facts of this case are the same, except she never underwent an endoscopy; but everything else is the same. Would you still think that she had ASD-GI?

A Again, that's too many "ifs". What if she had two heads?

Q I mean, the facts of the case are exactly the same. It's just she had never undergone any of her five endoscopies. Would you still think she had ASD-GI?

A I'd have to give that some serious thought.

Q So you don't know?

A I don't know.

Q Doctor, on the last page of your report, you list the relevant facts to you in this case. In the first one, you state that the relevant facts in Michelle's history are (1) the appearance of classic ASD-GI disease, together with other signs of systemic illness, close to following within seven days the administration of the MMR vaccine.

So if I'm understanding, Doctor, you are saying that a significant fact for your opinion that

the MMR vaccine caused Michelle's enterocolitis; that Michelle had symptoms of systemic illness, within seven days of her MMR vaccine?

A No, that's a misquote. What I'm saying is that the appearance of her ASD-GI symptoms, the symptoms made their appearance, and time has shown that they were chronic. They never really remitted. She's had GI symptoms from the very onset of this period.

Q What symptoms are you referring to?

A Well, initially, she had vomiting and diarrhea. the vomiting improved. The diarrhea reverted to constipation. At that point, it went back to diarrhea, and it has remained diarrhea for many years. So there's never been a period of time in Michelle's history where she's been free of GI symptoms.

Q Is it your understanding that she had GI symptoms, the vomiting and diarrhea seven days after the MMR vaccination?

A With seven to fourteen days. That's the history I got -- so very soon, yes.

Q Would your opinion be different if the onset of vomiting and diarrhea was one month later?

A No, not in one month.

Q What about two months?

A I would say six months, and let me explain myself. This question I will answer even though it's hypothetical, because in our experience, we've seen many cases of children with autistic enterocolitis. We've advised biopsy and confirmed on biopsy to have it, who when you get a careful history from the parents, the GI symptoms don't appear until many months after MMR.

Even in those cases who had a regression immediately after MMR, some of them don't manifest the symptoms, like the diarrhea, until months after that. And all we can rely on is the symptom presentation. You can't know what's in there obviously. So that's why I would answer you that if the appearance of GI symptoms occur in and last as four to six months afterwards, I still would consider it related.

Q So anything after six months though, you would consider unrelated to the MMR vaccine?

A Now we have kits even after six months?

Q I mean, what's your limit. I mean, you just said six months. Would it be seven months?

A No, again, this has to do with our -- we haven't quantified, so I can't give you an exact number. But in my experience, thinking back over all

of the cases we've seen, that's how I'm going to be answering your question -- that the majority of them, of the children, who thought they had been diagnosed with enterocolitis and biopsy.

The majority of them have presented with GI symptoms within six months of their MMR. This is an opinion, because it asked me for one and we don't have it. I can't cite you data. But I also know from our experience that the onset of GI symptoms -- many of the children with plastic regressive autism occurred even over a year, after the onset of their aggression. So there's a lot about bowel disease that we don't understand.

Q From my understanding, if Michelle's diarrhea and vomiting occurred one year, post-MMR, would you opinion be different?

A The opinion of what?

Q That the MMR vaccine caused her enterocolitis.

A No, not if we found the virus there.

Q I thought you just said that it's not necessary to find measles virus; whether or not there is a positive finding in measles virus is not a necessary part of your opinion. You said that it doesn't matter to you if the results from the

Unigenetics Lab were found to be unreliable.

A That's not what I said.

Q What did you say?

A I'm not sure what you're referring to.

Q I asked you a question, that if it was shown that the results from Unigenetics are shown to be unreliable, would your opinion that she has persistent measles virus in her lymphoid tissue of her bowel be different? You said, no.

A Well, we have our own experience with that. So what I said was that I would strongly suspect, based upon our experience, that that's what caused it.

If you asked me if I would know that for certain, the answer is no. Because without getting a result on Michelle, and your question was hypothetical, where there was no Unigenetics result, but I still think she had it. I couldn't know that she had it, unless I had a result.

Q So a positive finding of measles virus is a necessary component, measles virus R&A in the lymphoid tissue of the bowel is a necessary component of your opinion that a child has persistent measles virus due to the MMR vaccine?

A That's correct.

Q Okay. Now, Doctor, at the end of your

testimony, you were referring to a poster presentation that was presented at the IMFAR conference in 2006. I'm referring to Petitioner's Exhibit 59 at Tab K. You describe it as a study that you do with Dr. Steven Walker and Dr. Karen Hepner. Who was the other person?

A Dr. Jeff Segal.

Q Jeff Segal -- now you presented on the poster preliminary data, correct?

A That's correct.

Q This is not a blinded study, is it?

A No, this work was not blinded.

Q Okay, and are you still in the data collection phase?

A We are.

Q Doctor, who funds this study?

A This study is funded by a variety of sources. As best as I recall, it was money that came from the Autism Research Institute. There was some private funding from individuals, and there was that private funding from also a private foundation.

Q Do you have an autism expert in the study?

A An autism expert -- do you mean a neurologist?

Q A neurologist.

A No, we have no neurologists involved in the study.

Q A psychiatrist?

A We have no psychiatrists involved in the study.

Q Do you have somebody who can verify the diagnosis of progressive autism?

A They will have been seen. They will have been evaluated.

Q Do all these children in the study have the diagnosis of regressive autism?

A No -- I'm not sure. I'm not sure. I don't know if these kids were all regressive or if these kids were just autistic.

Q How do you select the kids that participate in the study?

A Basically, it's just the kids that presented for an endoscopy, colonoscopy, based upon their GI symptoms, who we obtain biopsies of the ilium.

Q Presented to you, or do other people contribute tissue samples to the study?

A No, these are all patients that were biopsied by me.

Q By you -- did you charge them for the endoscopies?

A Yes, sure. But we did not charge them for any research-related cost. So whatever costs are involved, to process the specimens for the research or to test them is not billed to the patient. They are only billed for that portion of the endoscopy which is clinically indicated.

Q What's the sample size?

A We have over 275 specimens that are picked and have been preserved properly. So that's the potential pool that was indicated in the poster.

Q Have you submitted this at all for publication, yet?

A I mentioned before, it's still a data gathering process.

Q Now Doctor, were you at IMFAR conference in 2006?

A No, I was not there.

Q Okay, so this poster was not presented by you, correct?

A Correct, Dr. Steve Walker was there.

Q Now do you know the doctor that right next to your poster at the IMFAR conference in 2006, there was a poster contradicting your findings?

A I had heard that, yes.

Q And that was from Doctors Susan, Fombord,

and Ward?

A Correct; it didn't quite contradict the findings. That's a misstatement.

Q They have since published the results of their study in Pediatrics, correct?

A That's correct.

MS. RICCIARDELLA: I have no further questions; thank you.

SPECIAL MASTER HASTINGS: All right, let me take a look and see if I have any questions that weren't asked, if you'll bear with me for a moment, Doctor.

Did I hear you, Doctor, talk about Theresa Cedillo's difficulty in finding a pediatric gastroenterologist close enough to treat Michelle?

THE WITNESS: Close enough, yes.

SPECIAL MASTER HASTINGS: As I understood her testimony, there was no pediatric gastroenterologist in Yuma.

THE WITNESS: Correct

SPECIAL MASTER HASTINGS: And that was part of the reason she ended up seeing you. But did I recall that you were helping her to try to get somebody closer to home than New York City?

THE WITNESS: I spent hours on the phone,

coordinating Michelle's care, not just with other gastroenterologists, but with the rheumatologist, and the ophthalmologist, and the pediatricians, and the radiologists. We put a lot of time and effort into making sure that Michelle got to the people that were able to help her.

SPECIAL MASTER HASTINGS: Refresh my memory, you testified, I think, to helping her get in touch with a new treating pediatric gastroenterologist who was closer.

THE WITNESS: That's correct.

SPECIAL MASTER HASTINGS: Somewhere in California, I think.

THE WITNESS: That's where she ended up.

SPECIAL MASTER HASTINGS: Can you tell me who that was?

THE WITNESS: Davis Ziring at UCLA.

SPECIAL MASTER HASTINGS: That was the one in Los Angeles.

THE WITNESS: Right, right.

SPECIAL MASTER HASTINGS: All right, now I'm just curious. My geography isn't that good. But I would think that Phoenix or San Diego would be a lot closer than Los Angeles. Was there nobody in those areas that would be qualified?

THE WITNESS: That's more of a question for Theresa. You know, she would tell me who she wanted to go see, based upon her insurance plan. Before she ever sees anyone, she researches them, as you may have understood from hearing her talk.

So she would look for people with an academic background in inflammatory bowel disease, and a track record of an inquisitive mind. Those are the ones who she singled out and pursued them.

SPECIAL MASTER HASTINGS: Okay, bear with me a minute. I think all the questions I was going to ask have been asked by one counsel or the other. Do any of the Special Masters have questions?

SPECIAL MASTER CAMPBELL-SMITH: I do.

SPECIAL MASTER HASTINGS: Okay.

SPECIAL MASTER CAMPBELL-SMITH: I have a couple of questions. Doctor, I have just a couple questions regarding your poster presentation. For the record, this is Special Master Campbell-Smith.

You indicated that you were not certain whether the study just was restricted to kids with regressive autism, or if it was a broader set of autistic kids.

THE WITNESS: Right; I'd have to check with Dr. Walker about that.

SPECIAL MASTER CAMPBELL-SMITH: Okay.

THE WITNESS: I seem to recall it was limited just to regressive autism, but I don't want to say that with certainty.

SPECIAL MASTER CAMPBELL-SMITH: That point of clarification would be appreciated.

THE WITNESS: Okay, certainly.

SPECIAL MASTER CAMPBELL-SMITH: Of all the kids that were included in the study, you indicated that they all had GI problems, including there was a reference to the four postmortem specimens, or ones that had GI problems, as well?

THE WITNESS: The postmortem specimens?

SPECIAL MASTER CAMPBELL-SMITH: They're in the larger -- I'm referring to the paper presentation at page nine.

THE WITNESS: Oh, the controls.

SPECIAL MASTER CAMPBELL-SMITH: Yes, they're controls. I'm sorry. For the record, I'm referring to Petitioner's Trial Exhibit 3, at page nine. You indicate that you currently have 15 non-autistic pediatric controls; four of which were postmortem specimens of nonautistic children. Those specimens, were they associated with children who had GI problems?

THE WITNESS: No, no, they were not. The four postmortem specimens were obtained from a Government program called the CHTN. That's the acronym. I forget what the "C" stands for. But HTN is Human Tissue Network, and it's a program you apply for with a formal application, and there are participating hospitals.

You specify what you want; what kind of tissue and how you want it preserved, how you want it processed, how you want it sent, where you want it sent to. When the patient expires at a participating hospital, they then go and they harvest the organ that you requested and send it to you for research purposes. The "C" is for Cooperative -- Cooperative Human Tissue Network. So we received four postmortem specimens from them. That's what that is referring to.

SPECIAL MASTER CAMPBELL-SMITH: Okay, and they were non-autistic and did not have GI problems?

THE WITNESS: That's correct.

SPECIAL MASTER CAMPBELL-SMITH: Okay, another matter, you indicated that it did make some difference to you regarding the onset of gastrointestinal problems after the receipt of the MMR vaccination. Outside of six months, longer than six

months was, in your view, perhaps too long.

THE WITNESS: I didn't quite say that. I said most of the kids. In looking back at our experience, we haven't quantified that data and looked at that question specifically. But a lot of parents ask me this question. So I've thought about it, and our experience with many hundreds of these children, the majority of them have an onset of their GI symptoms within six months of their regression.

So to say it was within six months of that memo, it may actually be inaccurate. But I asked the question. I don't really ask, you know, how in relation to MMR did the GI symptoms present themselves. My real interest is in terms of the regression; whether the GI symptoms precede the regression. In other words, the time that the parents, in retrospect, note that the child has lost milestones.

Did the GI symptoms precede that period? Did it occur at about the same time; or did it occur after the regression? That's the question I really ask all patients. I don't ask what the chronologic association was between the MMR vaccine and the GI symptoms.

When I ask parents about the correlation

between the onset on regression and onset of GI symptoms, most parents will say that the GI symptoms occurred within six months of the time that they noted that their child has regressed. That's what I say.

But as I mentioned, that's most of them. There are a number that have GI symptoms presenting a year later, or over a year later.

SPECIAL MASTER CAMPBELL-SMITH: Is that something you're tracking with respect to your ongoing study?

THE WITNESS: Yes, we have that data. We have it entered. We have a very detailed data base that's in the process of being improved. We get very specific histories from our patients, specifically for this purpose.

SPECIAL MASTER CAMPBELL-SMITH: Is that primarily from parents, or is that from physicians?

THE WITNESS: It's all parents. I mean, our experience has been that what it comes to these symptoms, the parents are the most reliable source of information.

SPECIAL MASTER CAMPBELL-SMITH: Doctor Krigsman, there was an issue that you declined to want to address earlier during your direct examination. That was the occurrence of lymphonodular hyperplasia,

whether or not that's a normal finding.

In your experience as a pediatric gastroenterologist, I've read quite a bit of submitted material that seems to suggest that this phenomenon can occur, or there's a correlation between the number of invasive techniques and endoscopies, colonoscopies, that have been administered. Do you have a view?

THE WITNESS: Oh, yes, I have a very strong view about that. Lymphoid hyperplasia is the response of the immune system to something. It's a response. The lymphoid nodule, the germinal center starts replicating. The B cells are being produced, and there's a swelling that you can see visibly.

So it's an immune response. It always means something. The question is, whether it's a pathological process that needs to be treated; or does it indicate disease? That's an entirely different question.

So yes, in the course of day-to-day living, a child might ingest something; or become ill with a virus that clears after a week or two, and he may be left with residual small lymphoid hyperplasia, which clearly is not normal. It's a response to something. It's not pathologic. We don't need to address it or deal with it.

On the other hand, there are certainly a number of disease conditions that hyperplasia is an integral part of. So if you take a look at a patient with facile colitus, you'll find marked LNH. If you look at patients with H pilori gastritis, you'll find marked LNH. If you look at a page with Crohn's Disease, you find market LNH.

So these are all characteristic features of the many disease processes. A lot of the immunodeficiency states, HIV enteritis, also is accompanied by plasia of the small bowel and then the colon.

So it clearly is part of a pathologic process in many, many diseases. Now whether it's always pathologic is a matter of debate. As I say, it always means there's been an immune response. That's for sure.

But whether it means that there's disease is a different question; and the answer, I believe, is no. So having LNH, in and of itself, in a patient who otherwise is healthy and well, is not indicative of anything than that lymphoid nodules, once upon a time, saw something and responded to it. That something may or may not still be present.

But to therefore say that all LNH is there

for normal, it's grossly incorrect, since it's well described as being part and parcel of the description of so many diseases.

In our experience with these children, what convinces me that the LNH is part of the pathologic process is that I theorized that if LNH occurs in association with inflammation of the colon, and you can show a statistical correlation between them, that would be significant. That suggests that the LNH is not occurring in the absence of any other findings, but in the presence of inflammation. That suggests that the process is pathologic.

We have that data, and we have made that calculation. We reviewed well over 100 patients, and one of the analyses that we did was looking first at the statistical correlation between the LNH on the inflammation. We found that patients with LNH were more likely to have inflammation than those without LNH. So that's already in manuscript form. It has not been completed, yet. So to answer your question - -

SPECIAL MASTER CAMPBELL-SMITH: Pardon me, Dr. Krigsman. That early manuscript form, is this another paper distinct from your poster presentation?

THE WITNESS: Correct, yes, this is a

separate analysis that myself and other authors in collaboration have done as a retrospective review of our experience with our first large number of patients.

SPECIAL MASTER CAMPBELL-SMITH: Thank you.

SPECIAL MASTER VOWELL: Just to follow-up on that, Doctor, what retrospective review are you looking at a case control study?

THE WITNESS: No, it's simply a large number of patients, and we reviewed our findings and report. So we had "X" number of patients, what did we find in them, and to report it.

SPECIAL MASTER VOWELL: And so you're comparing the findings on inflammation versus the endoscopy findings, versus normal statistical -- I'm not sure I understand what you're comparing.

THE WITNESS: Not even that; not even that -- it's strictly a report. This is what we did in "X" number of patients. This is what we found, and the results, without a control, without being perspective, it puts certain limitations on the value of that study. That's understood. But a retrospective review of this group of kids, in a large number, will stand on its own, just as a very important piece of information towards the puzzle.

SPECIAL MASTER VOWELL: We don't commonly perform endoscopies on kids without GI symptoms, correct?

THE WITNESS: You never should.

SPECIAL MASTER VOWELL: Thank you.

SPECIAL MASTER CAMPBELL-SMITH: I have one follow-up question. LNH can occur in the absence of a persistent irritant, a persistent virus?

THE WITNESS: Yes.

SPECIAL MASTER CAMPBELL-SMITH: You alluded to something that is transient, that moves throughout the system.

THE WITNESS: Yes.

SPECIAL MASTER CAMPBELL-SMITH: As a matter of fact, and correct me if I'm wrong, in kids with food allergies, for example, does the LNH resolve once the kids stop with the particular foods?

THE WITNESS: I don't know if anyone has looked at that, in particular, to see whether food allergy-induced LNH resolves over time. I'm unaware of a paper that looks specifically at that.

But I'll tell you, from other areas of the body, any of your lymph nodes, if you have a sore throat and you get a swollen gland, even when you feel better a week later, that swollen gland could be

present for months and months and months.

Particularly, in kids, kids have their persistent tonsil alert. The tonsil is a lymphoid issue, also. Even in the absence of any ongoing inflammation, households are often very large and children are not considered pathologic. But it's the residual hypertrophy of lymphoid tissue which sometimes persists, even after the inciting agent disappears.

SPECIAL MASTER CAMPBELL-SMITH: Thank you very much, Dr. Krigsman.

MR. MATANOSKI: Dr. Krigsman, I'd like to ask another question, as well.

SPECIAL MASTER HASTINGS: Well, concerning your ongoing study that is at Tab K of your articles and your report and that you gave us a copy of the poster for it today, I'm referring to that study, from the quick looking at Tab K, it mentions that biopsy tissue was assay by the RT-PCR for the presence of measles virus RNA. Now, from that extent, it sounds very much to me like what the Unigenetics Lab did. Is it the same assays we are talking about, the same assay?

THE WITNESS: My answer to that would be yes, but I really would defer that question to Dr.

Hepner --

SPECIAL MASTER HASTINGS: Okay.

THE WITNESS: -- tomorrow, because she would have much more specific -- I don't want to answer incorrectly.

SPECIAL MASTER HASTINGS: Well, maybe that's really my next question. In the case of the -- the Unigenetics, we're talking about a specific lab. Usually when I see these kind of results, these kind of assays done in cases, it's usually reported by such and such lab. So, which -- is it Dr. Hepner's lab that -- what lab, if you know?

THE WITNESS: The lab, it was Wake Forest University.

SPECIAL MASTER HASTINGS: It is Wake Forest.

THE WITNESS: Wake Forest University. Dr. Steve Walker is the biologist over there. It's his lab.

SPECIAL MASTER HASTINGS: It's his lab?

THE WITNESS: Yes.

SPECIAL MASTER HASTINGS: Okay.

THE WITNESS: And the specifics of the assay, Steve used a number of different primers, so he was experimenting with a lot of them to see which one would be most productive versus least productive. And

as I say, that's demonstrated in the table. And, again, Dr. Hepner can give you much more --

SPECIAL MASTER HASTINGS: Okay.

THE WITNESS: -- much more detail about that. So, more primers we used in our study than in the Ulman study.

SPECIAL MASTER HASTINGS: All right. That answers my question. Any redirect for this witness?

SPECIAL MASTER CAMPBELL-SMITH: Yes, Special Master. Could we possibly take a five-minute break first?

SPECIAL MASTER HASTINGS: Let's take a five-minute break. Don't forget that we're going to go dark here and we want to get out before that happens. Okay, let's take a five-minute break.

(Whereupon, a short recess was taken.)

SPECIAL MASTER HASTINGS: All right. The folks, who were at home, we are back from our break here and Ms. Chin-Caplan for the Petitioners will be asking some more questions of Dr. Krigsman. Ms. Chin-Caplan, please go ahead.

MS. CHIN-CAPLAN: Thank you, Special Master.

REDIRECT EXAMINATION

BY MS. CHIN-CAPLAN:

Q Dr. Krigsman, are you aware that Michelle

Cedillo is now receiving Humira?

A I am.

Q What is Humira?

A Humira is a more recently manufactured anti-TNF drug, which has a lower side effect profile than Remicade that preceded it for a variety of reasons. And she is now receiving that.

Q And what are the indications for the use of Humira?

A Well, autoimmune diseases that involve tumor necrosis factor as a predominant cytokine would all be expected to respond to Humira. So, diseases such as severe arthritis, rheumatory arthritis and inflammatory. Bowel disease are two immediate diagnoses that come to mind that would be expected to respond to Humira, based upon their known predilection for tumor necrosis factor.

Q Did you order the Humira?

A No; no, I did not. Dr. Ziring, at the UCLA, the pediatric gastroenterologist over there ordered Humira, not at my urging. I have not spoken with Dr. Ziring, nor have I ever e-mailed him or he e-mailed me.

Q And Dr. Ziring is Michelle Cedillo's current treating pediatric gastroenterologist?

A That's correct.

SPECIAL MASTER HASTINGS: Doctor, before we leave that topic, can you spell the name of that medication for us?

THE WITNESS: H-U-M-I-R-A.

SPECIAL MASTER HASTINGS: Thank you. Go ahead, Ms. Chin-Caplan.

MS. CHIN-CAPLAN: Thank you.

BY MS. CHIN-CAPLAN:

Q Doctor, you were asked some questions about a situation that occurred at Lenox Hill Hospital. Do you remember those questions?

A I do.

Q Doctor, could you kindly tell the Court the circumstances of what occurred at Lenox Hill Hospital?

A Well, it's a long story, but the -- you know, the essentials of the story is that the hospital was concerned that the endoscopies that I was performing on children with autism and bowel symptoms, very similar to Michelle's history, same kind of diarrhea, same abdominal pain, they were concerned that those procedures were not medically indicated and were being performed for the purpose of research and that was their concern. And in response to that concern, they prevented me from performing further

endoscopies in the endoscopy unit and that resulted in litigation.

Q Doctor, when you perform an endoscopy, are there clinical signs and symptoms, which you rely upon before you would conduct that procedure?

A Absolutely. You know, the standard textbook indications, pediatric GI textbook indications for a diagnostic colonoscopy, for example, is the presence of abdominal pain that's chronic, with or without diarrhea, chronic diarrhea with or without abdominal pain. Those two findings, when there is no other explainable cause, you've looked at potential diagnoses and ruled them out based upon either laboratory testing, which includes blood and stool, if you rule that other diagnoses based upon the history and the physical examination, if you've ruled out everything you can think of and what is left is abdominal pain and diarrhea, then the next step is a diagnostic colonoscopy specifically to look for inflammatory changes as being the cause of the abdominal pain and diarrhea. What makes these children different from most other kids that even I had previously encountered in my career as a pediatric neurologist is that traditionally, and this is part of the confusion, traditionally, the way we're taught,

whether it's, you know, taught explicitly or just implied, is that the chances of having bowel inflammation that result in symptoms is unlikely if there is no bleeding or weight loss. This is something that most -- and this is something that I was taught and I believed for quite a long time. So, in the absence of any evidence of bleeding, either visible bleeding or microscopic bleeding or weight loss or low albumin or high sed rate, in the absence of any one of those findings, if you have chronic diarrhea and abdominal pain, you're very unlikely to find bowel inflammation as the cause of the diarrhea and abdominal pain. And that way of thinking is a prevailing way of thinking and it's even supported by a number of studies. It isn't like it's a myth.

But, these children have been shown to be different. These children have inflammation that is related to their symptoms, but usually it occurs, these symptoms of diarrhea and pain occur in the absence of gross bleeding, any visible bleeding, in the absence of even microscopic bleeding usually. There are some kids, who have bleeding; most of them don't. Most of the kids don't have an elevated sed rate, even though Michelle did. And because -- and these children, again, have been demonstrated, this

has been published, to have enterocolitis even though they didn't have the other markers that traditionally gastroenterologists have relied on in determining whether -- more likely to find colitis, which is a cause of their symptoms.

So, that's the way of thinking and this was the concern of the hospital, that they, therefore, concluded that I must be doing this for research-related reasons, meaning that these children did not, in fact, merit a diagnostic colonoscopy. I was just interested in some research project. And they moved to, and they did prevented me from scheduling any further colonoscopies. And that was the -- and I should mention that these children that I had scoped -- and by the way, it was -- at Lenox Hill, I should mention that it wasn't until after I had scoped more than 100 children there, more than 100 children was scoped at that hospital, that they moved to prevent me from doing further colonoscopies. And the pathologist at the hospital, and there were many of them, a variety of pathologists would read the biopsies, it wasn't just one or two, the frequency with which the hospital's pathologists found this non-specific enterocolitis was close to 70 percent. So, the majority of the children there, and this is all part

of the medical records of these children, it's not my diagnosis, this is the institutional pathologist's diagnosis, despite that, there was still this concern of the hospital that this is something that's different, that they wanted stopped. And that's the story.

Q So, Doctor, the children that you wanted to scope, they all had GI symptoms; is that true?

A Every single one. Every single patient, who gets a diagnostic colonoscopy, which is what these kids were getting, have chronic symptoms in the absence of an explainable cause.

Q And all of the causes had been ruled out, is that true?

A Yes. We routinely will do blood testing, stool testing, abdominal x-rays, dietary investigations, dietary changes, urine analysis, looking for urine infections. I mean, the common causes of pediatric GI symptoms are all ruled out. And when that happens and the symptoms persist and they impact the patient's quality of life, the next step is to do a diagnostic colonoscopy, looking specifically for bowel inflammation. And that approach, by the way, has been now adopted by a consensus of pediatric gastroenterologists. Since the

Lenox Hill incident, specifically in October of 2006, there was a meeting of leading pediatric gastroenterologists, and I attended, even though I'm not a leading pediatric GI doctor, I was invited to attend to be part of this meeting and it was held in Boston at the Harbor Club and attended by a number of very prominent pediatric gastroenterologists from this country.

And the purpose of the meeting was convened by Autism Speaks. It's an organization that many of you have probably heard of. And it was convened by them -- information about this is available on their website -- specifically to respond to the community interest, is the way the website phrases it, this parental concern that so many of these children are experience gastrointestinal problems. And what approach does a panel of leading gastroenterologists recommend, be taken to assess and evaluate these patients. And between October and I think January or February, the statement went back and forth amongst the various authors and eventually the consensus statement was published on the Autism Speaks website and it's available. We would be happy to distribute it to the Court. And it essentially advocates the exact work-up that I have just described to you:

careful history; careful physical exam; you can treat empirically for minor problems; constipation, treat it the way you normally would treat constipation; a little diarrhea, you can try giving some motility drugs temporarily; rule out other causes, other potential causes of these symptoms in these children.

But after you have done that, if all those tests are negative and you've done short-term therapy for irritable bowel syndrome and for constipation, and despite all of those things, the problem still persists, then the next step is to look specifically for inflammatory changes of the colon. So, that's becoming more of a consensus opinion. I'm happy to say that.

Q Now, Doctor, you mentioned that that meeting took place in Boston in October of 2006?

A Correct.

Q And was their a sponsoring organization?

A Autism Speaks.

MS. CHIN-CAPLAN: Special Master?

(Pause.)

BY MS. CHIN-CAPLAN:

Q Doctor, I am going to ask you to read along with me, please. Is this the letterhead of Autism Speaks?

A Correct, it is.

Q And, Doctor, is the title of this document, Autism Speaks Hosts Gastroenterology Workshop?

A Yes, it is.

Q And, Doctor, underneath this, does it say, 'responding to community interests, Autism Speaks hosted a workshop on autism and gastroenterology in Boston on October 13, 2006. The object of the workshop were to: (1) review current scientific evidence for GI issues associated with autism; (2) develop consensus scientific priorities for autism gastroenterology research; and (3) suggest an approach to establish best clinical practices for autism gastroenterology.' Have I read that correct?

A Verbatim.

Q 'In an effort to capture all perspectives on this topic, participants included members of the Autism Speaks Scientific Affairs Committee and leading experts on pediatric gastroenterology and autism. The discussion was comprehensive and productive. Please watch this space for a synopsis of the consensus recommendation.' Have I read that correctly?

A Yes.

Q And, Doctor, underneath it, it listed the participants in this gastroenterology workshop, didn't

it?

A It did.

Q And, Doctor, was Dr. Paul Ashwood of the University of California Davis Mind Institute present?

A Yes, he was.

Q Dr. Federico Balzola, Hospital Mullinet from Torino, Italy?

A Correct, he was.

Q Dr. Margaret Bauman, the Latters Clinic from Boston?

A Correct.

SPECIAL MASTER HASTINGS: Ms. Chin-Caplan, should we -- rather than read the list, can we just make this Petitioner's Trial Exhibit 5? I mean, you're going to read this whole list of --

MS. CHIN-CAPLAN: I thought that this was a consensus meetings of experts within the field --

SPECIAL MASTER HASTINGS: Okay.

MS. CHIN-CAPLAN: -- and these were the people, who participated.

SPECIAL MASTER HASTINGS: All right.

MS. CHIN-CAPLAN: So, it thought we should be comprehensive on this.

SPECIAL MASTER HASTINGS: Well, what I am saying is can we get this into the record just by

making it a trial exhibit?

MS. CHIN-CAPLAN: Oh, certainly, certainly.

SPECIAL MASTER HASTINGS: Yes.

MS. CHIN-CAPLAN: I'm sorry. I misunderstood you.

SPECIAL MASTER HASTINGS: Trial Exhibit 5.

MS. CHIN-CAPLAN: Would this be Krigsman --

SPECIAL MASTER HASTINGS: Well, no, no, no.

MS. CHIN-CAPLAN: No?

SPECIAL MASTER HASTINGS: You were mentioning as to the other ones Krigsman. Let's call Petitioners' Trial Exhibit 1, 2, 3, 4, and now No. 5.

(The document referred to was marked for identification as Petitioners' Trial Exhibit No. 5 and was received in evidence.)

MS. CHIN-CAPLAN: Okay.

SPECIAL MASTER HASTINGS: So, I was just saying, this list speaks for itself. It gives the names you're reading off and who they're from. So, go ahead.

MS. CHIN-CAPLAN: Thank you, Special Master.

BY MS. CHIN-CAPLAN:

Q Dr. Timothy Buie, Massachusetts General

Hospital for Children, Boston; Dr. David Burnham, PediaMed Pharmaceuticals, Florence, Kentucky; Dr. Stan Cohen, Emery College, Atlanta, Georgia; Dr. Andrew Conrad, National Genetics Institute, Los Angeles, California; Dr. Anil -- is that it -- Darbari, Kennedy Krieger Institute, Baltimore, Maryland; Dr. Gary Goldstein, Kennedy Krieger Institute, Baltimore, Maryland; Dr. Susan Hyman, University of Rochester Medical Center, Rochester, New York; Dr. Arthur Krigsman -- that's you, okay?

A That's me.

Q Dr. Alan M. Leichtner, Children's Hospital, Boston; Dr. Elizabeth Mumper, Advocates for Children, Lynchburg, Virginia; Dr. Leonard Rappaport, Children's Hospital, Boston; Dr. Ann Reynolds, University of Colorado, Denver, the Children's Hospital; Dr. Mark Roithmayr, Autism Speaks, New York; Dr. Andy Shih, Autism Speaks, New York; Dr. Andrew Wakefield, Thoughtful House for Children, Austin, Texas; Dr. Allan Walker, Massachusetts General Hospital, Boston. Have I read the list, Doctor?

A Yes.

Q And, Doctor, this indicates that there was going to be a consensus recommendation, is that true?

A That's correct.

Q And was that consensus recommendation issued?

A Yes, it was and it was available on their website. More importantly, it was mailed to all the pediatricians that are members of the American Academy Pediatrics.

MS. CHIN-CAPLAN: Should we mark this as Petitioner's Exhibit ---

SPECIAL MASTER HASTINGS: Trial Exhibit No. 6.

(The document referred to was marked for identification as Petitioners' Trial Exhibit No. 6 and was received in evidence.)

BY MS. CHIN-CAPLAN:

Q Doctor, I am not going to go through this. This is quite a lengthy document. It's seven pages long, am I correct?

A Correct.

Q And since you were the participant there, did you review the subsequent drafts?

A Subsequent drafts, yes. Yes, they were passed around as they evolved.

Q And did you review the finalized version?

A Yes, I did.
Q And it's a 'Dear Doctor' letter, is that it?
A Correct.
Q And what is your understanding of its distribution?
A I'm sorry?
Q What is your understanding of its distribution?
A As I mentioned, it was mailed out to all pediatricians, actually all members, all members of the American Academy of Pediatrics.
Q And Doctor, since you have reviewed the final version of this, could you just summarize to the Court what is contained within this Dear Doctor letter?
A Well, basically, it's a recommended approach to children, who have gastrointestinal symptoms, and it describes -- the introduction goes through some of the published data that suggests the very frequencies with which GI symptoms are found. The second page goes through the pertinent components of the history that the panel felt was most -- would be most suggestive or most likely to make any sort of a diagnosis, not just colitis, but as far as reflux and constipation. These children -- make no mistake, I'm

not saying that every child with autism and GI symptoms is enterocolitis. That's not -- that should not be the way you are interpreting what I am saying today.

Children with autism has a whole gamut of gastrointestinal diagnoses, including enterocolitis, and the main import of this meeting was to emphasize that there are symptoms, which may be not like symptoms that we're used to seeing in children, because of their communicative disorders need to be taken seriously. So, what questions need to be asked? What labs need to be drawn? What, if any, x-rays need to be done? What specific work-up should be done depending on the symptom presentation and three main symptoms are diarrhea, constipation, and bloating? What parts of the history would suggest that in a child with ASD? What part of the physical examination would be most pertinent to pursue depending on the symptom? And recommendations for empiric treating, brief empiric treatments are made, recommendations are made when to refer to a pediatric gastroenterologist. And there was a clear statement that endoscopy and colonoscopy may be indicated to make the diagnosis of a variety of different disease, among them the colitis that has been published and described in these

patients.

Q And, Doctor, this statement was the basis -- what a consensus statement of the individuals, who were present in this meeting?

A That's correct.

MS. CHIN-CAPLAN: Thank you. I have no further questions.

SPECIAL MASTER HASTINGS: Any more questions for this witness?

MS. RICCIARDELLA: No, sir.

SPECIAL MASTER HASTINGS: All right. Before we break, let's do one more housekeeping task. There were two of the documents that were used in cross-examination of Dr. Krigsman. Well, a number of them, most of them had already been filed. There were two documents, one was a page or two from the Thoughtful House website. The second was the licensure for the Texas, the minutes of that. Should we make those two as Respondent's Trial Exhibits 1 and 2, to put them in the record, since he discussed them today?

MR. MATANOSKI: I will leave that to your discretion, sir.

SPECIAL MASTER HASTINGS: Okay.

MR. MATANOSKI: What were you planning on doing on cross-examination, if we did have documents,

as we asked the questions first and depending on the answers, if we have to go to such documents to further elucidate the information that's necessary for the Court to consider? If you would like us to file those as trial exhibits, we would be happy to.

SPECIAL MASTER HASTINGS: Any objection to that?

MS. CHIN-CAPLAN: No.

SPECIAL MASTER HASTINGS: Why don't you do that ---

MR. MATANOSKI: Yes, sir.

SPECIAL MASTER HASTINGS: -- since we discussed them and we can see the whole document. These all can be filed after the trial, but if you keep a list of them, and mark those number one and number two, then, for the Respondent.

(The documents previously referred to were marked for identification as Trial Exhibit Respondent's Exhibit No. 1 and 2 and were received in evidence.)

SPECIAL MASTER HASTINGS: Anything else that we should -- anything?

MS. CHIN-CAPLAN: I just have one more.

BY MS. CHIN-CAPLAN:

Q Dr. Krigsman, what percentage of the patients that you currently see are non-autistic?

A Very few.

MS. CHIN-CAPLAN: Thank you.

SPECIAL MASTER HASTINGS: All right. Anything else we should take care of today before we break?

MS. CHIN-CAPLAN: Not from Petitioners.

SPECIAL MASTER HASTINGS: Okay.

MR. MATANOSKI: Nor Respondent.

SPECIAL MASTER HASTINGS: All right. And for the benefit of anyone listening out there, I understand that the order of business tomorrow, we'll hear from Dr. Hepner and Dr. Kennedy tomorrow for the Petitioners.

MS. CHIN-CAPLAN: That's correct.

SPECIAL MASTER HASTINGS: All right. With that, we are adjourned for the day. Thank you all.

(Whereupon, at 5:27 p.m., the hearing was recessed, to reconvene on Wednesday, June 13, 2007, at 9:00 a.m.)

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REPORTER'S CERTIFICATE

DOCKET NO.: 98-916V
CASE TITLE: Cedillo v. Sec., HHS
HEARING DATE: June 12, 2007
LOCATION: Washington, D.C.

I hereby certify that the proceedings and evidence are contained fully and accurately on the tapes and notes reported by me at the hearing in the above case before the United States Court of Federal Claims.

Date: June 12, 2007

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