AUTISM--WHY THE INCREASED RATES? A ONE-YEAR UPDATE

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C O N T E N T S

AUTISM--WHY THE INCREASED RATES? A ONE-YEAR UPDATE

WEDNESDAY, APRIL 25, 2001

House of Representatives,
Committee on Government Reform,
Washington, DC.

The committee met, pursuant to notice, at 11:07 a.m., in room 2154, Rayburn House Office Building, Hon. Dan Burton (chairman of the committee) presiding.

Present: Representatives Burton, Morella, Ros-Lehtinen, Horn, Davis, Weldon, Waxman, Maloney, Norton, Cummings,

Kucinich, Blagojevich, Tierney, Schakowsky, and Clay.

Staff present: David A. Kass, deputy counsel and parliamentarian; Mark Corallo, director of communications; John Callendar, counsel; S. Elizabeth Clay, Nicole Petrosino, and John Rowe, professional staff members; Robert A. Briggs, chief clerk; Robin Butler, office manager; Michael Canty and Toni Lightle, legislative assistants; Scott Fagan, staff assistant; Leneal Scott, computer systems manager; John Sare, deputy chief clerk; Corinne Zaccagnini, systems administrator; Phil Barnett, minority chief counsel; Kate Anderson and Sarah Despres, minority counsels; Ellen Rayner, minority chief clerk; and Jean Gosa, minority assistant clerk.

Mr. Burton. Good morning.

A quorum being present, the Committee on Government Reform will come to order. I ask unanimous consent that all Members' and witnesses' written and opening statements be included in the record. Without objection, so ordered.

I ask unanimous consent that all articles, exhibits, or extraneous or tabular material referred to be included in the record. Without objection, so ordered.

During the 106th Congress, I initiated oversight investigations to look at the dramatic rise in autism rates and the many concerns about vaccine safety. Autism rates have skyrocketed. Conservative estimates suggest 1 in 500 children in the United States is autistic. However, those rates are dramatically higher in some places such as Brick Township, NJ, where the rates are 1 in 150. I think Congressman Smith, who is going to testify today, represents part of that area.

In the first quarter of this year a child was diagnosed with autism every 3 hours in California. Last year, that rate was every 6 hours. Look at that graph. They are having an absolute epidemic out there.

Indiana is seeing a similar trend in increased rates; 1 in 400 children in my home State is autistic. Between December 1999 and December 2000, requests for special education services for children with autism went up 25 percent. That is a 25-percent increase in requests for taxpayer-provided services in just a year.

We have a national and potentially worldwide epidemic on our hands. It cannot simply be better reporting or an expanded definition of autism. There has to be more to it than that.

As with any epidemic, we need to focus significant energy and research on containing it. We need to locate the cause or causes. We need to determine if this is the same condition we understand autism to be or not. Could this epidemic of children who regress into ``autism'' be another condition being called autism?

We need to be aggressive in developing and making available appropriate treatments for both the behavioral issues and the biomedical illnesses related to this condition. And we need to

provide credible and timely information to the public. Has the public health sector responded adequately and appropriately to this epidemic? We will be hearing from witnesses over the next 2 days to find out.

Autism, or Autism Spectrum Disorder, is devastating to families. I know this from personal experience. My grandson, Christian, was born healthy and developed normally. His story is not much different than that of the thousands of families we have heard from over the last year. He met his developmental milestones. He was talkative. He enjoyed being with people. He interacted socially.

Then Christian received his routine immunizations as recommended by the Centers for Disease Control and Prevention and his life changed dramatically and very rapidly. We now know that through his shots, he may have been exposed to 41 times the level of mercury than is considered safe by Federal guidelines for a child his size. This was on top of other mercury exposure from earlier vaccinations.

Within 10 days of receiving his vaccines, Christian was locked into the world of autism--within 10 days. Is it related to the MMR vaccine? Is it related to the mercury toxicity? Is it the environment, including food allergies? Or is autism purely genetic? Some would have us believe that a child's regression into autism within a short time of vaccination is purely a coincidence. I ask those individuals to show me the science that proves this theory.

On Monday, the ``Measles-Mumps-Rubella Vaccine and Autism Report'' was released by the Institute of Medicine's Committee on Immunization Safety Review. We have Dr. Marie McCormick, the Chair of this committee, here today to talk about the findings and recommendations of the report.

I realize the headlines over the last 3 days have said that the committee found no connection between the MMR vaccine and autism. I would urge all of you to read the entire report and recognize that the committee found that there was insufficient evidence to conclusively prove or disprove a connection between the MMR vaccine and acquired autism. And yet, on television all across this country, every parent saw that there was no connection between the MMR vaccine and autism.

Yet, that is not what the report said. I believe a disservice has been given to the American people about this. Parents need to know the risks involved with certain exposures their children have to face. And they need to have all the facts, not part of the facts.

It should be noted that the committee notes in its conclusions that it could not exclude the possibility that MMR vaccine could contribute to Autism Spectrum Disorder.

In the scientific community, there is an accepted hierarchy of research methodology that builds a balanced foundation of the evidence. That is in attachment 1. What we learned from the

Institute of Medicine is that the research has not yet been conducted to build this hierarchy of evidence regarding the question of whether or not the MMR vaccine may be linked to the increased incidence of autism.

We have substantial parental observation, which should never be discounted. And we have several case studies and laboratory evidence showing measles virus in the guts of autistic children who have bowel dysfunction. And we also have several population-level epidemiological studies.

While the Immunization Committee noted that the epidemiologic studies do not support an association at a population level, their report stated that ``it is important to recognize the inherent methodological limitations of such studies in establishing causality.''

In essence, the studies that have been published and held up by the public health community as ``proof'' against Dr. Wakefield's hypothesis can never answer the question of whether or not MMR vaccine is linked to autism in some children. We do not have enough research to make an evidence-based final conclusion. What we have is a clear indication that a problem exists for some children. We need to do the research to get our arms around that problem, so that we can prevent any further escalation of this epidemic of acquired autism.

When the Institute of Medicine formed their committee, we were assured that there would be no one on the committee who had ties to the vaccine industry. We were told there would be nobody connected to the vaccine industry involved in the research done by this committee. So I was disturbed to learn that the committee sent this report out for review and comment prior to becoming final to numerous individuals who have ties to the vaccine industry, including the manufacturer of the MMR vaccine.

They sent it out for critiquing, and there were changes made by these other people outside. They also sent it to at least one individual who presented to the committee, but not to Dr. Wakefield and the rest of the presenters. This preferential treatment is disturbing, and I would like to know why they did not send it to everybody who was a presenter.

I am including in the record a letter I received from one of the reviewers, and a previous witness to this committee regarding his concerns about flaws in the evaluation of the published research. He is with the University of Oklahoma, the Health Center. And that will be included in the record.

[The information referred to follows:]

[GRAPHIC] [TIFF OMITTED] T6856.001

[GRAPHIC] [TIFF OMITTED] T6856.002

Mr. Burton. I want to read just one part of his letter.

``The report highly criticizes the peer review publications

that cite a causal association of the MMR vaccine and autism and does not provide a similar critique of the peer review publications that cite a lack of association of the MMR vaccine and autism.''

It also says, ``One of the publications that are used to support the lack of the MMR vaccine and autism cites support of Merck and Company in the acknowledgements.'' They are the producer of the MMR vaccine.

This is not mentioned in the Institute's report and could be considered potentially as a pre-existing bias. We want to ask the person who is going to be testifying about the report why that happened.

They also sent it to at least one individual who presented to the committee, but not Wakefield.

I am including in the record this letter I received from the reviewer about what he believes to be the flaws in the evaluation of the published research. He also raises concerns about the lack of the Institute's acknowledgement in their evaluation that one of the publications used to support a lack of a connection between the MMR vaccine and autism was sponsored by Merck, the manufacturer of the MMR vaccine.

witnesses to stick to the time limit so we can get through all the panels and have time for questions. We will be hearing first from my colleagues and friends, the chairmen of the Autism Congressional Caucus--which I am proud to be a member of--Congressman Christopher Smith of New Jersey, and Congressman Mike Doyle of Pennsylvania.

The record will remain open until May 11.

I apologize to Mr. Waxman for talking so long, but I feel very strongly, as you know.

Mr. Waxman, you are recognized for an opening statement.

[The prepared statement of Hon. Dan Burton follows:]

[GRAPHIC] [TIFF OMITTED] T6856.003

[GRAPHIC] [TIFF OMITTED] T6856.004

[GRAPHIC] [TIFF OMITTED] T6856.005

[GRAPHIC] [TIFF OMITTED] T6856.006

[GRAPHIC] [TIFF OMITTED] T6856.007

[GRAPHIC] [TIFF OMITTED] T6856.008

[GRAPHIC] [TIFF OMITTED] T6856.009

[GRAPHIC] [TIFF OMITTED] T6856.010

[GRAPHIC] [TIFF OMITTED] T6856.011

[GRAPHIC] [TIFF OMITTED] T6856.012

Mr. Waxman. Thank you very much, Mr. Chairman.

The issue of autism has been getting increased attention in Congress over the last several years, and this attention is overdue. I want to commend you, Mr. Burton, for your efforts to increase public awareness about autism through these hearings.

Autism is a particularly frustrating disease. We still do not understand what causes it and we still do not have a cure. All we know for sure is that its impact on families can be devastating.

During the hearings held in this committee, we have heard parents tell tragic stories of children who appear to be developing normally and then all of a sudden retreat into themselves, stop communicating, and develop autistic behavior. Other parents have testified that their children never start to develop language skills, and instead early on manifest symptoms of autism.

I can only imagine how frustrating and difficult this must be for families. And I appreciate how urgently we need to understand what causes autism, how to treat it, and if possible, how to prevent it.

Fortunately, Congress is beginning to respond. Last year, I co-sponsored a bill to increase NIH's funding for autism research. This funding was authorized as part of the Child Health Act, which I also supported.

This year, Congress' challenge will be to appropriate the funding authorized by the Child Health Act. We will not make real progress until we make sure NIH has the funding it needs to research this debilitating disease.

At our first hearing last year, we heard moving statements from the chairman and several witnesses that they had firsthand experience with observing signs of autism shortly after children received the MMR vaccine. These witnesses voiced their suspicion that autism was caused by the vaccine.

I was deeply concerned about these remarks. Vaccines are unique in medicine. Other medicines are administered to sick people to make them better. But vaccines are given to healthy children and they are mandatory in many States. When I heard the chairman's concerns, I was disturbed by the possibility that a vaccine that States mandate could be making healthy children sick.

But at the same time, I was also worried for another very different reason. Vaccines are one of the greatest success stories in modern medicine. Because of vaccines, children no longer suffer brain damage or die from measles or are paralyzed by polio. I realize that publicizing fears that vaccines may cause autism could cause some parents to stop vaccinating their children. And I worry that this could be counterproductive. In

the name of protecting our children from autism, we could actually be subjecting them to much greater risks of deadly or debilitating diseases such as measles, rubella, damage affecting developing fetuses or brain damage from meningitis.

The theory that the MMR vaccine may contribute to autism had been carefully reviewed by the British Medical Research Counsel, which found no evidence to support it. However, what we needed, I believe, was more study. That is why I proposed during last year's hearing that Chairman Burton join me in requesting that the Secretary of Health and Human Services convene a panel of experts to examine the theory that the MMR vaccine could cause autism.

HHS responded to our request by contracting with the Institute of Medicine, a branch of the National Academy of Sciences, to convene a panel of independent experts to review vaccine safety issues. The Institute of Medicine identified potential experts and then subjected the experts to strict criteria that excluded anyone who had financial ties to vaccine manufacturers or their parent companies, previous service on the major vaccine advisory committees, and prior expert testimony or publications on issues of vaccine safety.

The first issue this independent panel considered was the relationship between the MMR vaccine and autism. This panel of independent experts convened by the Institute of Medicine issued its report on the MMR vaccine this Monday. The report is careful and analyzes all the scientific information available and it concludes that there is no credible scientific evidence establishing a link between the MMR vaccine and autism.

The Institute of Medicine report is consistent with the findings of the British Medical Research Council. It is also consistent with the conclusions of the World Health Organization, the American Medical Association, and the American Academy of Pediatrics. Taken together, the evidence clearly demonstrates that the MMR vaccine is highly unlikely to be a cause of autism.

The next vaccine issue the Institute of Medicine will examine is whether there have been adverse effects from thimerosal, a mercury-containing vaccine preservative. Because of concerns about mercury in vaccines, FDA has acted to remove thimerosal from the childhood immunization schedule. In fact, the entire vaccine schedule is currently available without thimerosal. From a public health perspective, the remaining issue is whether FDA made the right decision in choosing not to recall the thimerosal-containing vaccines that are still on doctor's shelves.

FDA made the decision not to recall the vaccines because of concerns about a potential vaccine shortage. While there may be a theoretical risk to children from the thimerosal, FDA knew that there is a very real risk to children if there is not enough vaccine available to protect them adequately from

dangerous diseases such as whooping cough or diphtheria. Moreover, FDA was also aware that the Centers for Disease Control's surveillance has not shown any relationship between thimerosal and developing mental delays.

Based on these facts, FDA's decision seems right, but I will welcome any further insight that the Institute of Medicine is able to offer.

I sympathize with the parents who have testified at our hearings and who will testify today. I want them to know that I am committed to doing everything Congress can to address the problem of autism. It is clear to me that we need to research aggressively the causes and treatments of autism. Unfortunately, I believe the answers must come from science.

I thank the witnesses for appearing today and I look forward to their testimony.

Mr. Burton. I thank the gentleman from California.

Mr. Horn, do you have an opening statement?

Mr. Kucinich, do you have an opening statement?

Mr. Kucinich. Thank you very much, Mr. Chairman, for holding this hearing. And thank you very much, Mr. Waxman, for making it possible for me to be a member of this committee.

I have to say, in having the opportunity to sit through these committee hearings, I am taken with the concern for public health that both of my esteemed colleagues have, Mr. Burton and Mr. Waxman. I cannot say that I have formed any conclusion about this because I think it is important to be open to new evidence.

I do think it would be significant and important at this moment to read from the summary from the Immunization Safety Review from the Institute of Medicine, which says, ``The Immunization Safety Review Committee concludes that the evidence favors rejection of a causal relationship at the population level between MMR vaccine and ASD. However, this conclusion does not exclude the possibility that MMR vaccine could contribute to ASD in a small number of children because the epidemiological evidence lacks the precision to assess rare occurrences of a response to MMR vaccine leading to ASD and the proposed biological models linking MMR to ASD, although far from established, are nevertheless not disproved.

Because of the limitations of the evidence, the significant public concern surrounding the issue, the risk of disease outbreaks if immunization rates fall, and the serious of ASD, the committee recommends that continued attention be given to this issue. This committee has provided targeted research and communication recommendations. However, the committee does not recommend a policy review at this time of the licensure of MMR vaccine or of the current schedule and recommendations regarding administration of MMR vaccine.''

It seems to me that this summary, which comes from the document that is under discussion, does have an inconclusive

nature to it in the overall issue, even if it does not recommend removal of licensure of the vaccine. So in exploring the issue of this hearing, why the increased rates, I think the persistence of our chairman on the issue of autism and holding these hearings to update last year's work is well taken.

Often, hearings such as these raise more questions than they give answers, and a determination for finding answers is an example that researchers need to follow. In order to find more answers, I do not believe we should narrow the scope of the research. Rather, it is my hope that through the testimony of parents, Dr. Wakefield, and others we will be able to gain a broad view of the factors that may cause autism.

A recent report released by the Immunization Safety Review Committee at the Institute of Medicine is important in this regard because, again, I want to state the conclusion of the committee that the evidence favors rejection of a causal link between the MMR vaccine and ASD is not the whole story. Media reports have seemed to focus on the first part of the conclusion.

The second part of the conclusion, which is perhaps equally important, is that there is not enough evidence. The committee also concludes that the epidemiological evidence is lacking in both breadth and precision. That, by definition, means that we need to do more research. It means we need to do more specific research.

And while I would agree with Mr. Waxman that given the benefits of the vaccine, we do not want to be in a position where we take the position for challenging health risks to a broad spectrum of America's children, I believe we also need to look at these increased incidents with a sense of mission to find out exactly what is going on. The conclusion that the review made also notes that biologic models that link the MMR vaccine and ASD are fragmentary. The committee identifies the limitations of the available evidence, which can only mean that it is too soon to narrow our scope of possible answers.

Currently, there is $58 million in autism research funds at NIH. Congress needs to focus on more funding for more research. I would submit, instead of focusing just on the brain as the sole search of autism research, we need to have a more holistic approach and review the entire body system. Indeed, there is some evidence--admittedly, limited--that shows that vaccine may cause a physical reaction in the digestive system that may cause autism.

Also, as I understand it, there is no conclusive research on whether or not autism is caused by genetic factors or environmental factors. We may need to look at food allergies, vitamin deficiencies, and pollutants for their potential role in causing autism. By looking at the entire human body and not just the brain as the subject of research, we may find answers to questions that we, as Members of Congress, the Autism

Congressional Caucus, parents, researchers, and others seek.

I look forward to the testimony of the witnesses. I encourage Federal agencies and Congress to acknowledge their testimony and have a broad scope in working to uncover the cause of autism with additional and improved research.

Again, I thank the Chair.

Mr. Burton. Thank you, Mr. Kucinich.

Ms. Ros-Lehtinen.

Ms. Ros-Lehtinen. Thank you so much, Mr. Chairman.

I merely wanted to congratulate you once again for your valiant efforts in helping bring this potential connection to light. Perhaps there is a connection between the onset of autism and the vaccinations, perhaps not. But I know it is an important issue for this committee and it is something that should be taken seriously.

I congratulate you for sticking to your commitment on this, in spite of the overwhelming pressure you must be under from the mainstream scientific community to let it go. I know in my community we have many cases of autistic children, children being tracked by the school system in a different manner. Maybe we are just getting better with diagnosis, but it just seems alarming to me, in my area of south Florida, the high number of children with autism.

I think it is an important issue for our committee. I think you have been a valiant leader in this fight. We do need to improve the scientific evidence. We need to fund the research. We need to educate doctors in a better way because many times those symptoms are going by unnoticed and the pediatricians just shrug their shoulders and say, don't worry, this is just a phase that child is going through. So we need to improve funding and we need to improve the education for the medical community as well.

I want to thank you, Mr. Chairman, for being brave enough to stick to your agenda and to keep our committee seriously looking at the connection between vaccination and autism and just raise the awareness on the issue of autism itself. And I congratulate our colleagues, Mr. Smith and Mr. Doyle, for forming this coalition, of which I am proud to be a member and with which I am proud to be associated.

Thank you, Mr. Chairman.

Mr. Burton. Thank you, Ms. Ros-Lehtinen.

Mr. Clay.

Mr. Clay. Thank you, Mr. Chairman.

I welcome the opportunity to meet with the committee today. I also welcome the opportunity to meet with my fellow Members of Congress who are co-chairs of the Autism Caucus, Representative Christopher Smith and Representative Michael Doyle. I especially welcome the parents of autistic children who are witnesses. It is noted that all of the parents on the panel are doctors. Additionally, I welcome all other witnesses

of panels three and four.

Mr. Chairman, my No. 1 focus while I am in office is children. I am a father, as are you, and I am especially grateful that you extend that parental concern through this committee. Autism is a developmental disorder that appears within the first 3 years of a child's life. The exact causes are unknown. Many scientists who study autism find that it occurs during fetal development, while some speculate that there may be a form or forms of autism that occur in the early years of a child's life.

Some parents and researchers subscribe to the theory that this form of autism may be caused by vaccinations. Presently, no confirmed scientific basis links vaccinations with autism and some of the studies that support some of these theories have been discredited.

These are questions to which we must have answers. I have a 4-month-old son and a 7-year-old daughter. To you parents who are witnesses today, your children could just as well have been my children. This is an area that must be given all the resources and attention necessary to find causes, effects, and solutions.

At this point, Mr. Chairman, I would yield back the balance of my time and ask unanimous consent to enter my statement into the record.

Mr. Burton. Without objection, your prepared statement will appear in the record.

[The prepared statement of Hon. Wm. Lacy Clay follows:]

[GRAPHIC] [TIFF OMITTED] T6856.013

[GRAPHIC] [TIFF OMITTED] T6856.014

Mr. Burton. Dr. Weldon.

Mr. Weldon. I just wanted to mention my good friend from Ohio, Mr. Kucinich, said earlier that NIH funding for autism research is at $58 million. I believe that actual figure is substantially below that, more in the range of $15 million. I think there is going to be another hearing to get at that issue, but I just wanted the record to reflect that.

Indeed, that is a big part of our problem. We are not funding enough research in this arena. I thank you for calling this hearing, Mr. Chairman.

Mr. Burton. Thank you, Dr. Weldon.

Mr. Cummings.

Mr. Cummings. Thank you very much, Mr. Chairman. Thank you for holding this hearing today.

During the 106th Congress, the Government Reform Committee held numerous hearings on vaccine safety and the theories on the correlations between vaccinations and autism. Earlier this week, the Institute of Medicine Committee on Immunization Safety Review released a study that reported ``there is little

evidence of a causal link between vaccinations and autism.''

I agree with Dr. Steven Goodman of the Johns Hopkins University of Medicine--which so happens to be located in my district--who was a member of the IOM panel, when he said that ``the risk of not immunizing is much greater than any risk from immunizing.''

Vaccinations provide important health protections so that our children will not be at risk for a variety of illnesses and diseases. Without vaccinations, the diseases we are now protected from will return.

I applaud the CDC, the National Institute of Child Health and Human Development, the National Institutes of Health, the Food and Drug Administration, as well as the Kennedy Krieger Institute and the Center for Development and Behavior Learning at the University of Maryland School of Medicine in Baltimore for their continued research in this area.

The causes of autism are unknown. There are some effective treatments for some children, but there is no cure. My heart goes out to parents, grandparents--like you, Mr. Chairman--and families of autistic children. I am convinced that with further research a cause and cure will be found.

I am also concerned that there have been approximately 2,800 cases of autism reported in my home State of Maryland. I am also concerned about the rise in the number of autism cases in California, New Jersey, and other States.

As such, I strongly believe that all theories for the cause of autism must be objectively and thoroughly researched. I echo the sentiments of the ranking member of this committee when he expressed last year in the Los Angeles Times that autism must not alarm the American people and steer them away from vaccinating their children.

I welcome the witnesses here today. I look forward to the testimony.

Thank you very much.

Mr. Burton. Thank you, Mr. Cummings.

Ms. Davis, do you have a comment?

Ms. Schakowsky.

Mr. Burton. If not, Congressmen Smith and Doyle, would you come forward, please?

We will start with you, Mr. Smith. We normally swear in our witnesses, but I do not think we need to do it with you, too.

Mr. Smith.

STATEMENTS OF HON. CHRISTOPHER H. SMITH, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY; AND HON. MICHAEL F. DOYLE, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA

Mr. Smith. Thank you very much, Mr. Chairman.

I thank you and the members of the committee for allowing

my good friend and colleague, Mike Doyle, and I to be here on behalf of our Coalition for Autism Research and Education [CARE]. It is currently made up of 115 Members of Congress. It is bipartisan. It was formed recently and we have our first major briefing on Friday. The reason for the Coalition is to try to sensitize Members to the need for more research dollars, more focus on this very, very debilitating and heartbreaking tragedy that has been experienced by increasing numbers of Americans.

I think most of you know that autism is a developmental disorder that has robbed at least 400,000 children of their ability to communicate and interact with their families and loved ones. The disorder, at least the common, prevalent number used, is found in 1 of every 500 people in America, although that number may have to be ratcheted upwards, given some of the more recent evidence that is coming forward.

My interest in autism has been a 21-year interest. I first got involved when the Eden Institute and Dr. Holmes in Princeton, NJ brought me to one of their group homes and showed me the kind of work they were doing. I worked with him and others throughout the years to try to do what we could.

But, frankly, I have been amazed at what has not been done at the Government level through the 1980's and into the 1990's on this affliction, this disorder.

What brought me into it even more so in recent years--in one of my largest towns, Brick Township, I became aware through Bobby and Billy Gallagher, a very devoted husband and wife who have two children with autism. They did their own study, if you will, in Brick Township and found that there was an exorbitant number of cases of children with autism. They became alarmed and brought this information to me. They had the documentation and we spent the better part of 3 hours reviwing it. In subsequent meetings, it went on and on as we renewed it further.

We finally brought the CDC and other Government agencies into Brick. Frankly, I was amazed, shocked, dismayed, and saddened by how little the CDC and some of our great Government organizations knew about autism. It was as if the studies were passive, the information collected was little to nonexistent--and that includes in my own State. This began an effort to try to do more, to try to at least get a handle on the prevalence of autism.

What is happening? Is 1 in 500 real? Is it imaginary? Is it fiction? And as you pointed out, Mr. Chairman, what is the causation? Looking at your witnesses and knowing of your own deep, personal commitment, I want to congratulate you at your dogged determination to get at the reason. Why do we have this terrible disorder seemingly cropping up in larger numbers in our communities, as we saw in my own Brick Township, NJ? What was found--and this was very disconcerting--after a

professional study by CDC, was that rather than 1 in 500, the number was 4 per 1,000 in Brick. What are the reasons? Nobody really has any answers. The questions and the answers we have gotten in terms of numbers only bring about more questions about why the prevalence? Why does there seem to be a cluster or why do we have a higher number throughout the country?

Our own Department of Education in New Jersey has seen more cases. Maybe this is just better reporting or maybe we have a problem that is an epidemic that has gone largely unnoticed. In 1991 there were 241 cases. That has grown to an incredible 2,354 cases in 1999, an 876 percent increase. In just 4 years, the number of autistic children aged 6 through 21 has more than doubled. So we have a problem that really begs a significant increase in funding, commitment, and prioritization within our Government.

Last year many of us argued successfully that the amount of money going to the CDC and NIH be increased. We are doing it again this year, making a similar request to the appropriators that more money for prevalence and other studies be forthcoming.

Finally, Mr. Chairman, last year we did get a breakthrough with the Centers of Excellence in Autism Epidemiology that was contained in Public Law 106-310. I had introduced legislation that had that in it. We worked with a number of organizations and individuals. Mike Bilirakis, our good friend who chairs the committee, put it as title one of his child health initiative bill. Now that is awaiting full implementation so we can get a better handle on autism with these new centers of excellence looking at prevalence and other issues associated with it.

Again, I want to thank you for your leadership. Let me offer one note of caution. I know the IOM study suggests that there is not a link. And I know that one of their witnesses will be here today to amplify that. But I chair the Veterans Affairs Committee. I remember when the very first amendment I offered dealt with the Agent Orange issue. Tom Daschle, now the minority leader over on the Senate side, and I offered an amendment to try to provide service-connection disability and enhanced medical care for our veterans who had been exposed to dioxin, the contaminant contained in Agent Orange.

For years, what we thought was credible evidence was laid aside and they said there was no link, there is no link, there is no link. Finally, in the latter part of the 1980's, the evidence became so compelling that at least three anomalies associated with that contamination were finally deemed service-connected and were deemed worthy of compensation.

My hope is that this report not end the issue, but only lead to more studies to find out what that causation really is, because we really do not know. Again, it is encouraging. I am a great fan and believer in immunizations. For the record, back in the early 1980's, as a member of the International Relations

Committee--and you remember this well, Mr. Chairman--I offered the amendment to create the Child Survival Fund and put $50 million in it. Now it has grown to over $200 million to immunize the world's children against pertussis, measles, tetanus, and other debilitating diseases.

So I am a great believer that immunizations save lives. But if there is a problem, we need to be candid enough, aggressive enough, and honest enough, for the sake of our kids, to go at this and find out what is the causation. God willing, there is no connection. But we need to pursue that aggressively.

Thank you.

[The prepared statement of Hon. Christopher H. Smith follows:]

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[GRAPHIC] [TIFF OMITTED] T6856.017

[GRAPHIC] [TIFF OMITTED] T6856.018

Mr. Burton. Thank you, Mr. Smith.

Mr. Doyle.

Mr. Doyle. Thank you.

Chairman Burton and members of the committee, I thank you very much for inviting me to speak with you regarding autism and the goals and expectations for the Coalition for Autism Research and Education [CARE].

I want to personally thank you for your interest in expanding our knowledge of autism and autism spectrum disorders and increasing research funding as well as for your members in CARE. Your leadership has brought desperately needed attention to a major children's public health issue that has been neglected for the past 50 years.

As you know, autism is a life-long disorder that significantly impacts the lives of those affected with the disorder as well as the lives of parents and relatives. I need not tell you, Mr. Chairman, of the profound effects autism has on parents and loved ones who provide care for every 1 of these 1.7 million individuals. Autism changes lives forever.

Based on the latest evidence, we can safely say that autism and autism spectrum disorders are now at an epidemic level here in the United States with over 1.7 million individuals affected. That is 1 out of every 150 to 170 children born.

During my tenure as Congressman, I have had numerous meetings with concerned parents, researchers, and advocates who are struggling to get autism research and treatment issues to the forefront of lawmakers' minds. The vast majority are frustrated by the lack of research and essential treatment and services for their children. It is because of them, Mr. Chairman, that I became committed to forming a congressional organization for autism advocacy, along with my good friend,

Chris Smith, who I knew already had a strong interest in autism from his work on the ASSURE Act last session, and the Coalition for Autism Research and Education was born.

With CARE, our major goals are to ensure substantial increase in research funding while ensuring that families receive the highest quality treatment possible in accordance with today's knowledge. If we accomplish these goals, the number of children born with autism can be substantially reduced and the revolution biologic treatments of the future can be achieved for those who already have autism.

I join you in your grave concern of an autism-vaccine link and feel strongly that we must examine what vaccines may be doing to our children and thoroughly investigate the late onset autism-measles vaccine connection. Identifying a vaccine-autism link will help countless individuals who develop autism after a vaccination, but we need to fully explore all possible avenues to help those who develop the disorder by some other means.

In my view, we must learn to identify the genetic and biologic basis of susceptibility to vaccine complications so that children at risk can be identified and their vaccinations delayed, while children not at risk can continue to receive vaccinations and the protection from brain injury and death that they provide. In addition, identifying the causes of autism will not cure the 1.7 million individuals who already have ASD. Research must also strive toward the revolutionary biologic treatments of the future so that there is hope for these children and adults. The decoding of the human genome opens the door for the development of cures for autism in the lifetime of children born with autism today.

The bottom line is that we need a lot more funding for autism research. The opinions and testimony this committee will hear are proof of that. I am concerned that if we focus the lion's share of funding on one suspected cause of autism that we could unintentionally pass up vital advances in other areas. I want to provide a lion's share of the funding for research into both the treatments and causes of the disorder equally for the sake of all 1.7 million individuals and families that are now living with the disorder, many of whom were born prior to the introduction of vaccines.

Autism lasts a lifetime and often children with disorders outlive their parents. We need to care for and educate autistic children and adults, provide properly trained staff and educators to meet the highly complex and specialized needs of these individuals. All of this can become very costly over the lifetime of an individual with autism. Steps must be taken to reduce the disability associated with autism so that more and more individuals can work and live semi-independently.

In my home State of Pennsylvania, the Autism Society of America estimates that we have 73,686 individuals with autism. Autism costs Pennsylvania an average of $50,000 per person per

year. It makes good sense to invest in research now so that we can get quality services to families and realize the ultimate payoffs of prevention of this disorder in the future and cures for those children and adults who already have autism.

Continued funding of NICHD's 4-year-old Genetics and Neurobiology Network must be maintained if we are to achieve this goal. Combined with the creation and funding of at least five new centers of excellence and three epidemiologic centers, autism research in America can reach new heights and achieve new breakthroughs for autism. Congress must continue to fund existing autism research programs without taking away the much needed funding for them to pay for new ones. I believe that any expansion of research programs must come with a corresponding expansion of funding dollars.

In closing, Mr. Chairman, in western Pennsylvania, we are fortunate to have one of NICHD's collaborative programs of excellence at the University of Pittsburgh. This 4-year-old program is not only making a substantive contribution to the understanding of neurobiology and genetics of autism, it is providing guidance to State legislators in developing surveillance and treatment centers in our State.

I would like to extend a personal invitation to you, Mr. Chairman, and to each member of this committee to come and tour this facility, as I have, meet the researchers and staff, and speak to individuals with autism and parents about their struggles and needs.

Mr. Chairman, I thank you for holding this hearing today and for the opportunity to testify this morning.

[The prepared statement of Hon. Michael F. Doyle follows:]

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[GRAPHIC] [TIFF OMITTED] T6856.020

[GRAPHIC] [TIFF OMITTED] T6856.021

[GRAPHIC] [TIFF OMITTED] T6856.022

Mr. Burton. Thank you, Mr. Doyle.

Let me start with you Representative Smith.

In Brick Township, as I recall--and you may have to refresh my memory--there were some toxic chemicals or something there. What were those chemicals?

Mr. Smith. We had problems with a number of toxic chemicals. As a matter of fact, we invited the ATSR, the agency that looks for environmental pathways, to come in and they did their own study and ruled out--based on the proximity of where the children with autism lived and whether or not they were close to the river----

Mr. Burton. What were the chemicals? Do you recall?

Mr. Smith. PCBs--there were a number of chemicals. It was a

witch's brew in essence of chemicals. They did look for a number, and I could provide that for the record.

Mr. Burton. I would like to have that. Did they find any mercury in there?

Mr. Smith. I do not believe they did.

Mr. Burton. But they found PCBs?

Mr. Smith. Yes, and others. We are a very industrial State in the State of New Jersey. Many of those chemicals were dumped into the river and got into the water system.

But despite concerns about that, when an overlay of where the children were living was done, there seemed to be no causation that could be attributed to an environmental pathway. So they ruled that out.

Mr. Burton. How many were there?

Mr. Smith. There were 4 per 1,000.

Mr. Burton. So 1 in 250.

Mr. Smith. And 6.7 for the full spectrum.

Mr. Burton. Representative Doyle, you indicated that there were 170,000 children in Pennsylvania who are autistic?

Mr. Doyle. Mr. Chairman, 73,686.

Mr. Burton. And you said that it cost $50,000 a year to take care of those people that are autistic.

I guess the one thing I would like to point out to anyone from CDC or health agencies, or anyone connected with our Government--let's just say we reduce that $50,000 to half and we only had to spend $25,000 per person for the rest of their life to deal with their autistic problems. If 1 in 250 or 1 in 500 people are autistic, you are talking about so much money that we cannot afford it. We are going to have people walking around that are going to be lost and will be causing all kinds of problems for our entire society. It could cause tragic consequences for the entire country.

So there has to be more research done to find the causes and if possible to find ways to minimize the damage done to these people so they can be productive members of society.

I am very happy for both of you being here and for you sponsoring and supporting and starting the Autism Caucus. I am very happy to be a partner with you on that. Anything I can do to help you get more money for this research, just holler. We will be glad to do it.

With that, Mr. Horn.

Mr. Clay.

Doctor.

Ms. Schakowsky.

Any questions for any of our panelists?

If not, thank you both for being here. I look forward to working with both of you. I appreciate it.

Our next panel is Dr. James Bradstreet, who will be introduced by Congressman Weldon; Dr. Cindy Kay Schneider, of Southwest Autism Research Center in Arizona; Dr. Jeff Segal of

Greensboro, NC, formerly of Terre Haute, IN; and Dr. Sharon G. Humiston, of Plattsburgh, NY.

Would you all stand, please?

[Witnesses sworn.]

Mr. Burton. We want to try to confine the remarks. I know you have prepared statements that are much longer than 5 minutes. But if you would, I would like you to stick as close to the 5-minute limit as possible because we have 14 witnesses today and we want to have time for questions.

Let me start with Dr. Bradstreet.

Dr. Weldon, do you want to introduce him?

Mr. Weldon. Yes, thank you, Mr. Chairman.

It is a real pleasure and honor for me to be able to welcome and introduce my good friend and colleague--that is, medical colleague--from the Melbourne-Palm Bay area, Dr. Jeff Bradstreet.

Dr. Bradstreet is well known to the community I live in, both as a practicing family physician and also for a radio program that was carried nationwide, the Good News Doctor. He is a fellow of the American Academy of Family Physicians. With the development of autism in his son, he has emerged as one of the leading practitioners in treatments of autism and currently receives referrals from throughout the country from parents who have been devastated by this disease.

It is a real pleasure for me to be able to welcome you, and I am looking forward to your testimony as well as that of all the other witnesses we have today.

Mr. Burton. Thank you, Dr. Weldon.

Dr. Bradstreet.

STATEMENTS OF JAMES J. BRADSTREET, M.D. FAAFP; CINDY KAY SCHNEIDER, M.D. FACOG; JEFF SEGAL, M.D.; AND SHARON G. HUMISTON, M.D.

Dr. Bradstreet. As a minor introduction to myself, I had absolutely no interest in autism until it affected my son, at which time--in a very short amount of time because of a complete lack of local resources--I wound up having to dedicate myself full-time to this activity which, in the end, was apparently a blessing.

[Slide presentation.]

Dr. Bradstreet. This is just to remind us that we cannot over-focus our attention on just the vaccine issue. There is a host of environmental toxicological issues that may be interacting with the vaccine constituents to cause problems, and this U.S. News article points to that.

I want to point your attention to this, which is from the November 17, 2000 Oregonian. There are now over 3,000 children in Oregon--I am in Florida, but I was lecturing in Oregon and meeting with researchers at the medical school. That makes a

prevalence of 1 in 190 students. The national average, actually, based on recent statistics I have been able to acquire from the Internet--the reference of which are all in my written statement--may be as low as 1 in 140. That is an extraordinary prevalence.

I also want to point your attention to the red line, which shows the point in time that we introduce the infant HiB vaccine and shortly after that, the Hepatitis B vaccine to newborns on the first day of life--what happens to the prevalence of that disorder in Oregon during that period of time.

This is from the U.S. Census on Americans with disabilities. The blue arrow is slightly above, but that number is 1.8 percent of children under 3 being labeled as developmentally delayed--which is a synonym for autism, in many cases or certainly autism spectrum disorders.

If you go to the 3 to 5-year-olds, that is 2.7 percent of children that are labelled developmentally delayed by our U.S. Government. I would tell you that is a multi-trillion-dollar problem coming that you are going to have to deal with, and that is a huge prevalence. That is an epidemic by anybody's standards.

This is the British Medical Journal article that is so famous or infamous in terms of supposedly refuting the incidence of autism-MMR relationship. Again, I do not want to over-focus on any one particular vaccine, but look at when the infant HiB was introduced into England with that red arrow and what happened to the incidence at that point in time. Is there an interaction between MMR components and HiB? Is there science behind that? I would tell you that there probably is. This is from the Mayo Clinic. Briefly, this is a 2000 article that came out in the American Journal of Gastroenterology that said that measles virus infection is associated with inflammatory bowel disease. The IOM report states that no cases of vaccine encephalitis have ever been reported, but what about this case that came out in 1999 that says that measles-inclusion encephalitis caused by the vaccine strain of measles was proven using PCR data.

In addition to that, the IOM report also states that MMR may be associated with inflammatory bowel disease, but concludes that it is still safe. This is from the recent Journal of Pediatrics about a month or so ago that shows that there is in fact marked autoimmunity in these children's intestinal tract. This is most likely an autoimmune disorder in general.

This is the parent's view of what it looks like.

That is what for 4 years of my son's life I got to change about three or four times a day and my wife got to change another three or four times a day as he had chronic diarrhea. The parents have a rather dim view of what chronic inflammatory

bowel disease and autism look like.

I want to let you know that it can be fixed. This is part of my Christmas card from one parent thanking me for the fact that in fact it is nice to have a child with a well-formed bowel movement. And that child is doing extraordinarily better now that the enterocolitis is taken care of.

Autoimmunity is a process where the immune system gets confused and turned around and thinks that maybe the child is at fault for this.

Myelin, which is the insulator of the brain nervous system, is clearly a problem and there are many things that we are finding in the kids that are abnormal that are affecting melanization. The vaccine constituents may be part of that.

Just briefly, there is a host of credible science that autoimmunity and vaccines are related. We are seeing in our clinic of over 1,000 children in Florida, who come to us from all over the world--in fact, I will be leaving shortly to spend 2 weeks in Indonesia where, after instituting a World Health Organization vaccine program, they went from essentially no autism to an epidemic in Indonesia, as well. I have been hired to go over there for about 2 weeks to work with the government and teach doctors how to take care of this disorder.

I am a clinician and I have to take care of kids. This is a little difficult for you to read, but it is in my report. Let me just state that this is from the Utah State University. This is cerebral spinal fluid of a child who regressed after an MMR vaccine that shows autoantibodies to myelin basic proteins being positive as well as measles virus in the spinal fluid. All other variables were negative.

I would conclude from that--as did the physician and the researchers who have looked at this--that in fact that is an MMR reaction in this child since there was no measles in this child's history.

This just shows that it is not just Dr. Singh at the Utah State University, but myelin basic protein antibodies are prevalent and we can find them at many different laboratories.

We also know that Hepatitis B is an issue, and this shows that as early as 1985 we knew that Hepatitis B constituents had protein peptides that could in fact induce autoimmune encephalitis in rabbits through molecular mimicry. These are the same proteins we are injecting into our children.

We know that the French have identified a problem with demelanization following Hepatitis B vaccine. We see problems with melanization in autism every day in our facility.

This is a quickie just to show you that while there are a lot of different peptides out there, hemophilus peptides do induce autoimmunity to myelin basic protein from the Journal of Immunology in 1999.

Exposure to mercury and other constituents will induce the same autoimmunity to brain elements, and that is a review

article that has over 174 references. Is mercury a problem? It is certainly in the vaccines.

This shows just a brief overview of the amount of mercury that is available to children through the vaccines. It is a tragedy. There is a lot of mercury in our environment. It should not have been in the vaccines.

This is my son's first mercury test. That little dot on the fourth column on the left that says toxic elements is in fact a very high level of mercury. That is 15.7 parts per billion, which is extremely high. This is his first post-provocational urine using a standard procedure that has been developed; 24 micrograms per gram in his urine.

This is a New Jersey family--for Mr. Smith. This is a heavy metal study from a child.

This is a 6-year-old with autism.

That is his first post-provocational urine. It shows extraordinarily high levels of lead and mercury. One would conclude that perhaps this is an environmental exposure, so I tested the entire family, trying to be a good doctor.

Look at Mom. Mom is a nurse, Mom has had some vaccines, Mom has a lot of amalgams, but look at that. Mom's mercury is not too bad. Maybe it is not too bad.

Maybe Dad is a battery factory worker--actually, Dad is an engineer, but let us go to Dad. Dad shows very little. He does have some amalgams as well.

How about a 4-year-old sibling that has never been vaccinated that has grown up in the same household. There is essentially no mercury in that child. That causes me, as a physician and as a clinician great concern. In this situation, it looks like heavy metals are a problem. The only place I have to look--the only difference between one child and the other--is vaccination.

Is mercury toxicity a problem in autism? That bottom line on that graph is a mercury level that is so high it could cause neurological developmental disorders. The zinc level is almost at critical levels of deficiency. Those two combinations cause problems.

In summary, TH-1 and TH-2 imbalance where marked TH-2 insult has occurred through the vaccination program is well documented from researchers at the University of California at Irvine. TH-2 causes autoimmunity as vaccine-related. We see it in our kids every day.

That is basically the issue we think that thimerosal plus environmental mercury causes the initial TH-2 skewing and autoimmunity. Aluminum adjuvants, which are in the vaccines, adds to that infant. Infant HiB, again, is a strong TH-2 impulse agent. Newborn Hepatitis B is another TH-2 agent. All these so far have been associated with autoimmune reactions, with the exception of aluminum.

Pertussis is a TH-2 potent stimulator. This is an immune

system within the child that is primed to react so that when MMR does come along, we are going to see autoimmune reactions to brain and to bowel. We see it every day. This is an epidemic of neurodevelopmental catastrophe.

This is my son at the Smithsonian. That is what I think autism must feel like to children and to families. That is a T-Rex--big teeth, big problem. But we do know that with love, prayer, and sound medical behavioral action, this does not have to be a catastrophe and there is hope.

The last picture is how Matthew is today. He is a happy well-adjusted child, who is much better.

Thank you.

Mr. Burton. Dr. Bradstreet, thank you for that very informative testimony. I will have a number of questions for you.

Our next speaker will be Dr. Cindy Kay Schneider of the Southwest Autism Research Center.

Dr. Schneider. Good morning, Mr. Chairman and members of the committee. My name is Dr. Cindy Schneider.

I would like to express my gratitude and that of the hundreds of families I represent to Representative Burton for his scrutiny of the medical issues related to autism and his leadership in bringing these concerns to your attention.

In 1995, my son Derek and daughter Devon were diagnosed with autism. After visits to several specialists and series of medical tests, we were left with a diagnosis and nothing more. No treatment, no plan of action, and no hope.

The following year, Dr. Ron Melmed, Denise Resnik, and I founded the Southwest Autism Research Center, a nonprofit organization dedicated to serving the needs of individuals with autism. We developed a questionnaire for the purpose of obtaining medical, developmental, behavioral, and family histories. We began to send laboratory specimens to researchers around the world.

This became the infrastructure of a data base which now contains information on approximately 500 children with autistic spectrum disorders, their siblings, and 200 unrelated controls. Many of these children have undergone extensive psychological testing through our center and hundreds have participated in clinical research trials. In this very limited time, I would like to share with you the highlights of our findings.

We looked first at patterns of development; 60 percent of children in our data base spoke their first word prior to 18 months of age, indicating that early language development was usually intact. The majority of children acquired motor skills at the expected age as well.

Because my children experienced a distinct loss of language and deterioration in health after their first year of life, I looked for this pattern in other children. When asked if their

child had a normal or near-normal period of development followed by regression, nearly 80 percent of parents told us yes.

The most frequent age of regression was between 13 and 18 months. Consider the possible explanations for this deterioration. These might include a metabolic defect which over time results in neurological damage in a previously healthy child. Exposure to toxins in the environment could do the same. Infections, either naturally occurring or acquired through vaccination, must also be considered.

For the past 3 years, we have collaborated with researchers in Rome on a genetic screening project. Antonio Persico and Flavio Keller have conducted detailed evaluations of 184 families in Italy and the United States, including 44 of our children at SARC. Investigation of four candidate autism genes revealed that three have little effect on a child's risk of developing autism. The fourth gene is related to reelin, a protein critical in early brain development.

In the Italian population, carrying a variant of this gene more than doubled an individual's probability of having autism. In the American subjects, the risk of autism associated with the inheritance of this allele is 19 times the usual risk; 20 percent of individuals with autistic spectrum disorders carry this gene. The inheritance of the long allele of this gene results in a lower production of reelin. Interestingly, viral infection further reduces reelin production and may explain frequent reports of children's deterioration into autism following illness or vaccination.

Other research at SARC has focused on the health problems associated with autism. Of the 500 families interviewed, 48 percent reported that their children have a history of chronic diarrhea, chronic constipation, or alternating gastrointestinal symptoms. The increased incidence of bowel disease in individuals with autism has been confirmed by multiple investigators over the past 4 decades, yet has been largely dismissed by the physicians caring for these children.

Our interest in the gut-brain connection intensified in 1997 when we learned of several children with autism who experienced remarkable improvement following the administration of a gastrointestinal hormone called secretin.

In 1998, we initiated the first clinical trial of the safety and efficacy of synthetic human secretin in the treatment of autism; 30 children were enrolled in this phase one study. Improvements were noted in language, social awareness and interaction, sleep pattern, and gastrointestinal but were not captured on standardized psychological and language tests. We saw that some children benefited from this treatment, yet the study of this heterogeneous group failed to demonstrate this benefit.

Over the past year, we have collaborated with Repligen

Corp. and four other sites across the country in the first phase two clinical trial ever performed in the treatment of autism. There were 126 children who completed this double-blind, placebo-controlled study. Each child received three doses of either synthetic human secretin or placebo at 3-week intervals.

Unlike previous secretin studies, enrollment was restricted to children between the ages of 3 and 6 who met strict inclusion criteria. These criteria included a diagnosis of childhood autism, a moderate to severe level of impairment, little or no language, and significant gastrointestinal symptoms. In addition to formal psychological testing, we asked parents to report their children's status at the completion of the study using a clinical global impression scale.

Treatment with three doses of secretin produced a significant decrease in the symptoms of autism in 42 percent of children, while 27 percent in the placebo group improved. Further data analysis is underway and will take several months to complete, but early findings indicate a biochemical market which may predict secretin response.

Additional research planned at the Southwest Autism Research Center includes expansion of our current data base through recruitment of additional families and extensive medical and behavioral assessments of these children. Genetic testing for candidate autism genes and screening for several metabolic defects will be performed.

An associated research priority will be the establishment of a sibling screening clinic in which younger siblings of children diagnosed with autism will undergo the same testing. The recurrence rate of autism is approximately 5 percent, meaning that parents of a child with autism have a 5 percent change of having another affected child. Siblings age zero to 3, the age of onset for autism, will be evaluated every 3 to 6 months. In this way, identification of risk factors will facilitate diagnosis and treatment at the earliest possible age. This program will also allow prospective data collection related to the natural history of autism, its associated biochemical distinction, and the role of suspected environmental variables.

The establishment of these programs on a national level could allow the genetic environmental variables responsible for the development of autism to be identified in the foreseeable future.

I thank you for your attention to this subject and look forward to participating in the materialization of this vision.

[The prepared statement of Dr. Schneider follows:]

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Mr. Burton. Thank you, Dr. Schneider, Dr. Bradstreet, and the others.

Do we have copies of your studies? I would like to have as much documentation from all of you as we can get because we are going to have the people from HHS and FDA here. I want to submit your studies to them--along with Dr. Wakefield's and others--and ask them to give us an evaluation of those studies based on their report and their research. In other words, I want to get a comparison.

They are saying one thing and you guys are telling us something else.

Dr. Segal, welcome. It is nice to have a Hoosier here--although we love you guys, too.

Dr. Segal. I was born in South Bend, by the way.

Mr. Burton. Once a Hoosier, always a Hoosier. [Laughter.]

Dr. Segal. Mr. Chairman and members of the committee, thank

you for the opportunity to speak.

In October 1999, I became a member of a club I never wanted to join. My son was given a diagnosis of regressive autism.

I am the father of 4-year-old twins, a boy, Joshua, and a girl, Jordan. I practiced as a neurosurgeon. My son developed normally and hit all of his milestones. He was jolly, sweet-natured, and very bright. Before his second birthday, he started losing the language he had acquired. He became hyperactive and inattentive to the point that I though he was deaf.

By the time a physician confirmed the diagnosis, my wife, Shelley, and I already knew. We were devastated.

I investigated treatment options. The first treatment consisted of occupational therapy to address his sensory issues. The other early intervention that we chose was called ABA, or applied behavioral analysis. ABA breaks down everyday actions into discrete steps. The training is delivered as one-on-one therapy and involves 40 hours of work a week. It is expensive, exhaustive, and extremely time-consuming. Most families we spoke with were on waiting lists for ABA treatment. As time was our enemy, we moved to North Carolina. I quit my practice and devoted my time to investigating biomedical options.

At this point, I am pursuing three main projects. First, help my son. If I can help him, I can help others. Next, I am researching toxicologic causes and treatments as it relates to autism. I am doing this in concert with the Department of Physiology at Wake Forest School of Medicine. Finally, I am exploring pharmaceutical options. I dug deep into my right pocket and started a drug company based on medications that are likely to be relevant to helping those with autism. At the same time, it turns out it is probably relevant to treating Parkinson's, schizophrenia, and other illnesses.

I have a few observations I would like to make.

The number of children with autism or related disorders is rising. Do not take my word for it and do not ask physicians. We need to ask teachers. These kids are filling regular and special education classrooms to over-capacity.

We have heard the argument that the number of kids with autism is static and that doctors are just better diagnosticians. I have two points. Where are the autistic adults who were never diagnosed 20 years ago? Surely they have to be somewhere. Also, physicians spend less time than ever truly talking with patients and families. More diagnoses are made by tests and machines. No laboratory test exists for autism. The diagnosis is based strictly on clinical examination. Finally, the average time between onset of autistic symptoms and diagnosis is still years. We are not better diagnosticians.

The California Department of Developmental Services is

adding one new child with full-blown autism every 3 hours. Estimates vary, but we are looking at approximately $2 million to raise an autistic child to age 21.

The number of physicians who have a deep understanding of autism treatment is small. These doctors are overworked and it takes months to get an appointment. Many of these doctors have affected children of their own. Since autism is a systemic condition that involves that GI tract, immunologic system, and central nervous system, it requires expertise by multiple specialists. Finding all the specialists who have an interest in treating autism can be a daunting task.

The statistics quoted by academicians are at odds with reports by parents. For example, the standard autism literature does not even recognize a general connection with the GI tract and autism. However, families report that up to 80 percent of their children have GI problems. Standard literature suggests that only 20 percent of autistic children regress, that is, they develop normally until age 2 and then become autistic. The majority of parents that we see report that their children fall into the regressive or acquired category.

Andrew Wakefield has theorized about a connection between GI problems and autism. His work suggests that the measles virus from vaccines might persist in GI tissue. This association might also have a causal role in autism. This work urgently needs replication, yet many gastroenterologists conveniently dismiss his work rather than test his theory. Incidentally, it would not be difficult to validate or refute his hypothesis.

Eighty percent of autistic children have abnormal EEG activity in brain areas associated with speech. It is believed that these abnormalities might contribute to language deficits. Correct diagnosis requires at a minimum an overnight EEG. Most kids are given a 1-hour EEG, informed that it is normal, and never properly treated. Not infrequently, the EEG is normal, and a more sensitive test called the MEG is abnormal. MEG is located in only a handful of cities and is quite expensive. Insurance companies do not readily pay for this test. Once correctly diagnosed, children may be given anti-seizure medication, which can help.

Speaking of insurance companies, they do not readily pay for much of anything that is autism-related. Laboratory tests are paid out-of-pocket by parents and most research is being borne at the parent's expense.

ABA treatment is extremely expensive. It works for about half of the children. Costs are approximately $30,000 to $70,000 a year. The parents will frequently turn to school districts to make these treatments available. Where one lives determines the type of treatment one receives. It is not uncommon for the school district to litigate against parents so they will not have to provide that service. The alternative is

placing children in large classrooms. This effectively warehouses the child and minimizes potential for future gain. Waiting lists for services are all too common.

I could spend a lot of time talking about the need for toxins research, but I would like to touch on this for just a second.

The Centers for Disease Control recently reported that 1 in 10 women of childbearing age in the United States are at risk of having newborns with neurological problems due to mercury exposure. Until recently, vaccines had thimerosal as a preservative. Thimerosal is a preservative that contains organic mercury.

Organic mercury is widely recognized as a neurotoxin. In one study, lower or scores neurologic function tests were found years later in children who had been exposed prenatally to intermittent doses of methyl mercury. These doses happened to be from dietary exposure at levels that had been previously thought to be safe.

The vaccine manufacturers, to their credit, have stopped making new vaccines with mercury as a preservative. But many of these vials still sit on doctors' shelves. Also, RhoGAM is given to RH negative mothers and this medication still has thimerosal.

As an anecdote, I spoke with two fertility doctors. They were not aware of the mercury issue. They were livid that this type of medication had a preservative that had ``cleared'' safety tests and was being given to a pregnant woman.

With more vaccines being recommended to an already-full vaccine schedule, and many vaccines administered earlier in life, the potential for mercury toxicity in children is quite real. The symptoms of mercury poisoning and autism are quite similar.

I recently analyzed 250 hair samples and found that 30 percent of these children had tested two standard deviations above the mean for various metals: aluminum, arsenic, and antimony. These agents are ubiquitous in the environment. It is my belief that autistic children may not be able to clear these toxins from their bodies.

Chelation treatment is one way to remove metal toxins from the body. It uses compounds that have a propensity to grab metal toxins. There are many unanswered questions regarding chelation. I say that historically the reputation for chelation is quite poor. And I say this as a physician who had never previously entertained the idea of chelation for any chronic condition. It is extraordinarily difficult for a practitioner to get funding to study chelation. It is just as difficult to get doctors to consider it as a viable treatment.

My scientific work is focused on analyzing genes and proteins that detoxify heavy metals in autistic children. My hypothesis is that some children are genetically predisposed to

the inability to detoxify the metals to which they are exposed to in the environment. These metals may come from vaccines, food, or the environment. The major detox pathway for heavy metals is metallothionein or MT. I am researching whether or not these children have defective MT genes or if they are unable to make appropriate amounts of this protein in response to the insult. This could explain why not all children exposed to the same environmental insult develop autism.

I will close, knowing I am well over the time.

We need immediate and abundant funding for research, particularly treatment. We need to fund fellowships to increase the number of skilled doctors who are treating autism. We need to mainstream autism as it relates to insurance payments. It is a biological condition and should not be constrained by policy limits on mental health coverage.

We need to standardize payments for ABA treatment across the country. It is unfair that some families are on waiting lists for 2 years to access coverage.

We need to get the vials of thimerosal-containing vaccines off the shelves through recall.

Mr. Burton. Amen.

Dr. Segal. We have adequate stocks of vaccine. It is not a problem at this point. We need to clear the shelves. And doctors do not know what is sitting on their shelves. We also need to remove thimerosal from RhoGAM.

We need to seriously test the hypothesis that vaccines are not always as safe as is currently believed. In addition, combinations of vaccines have potential risks that have never been explored. I clearly understand the public health import of diseases we are preventing, but we need prospective studies.

Finally, licensing boards need to be less heavy-handed to doctors offering off-label treatment to families that are desperate for treatment. Off-label use of medications is common in all fields of medicine. The standard by which these physicians should be judged is risk versus benefit.

Thank you for your time.

[The prepared statement of Dr. Segal follows:]

[GRAPHIC] [TIFF OMITTED] T6856.042

[GRAPHIC] [TIFF OMITTED] T6856.043

[GRAPHIC] [TIFF OMITTED] T6856.044

[GRAPHIC] [TIFF OMITTED] T6856.045

[GRAPHIC] [TIFF OMITTED] T6856.046

[GRAPHIC] [TIFF OMITTED] T6856.047

Mr. Burton. Before we go to the next witness, let me tell

you that every Congressman who got a flu shot from the Capitol Hill physician--they do not know this--but they all had thimerosal injected into their bodies. They all had mercury put into their bodies. I got the shot and afterwards I looked at the insert and found that.

There are a lot of people who believe--like you do--that a number of senior diseases, like Alzheimer's, could be contributed to by us having injections of mercury. And nasal sprays the doctor gave me, the preservative was thimerosal. So we are getting mercury in all kinds of things, not just for children, but for adults as well.

So to my colleagues, if you had a vaccination for flu--and I went over to see the doctor, who is a wonderful doctor and a good friend, and he did not know it was in there.

Dr. Segal. And it is followed with a tuna fish sandwich, to boot. [Laughter.]

Mr. Burton. Now, do not start telling me I cannot eat tuna fish. [Laughter.]

Dr. Humiston.

Dr. Humiston. Thank you for inviting me to speak on behalf of my son, Quinn.

I wish you could meet Quinn. He has big eyes as brown as chocolate, and when he grins, you see those two big front teeth. He has the smooth, lean, muscular limbs of a child for whom movement is perpetual. You would never guess when he is sleeping that with that perfectly handsome face and that perfect 8-year-old body that Quinn has almost no language, that Quinn will bite and claw people in fits of aggression, which at times, appear as spontaneous and uncontrollable as a seizure, and that Quinn, on a bad night, can get along on as little as 3 hours of sleep.

You think you have all the answers until you become a parent. I did not even know all the questions. The main question my husband and I have had to address is, what are we going to do now to help?

We initially decided to use behavior analytic treatment, an educational technique derived from research on operant condition. A one-on-one therapist gives the child short and clear instructions for a desired behavior. For example, Say ``Hi.'' A correct response gets an immediate reward. For example, the therapist smiles and says, ``Great job.'' An incorrect response may be ignored or may trigger the therapist to prompt the child. As recommended, Quinn received 40 hours each week of one-on-one therapy. Studies at UCLA had shown that many children had significant improvement with this technique and replications at three other sites confirmed their findings.

When I say this, it sounds so rational. We were faced with this devastating diagnosis and we went through the literature and talked to every expert we could find. We found an intervention on which there was encouraging evidence, so we

threw ourselves, day and night, into getting and keeping the therapy in place. I assure you that it did not feel rational at the time. I had the panic-stricken urgency of a person staring down the barrel of a gun. My son's brain development, I believed, depended on me finding the right therapy in time before we was too old to be helped.

Autism and mercury experts at the University of Rochester have advised us not to get chelation therapy for Quinn. I was told that chelation is not recommended even for acute mercury poisoning. Brain damage done by mercury poisoning is irreversible. You do not see improvement after chelation. Finally, I was told that the safety of this intervention is not known.

My husband and I have tried other interventions: a phenol-free diet, a gluten-free and casein-free diet, medications including Ritalin and Prozac, and cranio-sacral massage. We tried to get secretin and found a place where we could get a dose or two for $10,000, but by then evidence was accumulating that it was not effective.

There have been more questions. Because I am a pediatrician, and particularly because I used to work for the CDC National Immunization Program, many people have asked me if MMR causes autism. As you are well aware, two exhaustive independent reviews have become available on that topic. The American Academy of Pediatrics, of which I am a fellow, has made a summary of their review available to all pediatricians. They report that the available evidence does not support the hypothesis that MMR vaccine causes autism or associated disorders. Separate administration of measles, mumps, and rubella vaccines to children provide no benefit over administration of the combination MMR vaccine and would result in delayed or missed immunizations.

The American Academy of Pediatrics is dedicated to the health, safety, and well-being of children. The AAP has proven itself to be absolutely dedicated to vaccine safety. They quickly withdrew their recommendation for rotavirus vaccine at the first sign of a problem and recommended the move away from thimerosal-containing vaccines even during the information-gathering period.

These actions have given me added assurance of their open-mindedness regarding the MMR-autism hypothesis and have added weight to their findings.

Similarly, the Institute of Medicine, the supreme court of medicine, convened the Immunization Safety Review Committee to address this issue, and they found ``that the evidence favors rejection of a causal relationship at the population level between MMR vaccine and ASD.'' The committee felt that the relationship been MMR and autism would be extremely rare, if it occurred at all.

The next question is about thimerosal. And we all look

forward to IOM's review of this topic. I am aware of an interesting recently published report from the University of Rochester that shows that none of the blood mercury levels observed in full-term infants studied shortly after vaccination exceeded the most recently revised lowest level of maternal blood mercury considered to represent potentially significant exposure to the developing fetus.

So what are we going to do now to help? Despite intensive therapy, my son has not been helped dramatically. And that is why I am here today. I am absolutely certain that we need more research. I am pleased that IOM was asked to review the question of MMR and autism, and I am pleased that they will review the thimerosal question. I am pleased that NIH is proceeding with the scientific evaluation of alternative and complementary medicine. I am delighted with the progress made by the collaborative programs of excellence in autism and I trust that funding is assured for the future.

I am excited by the creation of the congressional Coalition for Autism Research and Education and most especially by the Children's Health Act of 2000. I am encouraged to hear that the CDC has created a new Center on Birth Defects and Developmental Disabilities. All this activity is especially heart-warming for a parent because autism research has been significantly neglected up to now.

We need good autism epidemiology in the United States to determine risk factors and true rates. We need basic science research into the nature and causes of this disorder. And we need clinical research to determine what works and what does not, what is safe and what is not.

As we all know, appropriations are the key. A financial investment now could, in maybe just a few years, prevent another mother from having to face the questions I have had to face. There is a motto: ``You can have it fast, good, or cheap, pick two.'' In autism, research, we cannot afford to go slowly or have poor quality. That is why parents want Congress to fund high-quality research at the high level it deserves given the disorder's frequency, its devastation, and notable past neglect.

And we need significant research funding that comes with a commitment to the long term. Scientists are poised on the brink of success, but it may not come tomorrow. Like the families of autistic people, Congress has to be in this for the long haul.

How should the autism research agenda be set? Foremost, scientists should be encouraged to follow the cues of epidemiology and basic research. Listen to parents carefully, but do not neglect to follow through based on the leads from science.

Autistic families need better services--educational services for the autistic individuals, parent training for handling autistic offspring through their lifetime, and respite

services that are so essential in coping. Finally, parents need to see residential care facilities in place that will help with the question my other child asked me, what is going to happen to Quinn when you and Daddy die?

The question for this committee and all of us is the same as the initial question my family faced, what are we going to do now to help?

[The prepared statement of Dr. Humiston follows:]

[GRAPHIC] [TIFF OMITTED] T6856.048

[GRAPHIC] [TIFF OMITTED] T6856.049

[GRAPHIC] [TIFF OMITTED] T6856.050

Mr. Burton. Let me just say that I admire your view, Doctor, that the health agencies are doing a good job. And I think for the most part they are, but I would like to bring to your attention that the rotavirus vaccine--the advisory committee that recommended that--was kind of split. Some of the people thought there should be more testing done on the rotavirus vaccine. But the chairman of the committee had financial interests in the company that manufactured a rotavirus vaccine.

Dr. Humiston. The chairman was John Motley, who had no conflicts of interest at all.

Mr. Burton. Let me just tell you that we have already checked. We looked at the financial disclosure forms. The chairman----

Dr. Humiston. It could not have been the Chair. He has no----

Mr. Burton. Well, there were a number of people on there who had financial interests in the rotavirus vaccine. And that vaccine was put on the market. Within a year, we had one child die and a number of them had serious problems. We are looking at and have found some financial conflicts of interest among other people who are in the decisionmaking process.

That is one of the reasons why many people in Congress are very concerned about things like the report we just received. And that report was not categorically saying that the MMR vaccine was not a cause of autism. It did not conclude that, if you read the whole report.

Let me just ask a couple of questions here.

First of all, does the MMR vaccine, when it is being produced, does it include in any way in the production mercury? Do any of you know that?

Dr. Humiston. It does not. MMR does not contain thimerosal. It contains no preservative because it is a live vaccine.

Mr. Burton. I am asking in the manufacture of it because in the manufacture, we have been told--and I do not know that it is true--there was mercury in some of the production of the

vaccine.

But you are saying that categorically, that is not----

Dr. Humiston. No, because it is a live vaccine. The live vaccines do not need preservatives.

Dr. Segal. I would say that we do not know. I would say also that in the manufacture of the drug we are working on, there is mercury in the process and we take pains to remove it at the end. We think that it is all out.

But I think the answer to your question is that we do not know. I do not know that----

Mr. Burton. But there is mercury used in the process?

Dr. Segal. I do not know. I do not think anyone here knows.

Mr. Burton. We want to check on that and find out about that.

Mr. Bradstreet, are you stating that the combination of the thimerosal-containing vaccine with the MMR vaccine causes neurologic, immune, and GI problems in susceptible children?

Dr. Bradstreet. I think that would be incomplete, but I am saying that in part.

I think there are a number of environmental factors that are skewing the child's immune system toward a predilection along the autoimmune lines. I think that thimerosal is one of those issues. The aluminum adjuvants is another issue.

Then the other vaccines I discussed--the Hepatitis B vaccine and HiB--also are capable, as is pertussis--of pushing that TH-2 response so that by the time we get to the 15-month level or so and we give the MMR vaccine, it is the next TH-2 potential responding vaccine that the kids get. For some of the kids, it is just too much.

However, I have a number of kids who, immediately after the Hepatitis B vaccine--within days--seem abnormal and never recover and evolve autistic-like symptoms. I have heard the same thing after pertussis.

So it is not just MMR by any means, but there is a significant number--perhaps half of our families--who now claim they had a perfectly healthy child and within days--10, 14 days, whatever--their child was completely changed following the vaccine schedule.

That, in and of itself, is not conclusive. But it certainly causes one to look very, very hard at that subject. Epidemiology, in and of itself, is not going to give us that answer.

Mr. Burton. You talked about the mercury. That was in the Hepatitis B vaccine as well?

Dr. Bradstreet. Yes, as well as in the HiB vaccines. Almost all the HiB vaccines have mercury in them as well. So those are multiple sources for mercury.

Mr. Burton. That is exactly what happened with my grandson, within days after his.

Dr. Bradstreet, are you seeing improvements with the

treating of children to remove mercury? Do these children appear to be more vulnerable to other toxic metals?

Dr. Bradstreet. I think that something--and I am not sure what it is at this point in time--has wounded the body's normal and natural metallic defense. We have a system in the body designed to prevent environmental toxins like mercury and lead and other things from being toxins within the body. Many things protect the body. However, for whatever reason, certain children seem to be unusually vulnerable to that.

There is abundant data now available that individual variability at the time of the mercury exposure to thimerosal--we do not know how susceptible that child is. We do not know what other sources of mercury he has had, whether it was RhoGAM or diet or environment. We do not know how much he is going to get. And we do not know the status of his ability to defend against that mercury. We kind of cavalierly give it assuming that because it is below some sort of EPA threshold--although, with the combination of the multiple vaccines that is not true--that it is going to be safe.

I think that there is something about certain children that makes them very vulnerable to mercury.

Mr. Burton. I have some more questions.

Mr. Horn.

Mr. Horn. Thank you, Mr. Chairman.

Dr. Segal, I believe you mentioned RhoGAM, and the content of thimerosal.

Dr. Segal. That is accurate, yes.

Mr. Horn. What would be the behavioral changes if one used that consistently?

Dr. Segal. I am not sure I understand that question, but let me take a stab at it.

The medication is RhoGAM, which would be given to RH negative mothers to prevent a reaction with children in terms of attacking their blood cells.

Thimerosal is used as a preservative. It is given to the women--at this point--while they are still pregnant. The mercury preservative would be able to cross through the placenta and get into the developing infant. The theory would be that it would harm the developing fetus, at which point you would see neurodevelopmental abnormalities.

Mercury is an accumulative problem. That is, as you continue to be exposed to mercury, the body struggles with trying to remove it. When it builds up to some critical level, which cannot be predicted in the individual child, we have the potential to see neurodevelopmental problems.

Mr. Horn. So this is nothing to do with Rogaine, which relates to hair, and so forth? [Laughter.]

Dr. Segal. Not to my knowledge.

Mr. Horn. You have 2 million people across America who will wonder.

Dr. Segal. I think they can rest comfortably. [Laughter.]

Mr. Horn. Dr. Segal, do you think the genetic component of this problem may be the inability to these children to clear toxins and metals from their bodies?

Dr. Segal. I think that is the first step. I think there are multiple problems that are individually necessary but not sufficient. I think the first step is a genetic predisposition. I think that predisposition relates to the ability to detoxify against environmental insults.

Mr. Horn. Do you agree with the comparison of the symptoms of autism and the symptoms of mercury toxicity as similar? Do you see that?

Dr. Segal. I think the parallels are astounding, yes.

Mr. Horn. And that has been a lot of your research?

Dr. Segal. That is correct.

Mr. Horn. So you are speaking from scientific research?

Dr. Segal. That is accurate, yes.

Mr. Horn. Thank you very much for your testimony. I was very interested in it.

Dr. Schneider, are you seeing children with increased toxicity to other substances, such as arsenic?

Dr. Schneider. Absolutely. My own children have high levels of arsenic. After some research, I learned that is because I live in the State of Arizona where mining has been and still is occurring and our water supply comes from Colorado where the same can be said. Gold is mined with cyanide. Copper is minded with arsenic. It is so prevalent in the Phoenix water that no one is using Phoenix water. We have to get our water from Colorado, which really is not much better.

I have a reverse osmosis system in my household, and I mistakenly thought that removed heavy metals. I found recently that was not correct. I had to pay $5,000 to put in a water system which did remove arsenic and mercury from our water supply.

Mr. Horn. That is the Phoenix water system?

Dr. Schneider. Yes.

Mr. Horn. Do you see that throughout Arizona?

Dr. Schneider. I have not looked throughout Arizona, but certainly there are metal-toxic children throughout Arizona.

Mr. Horn. We see the same thing in Los Angeles where we have had various types of industries, small and large, where the metals just get into the underground water supply. That has become a major problem. I know EPA has studied this. What studies have you seen that lead to a different--arsenic as it goes around--some say you cannot deal with it because it is in this or that. I just wonder what kind of research you have seen where it is clear that it is hurting people substantially.

Dr. Schneider. Quite honestly, I do not do that kind of research and I am not as familiar with it as I intend to be because I was focusing more on the mercury aspect. But I find

now that mercury is not our only problem. We are exposing our population to many toxic metals.

Mr. Horn. We understand that typically children with autism are first diagnosed by a developmental specialist or psychiatrist and that the physical problems with these children are not addressed.

What do you think must be done to ensure that these children receive appropriate medical care?

Dr. Schneider. At our research center, we have initiated a physician outreach program, which is now in the stages of developing educational material for physicians, planning conferences for physician education. The reality is that most parents diagnose their children and then go to their pediatrician who tells them that they do not think so. Then they go back again and eventually get referred to the proper specialist and have the diagnosis confirmed.

In my own case, our pediatrician is a dear friend of mine and I have the greatest respect for him, but he did not know autism when he saw it. And that is very, very typical. We need to change that because, as many of us know, the earlier the child is diagnosed and the earlier the intervention is begun, the better the child's chances of having a partial recovery.

My own children are 8\1/2\ and 9\1/2\ years old now. I would say the clock is ticking.

Mr. Horn. In some of Chairman Burton's earlier hearings, we found there were a lot of medical journals of which there are probably a couple hundred--I have seen them in our library in Long Beach--that have glowing reports of this or that and they do not really tell you the effects on it. Do you have some feelings that the various professional groups and segments of this and that specialist, and some of their yearly meetings--they ought to have meetings that relate autism to all of the things that they might not--they go through medical school and there is great ignorance there in many ways, just like nutrition was, which was a simple thing. Doctors ought to know something about nutrition. Well, doctors ought to know something about this.

Now, how do we communicate with them where they read it, and they see it, and it means something?

Dr. Schneider. You are absolutely right because the reality is that pediatricians or family practitioners were not educated in the area of autism. Their image of autism is a child rocking and banging his head on the wall. Many of our children do not do that, thank goodness, yet still have autism.

So the physician outreach is a very important project for us. But what we realized when we spoke to the residency programs in our city is that pediatricians in training right now--a pediatrician has 4 years of college, 4 years of medical school, and 3 years of residency--in that training process, they talk about developmental disabilities for about 1 month,

and autism is only one portion of their focus. So there really is very little exposure to this area.

If you think about what happens in terms of medical education after training, it is primarily in the form of conferences. I am sorry to say that most conferences are sponsored wholly or in part by pharmaceutical companies. The message they want to get across has much to do with treatment of the condition for which they have a drug.

So you have to understand that it is up to the physician to educate himself or herself after training and to take into account the sources of the information they are receiving.

Mr. Burton. Thank you, Mr. Horn.

Mr. Horn. Thank you.

Mr. Burton. I will tell you my son-in-law is a doctor. And many doctors pretty much take at face value the recommendations and the research done by the CDC and the FDA. I can tell you that even here on Capitol Hill--like I was talking about the vaccine we get for the flu--I do not think any doctors up here even knew that there was mercury or thimerosal in it.

Mr. Blagojevich.

Mr. Blagojevich. Thank you, Mr. Chairman.

Dr. Humiston, our staff has just checked with Merck, the only licensed manufacturer of the MMR vaccine. The staff was told--and perhaps you can confirm this--that there is no mercury in that vaccine. Is that consistent with your understanding?

Dr. Humiston. Yes. My understanding is that there is no mercury and there is no mercury in the process of making it. It is thimerosal-free, as opposed to the vaccines that have mercury in the process but not actually in the vaccine.

Mr. Blagojevich. Thank you very much.

Thank you, Mr. Chairman.

Mr. Burton. We will check on that.

Dr. Weldon.

Mr. Weldon. Thank you, Mr. Chairman.

I have a question for Dr. Bradstreet.

You have been doing a lot of research--and really any of you can comment on this--and you have talked to a lot of researchers. Have you encountered any lack of willingness or intimidation to research in areas that might suggest that there are problems with vaccines in terms of its impact on the careers of researchers or their ability to get funding in the future? Have you encountered any comments to that effect?

Dr. Bradstreet. Yes. Actually, we work with researchers at several major university medical schools around the country. Many of them or their department chairmen have related back to us that there is significant fear and apprehension about doing a study that looks into vaccine safety for fear of being blacklisted by the pharmaceutical industry for future funding of research. Many pediatric departments or infectious disease

or immunology departments around the country at medical schools are completely dependent for a vast majority of their research budget and operating expenses on granting from the vaccine manufacturing companies. Many of those vaccine manufacturers make a host of different drugs.

If you look then at the potential liability issue--determining for example that thimerosal may be harmful to children--what that means from a liability perspective, a beginning of life neurologically damaged child that has a life expectancy similar to yours or mine, 70 or 80 years of care--that is cataclysmic. So they will go a long way to potentially suppress research along these lines.

It is something that needs to be addressed and there need to be independent sources of funding completely apart from the drug companies.

Mr. Weldon. Have any of the other witnesses encountered comments to that effect? Or would you rather not comment on this issue?

Dr. Segal. I would rather not comment on that issue. I would say, without getting into detail, the answer is yes. We have encountered that difficulty. But as we are trying to make in-roads in terms of additional research projects, I feel any comment I could make would be fragile.

Dr. Humiston. At the University of Rochester, because my developmental pediatrician is one of the researchers for the centers of excellence, I am aware of what they do. They are getting funding to look at vaccine safety issues.

Mr. Weldon. I have a question about the incidence.

The incidence in boys is four times higher than the incidence in girls. The incidence in the population is estimated at being--some say as high as 1 in 100--most likely 1 in 500 or somewhere in between, according to a lot of researchers. But that doesn't that mean that the incidence in boys is substantially higher? Aren't we talking about it being somewhere between 1 in 50 and 1 in 250?

Dr. Bradstreet. Just to be specific, we are talking about prevalence, which is the amount of disease in the population of children or boys. Incidence would be the new cases that are coming on-line per population on an annual basis. That is probably very high as well, although there is much less incidence research being done as compared to prevalence.

We know that it is very prevalent. A lot of children have this. If you look at Oregon as an example--and all the citations are on pages 5 through 8 of my testimony--clearly Oregon is very conservative. The State is run by a physician.

Mr. Weldon. If I could interrupt you for a second, the Oregon data you showed was less than 1 in 200. Is that correct?

Dr. Bradstreet. Yes, 1 in 190 in Oregon.

Mr. Weldon. What does that make it in boys?

Dr. Bradstreet. It is probably something like 1 in 50 or 1

in 70 in boys if you factor the four to one difference in occurrence rate in boys.

Mr. Weldon. Dr. Segal, you kind of made the comment as a joke, but this issue--I have had CDC officials in my office talking about whether we have an epidemic or not, and they cite how the DMS-3 was changed. But you made an excellent insight. If we are just diagnosing it better, what happened to all the adults? Is anybody researching that or looking into that?

Dr. Segal. If it is a question of diagnosis, the adults have to be somewhere. They did not disappear. The problem is that they are not there. The numbers have gone up. I think that is the only conclusion we can make.

Mr. Weldon. But nobody has done a research study looking at adults who are in institutional care, have some kind of psychiatric disability, who were perhaps previously diagnosed as mentally retarded, who may have actually had autistic spectrum disorders. Nobody is looking into that, to your knowledge?

Dr. Segal. To my knowledge, no one is. I would comment that Dr. McDougle, when he was at Yale, had a great deal of interest in adult autistic patients. So he may be able to comment on that further. He will be in the third panel.

Mr. Weldon. I know I am running out of time. I just have a question for Dr. Humiston.

You quoted from the IOM study that the committee concludes that the evidence favors rejection of a causal relationship at the population level between the MMR vaccine and autistic spectrum disorder. I fully expected them to say that because if they did not say that and it got out in the press, then parents all across America would start rejecting the vaccine and we could have a huge explosion of measles.

But then they did go on to say in the next section that they did note that their conclusions did not exclude the possibility that MMR vaccine could contribute to ASD in a small number of children because the epidemiologic evidence lacks the precision to assess rare occurrences.

I assume you agree with that section of the report as well.

Then they further went on to recommend further areas of research--and they have several areas of research they recommend--to include to develop targeted investigation of whether or not measles vaccine strain virus is present in the intestines of some children with ASD.

Essentially, they are calling for what I had encouraged them to do when I testified before them, to encourage NIH to fund the duplication of Dr. Wakefield's and O'Leary's work.

I assume you have seen Dr. Wakefield's micrographs and slides of inflammatory bowel disease in these kids, and you have reviewed Dr. O'Leary's PCR research showing the presence of measles virus particles in the intestines of these kids.

Dr. Humiston. I have not reviewed his micrographs. I am not

a gastroenterologist. I am an emergency medicine pediatrician.

Mr. Weldon. I am an internist, but I have ended up having to get very familiar with all this.

If you listen to all the press reports, they loaded up at the beginning of the press report that IOM says this is fine. Then they go on and--at least the better coverage of what I saw of all this--to say that further research is recommended. I do not want to accuse the IOM of talking out of both sides of their mouth. They were in a very, very delicate situation.

I have some concerns about the way the study was passed through some of the reviewers, or some of the witnesses who have had a track record of being critical of this work. But I think we have a very serious issue here. You cannot refute a clinical and pathologic report with an epidemiologic study. You cannot do that. It is bad science. You have to fund an attempt to duplicate the clinical study and the pathologic study.

Would you agree with that?

Dr. Humiston. I am in agreement that the study should be replicated. I am in agreement that epidemiology alone does not refute.

What IOM reviewed was not just simply two or three articles. It was many.

Mr. Weldon. I know.

Dr. Humiston. And I did have the privilege of being in the room during the IOM report. So I was privileged to hear about changes in autistic brains of children in areas where the brain develops and is used for different things at different times. So the neuropathologist was describing how this could explain how we see regression.

There was one researcher there who showed how blood spots taken on the first day of life had different levels of vaso-active intestinal protein present in day 1 of children with autism, different levels than controls. I think IOM took Dr. Wakefield's hypothesis very seriously, as I think it deserved to be taken very seriously.

I also do not think that when you say in a light way that this is what you expected of IOM--I have great respect for those scientists. They came from many fields. And many of them did not come from vaccines.

So I think that taking that lightly is a disservice to those scientists and to the work of people who are moving forward with genetic explanations.

Mr. Burton. We have to have a vote. We have 6 minutes left on the clock.

Mr. Weldon. I just want to clarify one thing.

You are accusing me of taking it lightly what they were doing. I do not like that at all. I consider this report a good report. I was pleased with the results of this report. But for them to spotlight and put the focus of public attention on the serious issues being raised about the safety of this vaccine by

Dr. Wakefield, it is going to cause parents--just like it happened in England--to quit giving the vaccine. So they were in a very awkward situation, in my opinion.

I personally believe that there is a problem with this vaccine. And there is a subset of children who have a genetic predisposition to having problems with this vaccine. But further research is needed.

I do not want to be accused of taking their findings lightly. I consider this basically what they should have done. They did what was needed.

Mr. Burton. Let me just conclude--and I hope you will come back for the third panel, Doctor, because I value your input.

Let me just say to you that they did send that report out for review to people from various pharmaceutical companies, and there were changes made, as I understand it, or corrections or perfections done on that report. I want to find out what those were.

Let me just ask two quick questions.

Does secretin cost $10,000 for two doses? I think my grandson got secretin and I know it did not cost that.

Dr. Schneider. There certainly are some practitioners who charge that much. That is absolutely true.

Dr. Bradstreet. Mr. Chairman, $200 to $300 for what used to be available is no longer available is a fairly common cost to the physician. Relatively commonly, physicians double the price of something that they buy. So if they buy a vaccine for $20, they would like to sell it to the patient for $40. So that is an outrageous price.

Dr. Schneider. Our regular pediatrician would not give it us. We were trying to find any source.

Mr. Burton. And my other question is, can chelation remove mercury from the brain?

Dr. Bradstreet. There is no evidence of that at this point in time.

Mr. Burton. Anybody else?

Dr. Segal. I agree. There is no evidence one way or the other. In fact, I spoke with two mercury experts. One suggests that mercury stays in the brain indefinitely. The other said that mercury is cleared within 50 or 75 days.

The bottom line is that nobody knows at this point.

Mr. Burton. We need some research on that point as well.

Dr. Segal. Yes, we do.

Mr. Burton. We will dismiss this panel. Thank you very, very much. We really appreciate it.

We would like to have your documentation and reports in total, if we can get those, so we can submit those to the health agencies.

Thank you very much.

We will be back. We will stand in recess to the fall of the gavel and go to our third panel as soon as we get back. It

should be about 10 minutes.

[Recess.]

Mr. Burton. We have a very large second panel. It is very, very important, though, that we cover all this territory. There will be other Members coming back from the floor in a minute.

[Witnesses sworn.]

Mr. Burton. We will start with Dr. McDougle. You are recognized.

STATEMENTS OF CHRISTOPHER J. MCDOUGLE, M.D., RILEY CHILDREN'S HOSPITAL, INDIANA UNIVERSITY SCHOOL OF MEDICINE; ANDREW WAKEFIELD, M.D.; WALTER SPITZER, M.D., FACULTY OF MEDICINE, MCGILL UNIVERSITY, MONTREAL, CANADA; BOYD E. HALEY, DEPARTMENT OF CHEMISTRY, UNIVERSITY OF KENTUCKY; DAVID G. AMARAL, MIND INSTITUTE, UNIVERSITY OF CALIFORNIA, DAVIS; DR. ELIZABETH MILLER, PUBLIC HEALTH LABORATORY, ENGLAND; AND DR. MICHAEL D. GERSHON, DEPARTMENT OF ANATOMY AND CELL BIOLOGY, COLUMBIA UNIVERSITY

Dr. McDougle. Thank you very much, Chairman Burton and committee members. Thank you for the opportunity to come and speak with you today.

In addition, I would like to thank you personally for your recent efforts to assist our work in autism at the Riley Hospital for Children in Indianapolis. It is very much appreciated.

I was asked to come today to talk a bit about our current clinical, educational, and research activities at the Indiana University School of Medicine. I am currently the chairman of the Department of Psychiatry as well as the director of the section of child and adolescent psychiatry and the chief of the Autism/Pervasive Developmental Disorders Clinic.

I have been doing research and clinical care in the area of autism for the past 12 years or so. I came to Indiana in 1997, and at that point wanted to establish a formal autism clinic. At that time, we had approximately 100 children with a diagnosis of autism and other pervasive developmental disorders in our clinic. We brought those children together into a formalized manner and then began to build a clinical team.

At that time, I was the only child psychiatrist on the team and we had one clinic coordinator. We soon realized--once we got the word out that we had a formal clinic--that we needed to expand our clinical operation significantly.

We currently have an active clinic census of over 500 children. So in 3 years the census within the clinic has gone from 100 to 500. The disturbing and alarming part of that is that our waiting lists are out 9 months in advance now to bring children and families in for a new evaluation. So we have 9 months of people on the waiting list to even begin to get in to see us. At the same time, we are still trying to provide good

care for the 600 current families within our clinic.

In an effort to meet some of these clinical demands, we have begun to hire additional faculty. I have added another full-time child psychiatrist, a nearly full-time behavior therapist, and a social worker to work with families to provide resources and help them with a number of the sticky issues they face.

Despite those additional clinical personnel, the waiting list persists. So I can certainly say firsthand that we are working very hard in Indiana. Autism is not rare. And we are having difficulty keeping up with the pace of personnel, despite adding additional personnel.

One problem with providing clinical care is that the reimbursement for such care is very poor. It becomes an issue as to how you are going to fund additional personnel to care for the growing population of your clinic when insurance reimbursement is often nothing or minimal. So that is an issue that I think needs to be addressed to a greater degree.

With regard to research, I am an expert in the area of psychopharmacology. I would say I am pretty good at diagnosing autism and related disorders and treating symptoms of autism that can become quite problematic. These symptoms--many of which have not been mentioned yet today--include aggression toward self, aggression toward others, property destruction, hyperactivity and inattention, interfering repetitive or ritualistic behavior, as well as the core disturbance of autism, which is a disturbance in the ability to relate appropriately to other people.

And we have a number of medicines we are studying in an effort to try to reduce some of these symptoms so that the child may be better able to participate in non-drug treatments, to be able to sit still and pay attention in speech therapy and other educational activities. But many times these symptoms I mentioned are so severe that the child cannot even get into a school or educational setting to benefit from these alternative treatments.

I would like to thank the National Institute of Mental Health. Approximately 3\1/2\ years ago they instituted a program to develop research units on pediatric psychopharmacology. They put out an RFA specifically to develop centers focused on autism. We were fortunate enough to be chosen as one of those centers in addition to four others across the country.

We recently completed our first study of a medication through this program with a medication called Risparidone, targeted really at some of the more severe symptoms of autism, including aggression, self-injury, and irritability. This was a double-blind, placebo-controlled study. We entered 101 children in adolescence into this study, which will make it by far and away the largest medication study ever conducted in autism to

date by at least half--twice as large. So the idea of having multiple centers working together to get a larger sample size more quickly makes a lot of sense. I would like to see the RUPP networks continue to be funded.

In addition, we have begun to explore a number of what we call investigator-initiated studies. When we read the basic science literature, we get ideas about medicines or compounds that might be helpful for some of the symptoms of autism. We then go and try to generate some pilot data that if there is something to it we then apply for Federal funding. We have initiated a number of studies with some of those compounds.

The other areas of research in autism to date that I think are hopefully going to be fruitful include those that have been successful in investigating disorders in other areas of medicine over time, and that includes genetics. Certainly there have been large dollars put into the genetic research of autism to date without really significant results.

What that tells us is that this is a complex disorder, that there may be multiple genes involved in autism, and my guess is that eventually we may find in fact that multiple genes might be contributing to just certain small populations of autistic children. So it is going to be very difficult to pin down a gene or genes for autism, although clearly there is a genetic basis.

But I focus most of my energy on treating people that currently have autism. That has been emphasized today, not only the need to find the cause but to treat those people we already have with autism. I would like to see more funding put into treatment--not just drug treatment, but other forms of treatment--for autism.

The question came up earlier--and Dr. Segal referred it to me--regarding adults with autism. When I began my work 12 years ago at Yale University, at the time I was not a child psychiatrist. Due to various factors, I was not allowed to see children--maybe for a good reason. But I really wanted to study autism, so I initiated a clinic for adults with autism, which was really unheard of at the time.

My colleagues looked at me strangely and said, why would you want to study adults with autism? I asked them what they thought happened to children when they grew up. Most people view autism as a childhood disorder. In fact, it is a childhood-onset disorder that lasts forever.

Those individuals, in fact, are out there. One of my moonlighting jobs while I was in Connecticut as a consultant to the Department of Mental Health--and I actually went to the State hospital and the ``back wards'' where adults were hospitalized, and not infrequently could I identify individuals that had a history consistent with an earlier diagnosis of autism.

So they are out there, often misdiagnosed with

schizophrenia or other disorders. But I will say that since I have been in Indiana and am now seeing kids, the ratio of kids coming to me versus adults is highly skewed in the direction of newer onset of cases in children. So the adults are out there, but there are many, many more kids and younger individuals who are being referred at this point. I have a sense that the numbers are increasing significantly. Again, I do not know the reason for that.

Mr. Burton. Can you sum up, Doctor, so we get to some questions in just a few minutes?

Dr. McDougle. Sure.

I have really touched on our clinical and research efforts. The other thing I would like to highlight would be our efforts in education. That is something else that has been brought up today.

Pediatricians and family practitioners are not adequately educated about autism. I never heard about autism in medical school at all and first learned of it during my second year of psychiatric residency. So what we are doing within our clinic is having all the medical students in fact rotate through our clinic with us so that--we are the second largest medical school in the country--a large number of students are at least now seeing individuals with autism and being exposed to those treatments. I think that is important.

Mr. Burton. Very good. I think we will come back and talk with you. You are doing a good job there and I am happy to work with you.

Dr. McDougle. Thank you.

Mr. Burton. Dr. Wakefield.

Dr. Wakefield. Thank you, Mr. Chairman. It is a great pleasure to be back here and provide you with an update and recommendations following last year's meeting.

[Slide presentation.]

Dr. Wakefield. Let me just give you my terms of reference, and that is that we are dealing with a subset of children on the autistic spectrum. What I am going to present to you is based upon the scientific data. It is not fragmented. It is based upon a logical, hypothesis-testing framework. It is not anti-vaccine. However, it is not based upon assumptions of safety or coincidence. It is not an isolated opinion. It is the opinion of a growing number of physicians, as you have heard today, and it is based on conventional methods of listening to the patients and parents and the new-kid-on-the-block in this context is public health.

Let's go to the clinical history, which I will just briefly review, and that is of normal early development, of developmental regression, and the majority of parents cite the contemporaneous regression of their child following MMR vaccination. There is onset of associated neurological and gastrointestinal symptoms. The children also suffer recurrent

infections.

You have heard that bowel symptoms are common in autistic spectrum disorder children, particularly in the United States, between 47 and 80 percent. So these findings may apply to a large proportion of the pediatric population with autism. The GI system are often masked by behavioral problems and if a history is not taken by an expert in gastroenterology, then these can be missed.

The question for the physician is, do these symptoms in these children reflect underlying intestinal disease? The medical profession hitherto have said, no, they do not. The answer is, yes, they do.

We have now published several papers, peer-reviewed papers. The first in the Lancet in 1988 and then in the American Journal of Gastroenterology in 2000, which was met with a very favorable commentary from the editor. And just a few weeks ago we published on the characteristics of this bowel disease in these children, comparing it with classical inflammatory bowel diseases, Crohn's Disease and enterocolitis, and normal controls, peer-reviewed and published data. We are presenting next week in Europe the discovery of not only a disease in the large intestine, but a disease in the small intestine as well.

And you have heard a great deal about autoimmunity. The disease in the intestine of these children is an autoimmune disease. There are antibodies in the blood of these children that bind to the lining of the bowel and seem to be part of an inflammatory reaction.

The key features are of developmental regression, swelling of the lymph glands in the bowel--this is consistent with a viral cause. The enterocolitis and inflammation throughout the gut is consistent with a viral cause. And the immunodeficiency we see in these children is consistent with a viral cause.

The important thing, though, Mr. Chairman, is that parents were right. The medical profession was wrong.

This issue of coincidence--and this is an important one--a child receives the MMR vaccine in the second year of life, and this is when the first signs of autism are noted. Bear in mind that we are dealing with regressive autism in these children, not of classical autism where the child is not right from the beginning. But coincidence is a situation you arrive at by due scientific and clinical investigation. It is not something that you assume from the outset. That is not good medicine; it is not bad medicine; it is nothing at all.

We will gain nothing from looking at children who had a single dose. But can we gain something from looking at children who had more than one dose? It is very important to raise this issue because this came up at the Institute of Medicine's review.

Here we have a group of children, each time line representing one child, and these children received not one

dose but two doses of the MMR vaccine. What we see is that in many cases the red square and circle represent their contemporaneous regression into autism and subsequent deterioration. The green square and circle represent their first and second exposures to the vaccine.

What we see in many of these children is a double-hit phenomenon. They regress after the first dose, and then they regress further after the second dose. Let me give you an example, that is the child with the larger icons.

This child did not receive his first MMR vaccine until he was 4 years 3 months of age. This is not just recognition. He then deteriorated into autism. Clearly, this was not even autism by definition, a disintegrative disorder. He then received his second dose at 9 years of age and disintegrated catastrophically. He became incontinent, his feces and urine, and he lost all his residual skills. This is not coincidence.

The reason I am concerned about this, Mr. Chairman, is that at the IOM's review there was considerable concern and anxiety raised over these double-hit issues, these double-hit cases. The data were requested from me to be discussed in the closed session of the IOM, such were the concerns of the committee members. However, they find little or no mention whatsoever in the IOM's report.

The IOM's report gives one and a half pages coverage to Dr. Fombonne, who was one of the co-presenters. It was sent to him for review subsequently so that he could make amendments. It was not sent to me. It was also sent for review--as you pointed out--to people who have a clear conflict of interest in the vaccine arena.

The reason it was not sent to me, I am certain, Mr. Chairman, is that these cases were not included. This analysis was not included. And that gives me great cause of concern.

Let me read you a comment from the IOM's report. ``However, well-documented reports of similar outcomes in response to an initial exposure to a vaccine and a repeat exposure to the same vaccine, referred to as challenge-rechallenge, would constitute strong evidence of an association.'' When we look at those, you see them. Those represent strong evidence of an association. They are well worked-up and well-characterized cases.

So the question is, is the virus present in the diseased intestine? These data were presented at the Cold Spring Harbor meeting earlier this year, and they were overseen by experts from the National Institutes of Health.

Is the virus present in the gut? Yes, it is. The viral gene and the protein are present.

Where is it located? It is located in the specific cells that we would recognize if it were the cause of this disease.

How much is there? It is certainly a low-level infection.

Can we confirm the presence of the virus with different technologies? Yes. We have now applied 10 different

technologies to this.

Does the presence of the virus distinguish these children with autism from controls? It is present in 93 percent of the children with autism and 11 percent of controls.

And can it be confirmed in independent laboratories? Bearing in mind that Professor O'Leary's laboratory was completely independent from mine initially, these further studies are underway, and the answer provisionally is yes.

The question we have now, Mr. Chairman, is, what is doing there? We are not saying it is the cause of this regressive autism, but the question is, what is it doing there? That is the next phase of our logical progression.

What is the link between the gut and the brain? We do not know, but it certainly is biologically plausible that one exists. It may be that it is an autoimmune process shared by the gut and the brain, or it may be that there are toxic contents of the gut that are getting through and hitting the brain in a situation similar to that which we see in patients with chronic liver disease.

Here is a child whose only treatments have been to the gut. He is an autistic child whose only treatments have been diet and control of his gastrointestinal inflammation. You can see that by solely treating the gut there is a demonstrable improvement.

What about the shortcomings in epidemiology? In short, Mr. Chairman, they have tested the wrong hypothesis. My colleagues and I have not proposed any hypothesis thus far that can be tested by epidemiology. We are still in the process of defining the parameters of this disease. In particular, we are concerned with what makes a child potentially vulnerable to a subsequent adverse outcome to an MMR vaccine. What sets the child up to then respond adversely to the vaccine?

What I have done is spent the last 3 years traveling the world and interviewing patients in our own clinic to try and establish from the clinical histories what those vulnerability factors might be. When we look, we see that there is a strong family history of autoimmune disease, particularly on the mother's side--of diabetes, thyroid disease, or Crohn's Disease, for example--that the child receives the vaccine in the presence of an infection or in the presence of recent or current antibiotic use, that the child has preexisting allergies, particularly food and milk allergies, and that the child receives many vaccines at the same time.

These are consistent elements that have emerged in the clinical histories that I now believe may represent vulnerability factors.

So let's look at what the data show. The hypothesis that has been tested and put down to me--which has nothing to do with me, whatsoever--is that if this is related to MMR vaccine, then at the point of introduction of the vaccine there should

have been a step-up in the numbers that should have levelled out as the vaccine uptake was saturated.

Is that a reasonable hypothesis? Can we assume that the background susceptibility of the pediatric population has remained constant? No, I do not. I do not think we can do that. What we actually see is an increasing incidence.

The time trend analysis for autism in the United Kingdom and California have confirmed the rise. The data are entirely consistent with an increasing vulnerability of infants to adverse reaction to an MMR vaccine. They are certainly consistent with the clinical histories of affected children. And again, I am not saying that this in any way proves causation. What I am saying is that we will gain insight into this disease from taking appropriate clinical histories and investigating and set up our epidemiologic hypothesis based upon that. Now we have a hypothesis that can be tested.

So in conclusion, Mr. Chairman, there is a group of children whose autism is associated with developmental regression, immunological abnormalities, intestinal disease, persistence of measles virus infection in the intestine, and onset following MMR vaccination. What I would recommend is that there be a high-level strategic meeting that is formed and a working group formed under the American Gastroenterological Association to investigate this specific group of children with the aim of providing appropriate and necessary clinical care for these children.

That is an absolute priority. The medical profession has let them down very, very badly thus far. And a research strategy needs to be defined by this group in order to understand this disease.

There needs to be immediate institution of active surveillance for vaccine-related adverse events. Passive surveillance has known to have failed. I believe that monovalent vaccines should be made available. This should be an issue of parental choice. I think it should be a priority that we identify those vulnerability factors--for example, a child who might be on antibiotics--and exclude them from vaccination until they have improved. We also need a policy for identifying and protecting susceptible children, and most importantly thereafter, informed choice.

It is ultimately a pro-vaccine argument, Mr. Chairman. If we have the ability with a single vaccine to prevent not only the acute disease, but this concurrent exposure, then we have the ability to protect children both against measles, mumps, rubella, and against this devastating consequence.

Thank you.

[The prepared statement of Dr. Wakefield follows:]

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Mr. Burton. Thank you, Dr. Wakefield.

Do we have your entire report?

Dr. Wakefield. Yes, Mr. Chairman.

Mr. Burton. We will submitting these reports to the health agencies of this country and we will get a response from them after they review the reports.

Dr. Spitzer.

Dr. Spitzer. Thank you, Mr. Chairman.

I would like to ask with respect that if I need to be cutoff--because there has been a lot of work done since I was here at this committee last year--that I be allowed at least to share with you what is in the future, the research that has been planned, some of it that has been called for, and which is going to be undertaken by an intercontinental group in nine countries and three continents to deal with some of the issues because this is the first time it has become public--and appropriately so--because 1 year ago, here in this room, I decided to commit the rest of my epidemiologic career to exploring these issues, if nothing else, out of admiration for the families.

Mr. Burton. We will allow you a little extra time. We have the other speakers. Because of time constraints, we have a little bit of a problem. But any additional information you have, you may rest assured will be put in the record and we will pass it on.

Dr. Spitzer. I will go as quickly as possible, particularly on those issues that are not specifically future-oriented.

The kind of research Dr. Wakefield does, with which I am familiar as much by the literature on an arms-length basis, is characteristic of laboratory and of clinical research which asks the question, can it happen? Epidemiology asks the question, does it happen? And then seeks answers in that direction.

The vast majority of the literature--and I have looked at pretty much everything the IOM looked at in the last 15 months on epidemiology--is inconclusive or uninterpretable answers. We are trying to remedy that, and I will explain why in questions or otherwise.

[Slide presentation.]

Dr. Spitzer. My perspectives are those of a professor of epidemiology and of public health medicine. I believe in immunization as the pillar of public health, but this does not mean that each new product can be exonerated from very careful evaluation, not just of effectiveness but of safety.

I have no sponsorship. The first time I have had coverage of my travel expenses was today. I work for no one. This is an initiative done without sponsorship and as neutral as I think can be attained normally. And I have no family members in the nuclear family or extended family with autism. That is not the motivation for my involvement, although that is a noble involvement.

Autism is an outcome--with very great respect for parents and families of children--that is as serious as death. It could not be less significant if I were involved in a mortality study resulting from MMR. The big differences are that the families of autistic children cannot grieve. It is their love, their commitment, and their undying optimism that masks the severity of autism. It is very important. It is part of the reason I made a commitment to the strategy for the future of autistic research.

The Institute of Medicine in a sense agreed. It said the disorders are incurable, permanent diseases that result in a serious developmental problem in children.

Incidentally, I was only able to get the executive summary. I came from overseas last night to be here. Where I was, I could not get the full report, so I can only quote the summary. If asked, I shall do that later.

I decided, having finished a review of much of the literature and the research literature on March 1st, approximately, when I submitted my paper to appear this month, that one has to really worry about autism based on the epidemiologic literature. And I will summarize it quickly. There is no evidence epidemiologically one way or the other that either rules in or rules out the problem.

A few days later, I was pleased to read the briefing document of Dr. Soto and his colleagues to the Institute of Medicine Committee, which reached pretty much the same conclusion--differences in words and emphasis--but pretty much the same. You cannot rule it in or rule it out.

Yesterday or the night before last, I saw that executive summary. You could interpret it the same way, but the wording and emphasis and what got to the press--the public relations version, if you wish--was that immunization is widely regarded as one of the world's most effective tools for protecting the public health and the evidence favors rejection.

If they are 48-52 percent, I am 52-48 percent. It is in the other direction. There has been no research that predicts the validity and interpretation of Dr. Wakefield's research, with which I have had nothing to do so far. Until that is set aside,

I could not make that statement, although we are within percentage points, probably, of the verdict looking at the same literature.

There is a great deal found in the report that alludes to causation. In biological population science, you have to demonstrate association before you get to causation. Normally, unless the results are very dramatic, you have to invoke the laboratory and the clinical science at the same time as the population science to reach those kinds of conclusions following criteria such as the Bradford Hill criteria, much as the surgeon general did with smoking of cigarettes 30 years ago or so.

So we have not gotten to association yet. None of the studies have gotten there, and certainly--say, the Taylor Study--cannot refute or confirm association, certainly not causation. That study mandated in the United Kingdom just does not prove anything. It is a preparatory, preliminary, hypothesis-generating study, not a hypothesis-testing study. And that is where we need to go.

These are the headings--I will go over them very quickly, Mr. Chairman--the issue of the epidemic of autism, natural history of autism--I will let you read them for a minute.

Speaking as an epidemiologist, there is an epidemic. It is not refutable on the evidence that is there. I am saying it, even though the great majority--except for one or two studies--they are all prevalence studies. A prevalence study is inexpensive and that is why one leans in that direction with the meek resources that are given for this kind of research. You need incidence to clearly demonstrate or refute an epidemic.

And the one peer-reviewed published study that did incidence--which is a case study out of the Boston Collaborative Surveillance Unit at Boston University, based on the British data base--it is an incidence study and it shows an epidemic. It is a seven-fold increase.

In California, you reported yourself, Mr. Chairman, that there are 700 new cases--which is incidence--in the past 3 months. Compared to the same seasonally adjusted period of 3 months 7 years ago, that is a 404 percent increase. That is an epidemic.

In Ireland, just the day before yesterday, there is a three-fold increase in prevalence done in the last few months. And in Cambridge University, a study showed a 10-fold increase in prevalence. These are numbers that are not the basis upon which you question an epidemic. We have an epidemic of autism and I assert that, as an epidemiologist, with confidence.

There is a widespread assumption that the autistic symptoms typically do not emerge until the child's second year, about the same time that MMR is first administered, a sensible observation made in the executive summary of the IOM. And you,

Mr. Chairman, in your introductory comments asked for the science about all this.

I have been working pro bono with the autistic families in the United Kingdom, who are challenging Merck, Smith-Kline, and others about the possible association. In documents I read of the attorneys of those companies, the statement was that 55 cases of autism were reported worldwide in the last 20 years of children with autism.

But I said, wait a minute. There are 505 cases in this list here. Where do they get that? Apparently, they are reported on the wrong color of paper to the yellow card system, so it does not make it into the official statistics.

So I decided that we should do an observational exercise--I barely call it a study--abstracting each of the medical records of these children and having some summaries to help us understand what is going on. We did it. I had an interdisciplinary team do this natural history of autism on a self-selected sample. I admit that. This is not representative of anything. We did not even do statistical tests for that reason.

The children had to be less than 15. They had to be free of symptoms not only before MMR but for the first 30 days after to bias it against us. All symptoms, signs, and diagnosis had to be in writing by a health professional, not just casual reporting--which is meaningful, but nevertheless difficult to validate.

We ended up with 493 medical records that could be used. I was sort of sobered. I entered a room that was full floor to ceiling and wall to wall with records. There was not enough space to work, but we did it anyhow. The average width of a chart was three volumes totaling more than 10 inches. That is what we were looking at.

This was looked at independently by the professor of family medicine of McGill, by a clinical psychologist from the University of Glasgow, by myself as an epidemiologist, and we had research assistants helping us with the tasks. It was a descriptive analyses only, as I said. I am reporting it for the first time. We met last Friday for the final analysis. We may end up by one-half percent because I questioned three records, which are being checked on now. That is what we were doing last Friday and we are writing the paper now, which should be sent in a week or so.

So there you see 493 medical records. The numbers there for exclusion, the 372 eligible subjects--most of the ineligibility was that they had symptoms early on and we wanted to bias it against us. We had 70 percent of those cases as classic autism; 7 percent were atypical autism; aspergoes were 8 percent. Of those cases, 40 percent were regressive, 40 percent were failure to develop, and 9 percent were both.

But most importantly--and that is with reference to the

evidence you were looking for--this is not good scientific evidence, but it is a start--if you see there, the median years from receiving the first dose to making the diagnosis was 2.6 years. That means that half the cases were 2.6 and greater. And there was great variation.

If you look at average, which is a bit higher, it is 3.2. But the median is more accurate because of the distribution. And the range is from 0.5 to 11.9 years of delay. The correlation does not even exist, the date of vaccination and the onset of this category of diseases.

I would just like to allude to this, Mr. Chairman. I have been looking for 17 months for studies with scientific admissibility that are adequate pharmacological-epidemiologic evidence of safety, which you would need when a concern has arisen in the community about safety of a particular drug. I have not found any. I have not found it. A proper study of safety under the current conditions, given the frequency of the disorder, would require about 450,000 children. I went through that with statisticians at Cambridge. And that has never been done.

And the ``safety studies'' published are of scores of patients. That is a type of sample size which is simply inappropriate, insufficient, and not a scientific way to look at the safety of a drug. I am astonished that the authorities in the United Kingdom, the United States, and my country of Canada are not requiring it the same way they have required us to do it for all contraceptives, for the right reasons.

The problem is incorrect length of followup as much as anything in these cases. For instance, the Medical Research Council report widely cited in the United Kingdom as setting aside the concern followed an unrepresentative subsample of the sample of children I looked at for 3 to 6 weeks when the range is from 0.5 years to 11.8 years. The study is simply not valid for that reason alone and cannot be invoked to demonstrate safety or the lack of a need for concern.

There is no problem if you do not look. The companies know that. Those of an opinion that there is no association say that epidemiologists have shown no evidence. Of course, they have. And they have all been small studies. I call them phyto studies to my students. Phyto means arenal products in the ocean. It doesn't make any difference in the levels in your understanding.

Nobody has looked. And the cost of looking is that of millions of dollars. Is that OK? Yes, it is OK. Look at the millions of dollars of profits. One way of pretending you are looking but not looking is by under-powering the studies. They are not powered sufficiently high to be able to deal with the no-difference issue leading you potentially to what we call a type two error statistically.

I will just tell you--and it is in the written record--the

Finnish study reported widely by the press in Britain--much like likely the IOM reports will be somewhat misrepresented--does not in any way demonstrate safety or lack of it because it is a passive surveillance study designed for other purposes and then reanalyzed for another reason. I give a page and a half of reasons why that study just does not mean anything one way or the other. It is in the written record, Mr. Chairman.

Research priorities--I will list them quickly and I will end up with the study.

Ongoing research in laboratory and the clinic--I will not say any more. A lot has been said about treatment, but I would add a word that I hardly ever hear and that is about palliation. The families need treatment as much as the children, and palliative strategies need to be undertaken. I am sure my clinical colleagues couldn't agree more with that. But it does not get priority in potential focus of support.

Correctly designed safety studies. Correctly designed incidence studies. And case-controlled studies.

This past Saturday and Sunday, we met at Heathrow Airport, representatives from six countries out of nine possible candidates, to decide go/no-go on a major intercontinental study. The IOM said the committee does propose targeted research efforts and more rigorous data-gathering procedures. Much of the problem in existing research is that you are going into data that were created for a purpose other than exploring that hypothesis. That is a lot of the problem. This is going to get around that.

Mr. Burton. Doctor, are you about to wrap up?

Dr. Spitzer. I need 3 more minutes, or less, if I can.

We reached a ``go'' decision on Sunday, a few days ago. We have been working on it since. I am going back to it.

We are going to explore risk factors other than MMR as well because there is no point going in 5 years and then deciding that we should have looked at something else. We are going to try to avoid that.

The candidate countries are on the slide, nine countries. Why so many countries?

In England, Canada, Denmark, and the United States there is such an overwhelming coverage that obtaining control is almost impossible. You have to have control. The contestants of clinical science and epidemiology and laboratory science as well is comparison. Without comparison, you have generation of hypothesis in the main, very seldom testing of a hypothesis.

You ask in epidemiology, how is your spouse? And you will probably hear something like, compared to whom? [Laughter.]

You have to have comparison, and that is why we are proposing a case-controlled study, and to do much of it in-country. Poland only has 35 percent coverage today. The rest is univalent. The same with Argentina and the same with France.

Selected features of the study--quickly--3,500 cases and

7,000 unaffected controls. Exposure risk factors: MMR, mercury, other vaccination, childhood diseases, genetic factors, not to be exhaustive but as examples. The outcome is the entire spectrum of autistic disorders.

Why 3,500 cases? Because, as has been said by many already--and I am pleasantly surprised--we will likely find the problem in a subset. It is a multifactorial problem, almost certainly everyone seems to agree. But we do not know what that subset is in advance.

I would propose that a subset of less than 10 percent--it is either not discoverable or not as important. So we are making 10 percent the threshold. That gives you 350 cases and the corresponding control that may give us important answers.

Finally, it is investigator-initiated. We are not responding to any request for proposal, therefore we have to create the protocol and then ``sell it'' to objective, independent organizations. The cost is estimated to be $17 million to $21 million over 5 years, $125,000 in the first year.

Is that a lot? It is the equivalent to the annual cost of care and support of 0.3 percent of autistic children in the United States alone. We have only methodological support from the United States so far. We have support from most of the other countries. We will do it. We would like to work with the United States. We do not need the United States or the United Kingdom, for that matter. We hope we can push ahead with this and look for some of the answers that are being called for.

I apologize for the delay. Thank you for your attention.

Mr. Burton. Thank you, Dr. Spitzer. We will take your whole program and submit that, along with the others, to HHS and ask them to take a hard look at that.

Dr. Haley.

Dr. Haley. I am probably one of the few people here who does not treat patients. I am a research scientist and I work in a lab.

I was asked some time ago to look and go to the bottom line. Are the vaccine mixtures that we are placing in the children toxic? If they are going to have an effect on autism or any disease or any neurological disorder, there is a good possibility, if it comes from the chemical level, that vaccines have to show some toxicity at the molecular level.

We did test vaccines, and I will make this very short because I know we are in a hurry.

We compared the vaccines with and without thimerosal from the same source, the same type of vaccine, and those with thimerosal present were remarkably much more toxic--over 10-fold to 100-fold more toxic than those without thimerosal. There was one outstanding exception, and that was the MMR vaccine. The MMR vaccine was as toxic as the vaccines with thimerosal, but there is no thimerosal in the MMR. We measured

mercury levels, and I think the thimerosal is not there, but we would want to do a lot more numbers of vaccines.

But there is something in the MMR vaccine that does inhibit the enzymes and the brain protein systems that we have very dramatically. I do not know what it is.

I would point out also that the toxicity is thimerosal in a vaccine mixture. In our studies, we looked at combined toxicities because we are not rats living in a pristine cage. Aluminum is a neurotoxin, formaldehyde is neurotoxic, and you throw that in with thimerosal, which breaks down to ethyl mercury, a well-known toxin. You do not know what you will get without doing studies. I have looked hard and cannot find them. I am surprised they were not done, but not totally. This is just something we do not know the answer to.

We do know that ethyl mercury is very, very toxic. Of the studies you can read about, of the three children that have been intoxicated that I have found--they all died with 1 microgram per ml levels. That is considerably below what they would do, but you just do not hit a point and then die. You start a linear progression of health effects.

The other thing, when we talk about the level of mercury that is toxic, you cannot compare mercury to ethyl mercury to dimethyl mercury. They are different compounds. Ethyl mercury, methyl mercury, and especially dimethyl mercury are much more toxic than an equivalent amount of mercury on the atom or mole basis. So you cannot compare them.

I would also point out that the reason mercury does not kill us immediately is that a lot of it depends on our health. We all live at a level where we have reducing equivalents this high when we are 20 years old. We are full of spit and vinegar. And the mercury level is down here and we are handling it real well. As we age, the level of glutathione, metallothione, and other proteins that we synthesize in our bodies--because the energy level drops down--gets to the point where we are getting more balanced. When we get too old or too unhealthy, then we pass this. Then the mercury can take over and start having the effect of damaging the healthy proteins, the proteins we really need in the body.

I would also point out that this level can drop precipitously if you have a viral, bacterial, or fungal infection. It will drop dramatically because it is fighting to take care of the oxidants because the molecule that removes mercury from our body is also the molecule that takes care of the reactive oxygen species, the normal aging products, and the materials we call oxidating stress products.

I am surprised, when I understand the data that they are presenting here--we know certain children are born that are autistic. These vaccines need to be cleaned up because even if they did not cause it, who would want to give ethyl mercury to a child that is destined to get autism? It is a very poor idea.

You really need to clean the vaccines up. I cannot imagine why they did not take the vaccine mixture and test it, on the very base level in a test tube against a bank of enzymes or against a brain homogenate to see whether or not they were injecting toxicants into these children. It is very clear that has happened.

I would also point out that we have a problem with combined toxicities. People that smoke are heavy in cadmium. And cadmium and mercury, if you combine them together in a test tube and test system against tubulin--which is probably the first protein affected in Alzheimer's Disease--that you can have a non-toxic level of mercury, a non-toxic level of cadmium, and you add those two together and you will get over 50 to 60 percent toxicity on a comparative basis.

Combined toxicities and the multiplicity of the events that are caused by mercury--mercury is somewhat similar to alcohol in that when different people get exposed to it they behave differently--so it is very difficult when you want to look just at someone who is an autistic. To me, that is a name and it is a tantology. Autistics do this. And yet, I say, do all autistics do that? No. Then there is a difference. They are not the same. You have to look at them differently. So we have a very confused issue here that I think we need to look at.

I would also point out that in the vaccine issued, the one thing that really makes the vaccines toxic to infants--you are giving the same shot to an infant that you give to a 180-pound soldier. Infants do not have bilary transport. They do not make bile when they are first born and for some time after that. The bilary transport system is how the body removes mercury from the system. Babies cannot do that. So it is the equivalent of drinking alcohol and not being able to metabolize it. It builds up. It would stay there and be much more damaging to an infant than to someone who is an adult who had the ability to rid the body of the mercury.

Aluminum is removed by the renal system. Infants have an immature renal system. They cannot handle heavy metals and get rid of them as fast as we can. If you give them multiple shots with high levels of mercury, I do not know how well they handle it. I have not been able to find any data where this has been tested. So the mercury and aluminum levels would buildup in these infants if they had multiple shots before they got to the point where their bilary and renal systems were totally mature.

The aspect of genetic factors--I was in New Zealand I talked to a doctor by the name of Mike Godfrey. He is a friend of mine and he and I have talked a lot about Alzheimer's Disease and the involvement of mercury. Johns Hopkins University showed several years ago that there is a risk factor, a gene called APO-E protein. There are three copies, two, three, and four. Two is protective against Alzheimer's Disease; four puts you at high risk for the disease.

If you look at the chemistry of the APO-E proteins, this can be reflected in the fact that it is a housekeeping protein that clears the brain of waste materials. If you have APO-E2, you can carry out two atoms of mercury for every atom of APO-E that goes out. If you have APO-E4, you can carry out none.

He took this and looked at autistic children. When he did the screen of autistic children, there was a huge preponderance of them that had APO-E4, indicating that there is a genetic risk factor which deserves further study. And it does implicate that the inability to detoxify the cerebral spinal fluid may be at least part of the neurological aspect of this disease. I am not a physician, so I do not go there to make answers about that.

I have also been in a fight with the pro-dental amalgam people for many years, as I did research about 10 years showing that mercury dramatically inhibited the same enzymes that are dramatically inhibited in an AD brain. And everyone says there is not enough mercury there to do it. Recently--and it is in the report I did--they have found that studies using neurons and culture, that levels of mercury approximately 100 to 1,000-fold less than you have in your brain, when you place it with neurons in culture will cause the formation of the two diagnostic hallmarks of Alzheimer's Disease.

I went to NIH and screened the grants they fund. We found one where they are funding the ability to make a better amalgam that would leave less mercury because there was some concern about the mercury being released, which, according to the ADA is a totally safe level. But there are no grants looking at the effects of low-level mercury exposures to Americans. But we are placing grams in our mouth and micro grams in our vaccinations.

I cannot say, nor would I say, that vaccinations cause autism. However, if the data holds up that I have been seeing with the relationship, I think it is an awfully good suspect, at least one of the co-factors that might aid in the onset of this disease. So I would really recommend and encourage you to put some pressure on NIH to look at the contribution of different forms of mercury we put in our medicines and in our dentistry to see what effect they have on the neurological health of Americans, especially autistics.

Thank you.

[The prepared statement of Dr. Haley follows:]

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Mr. Burton. Thank you, Dr. Haley.

You may rest assured that we are going to put as much information before them and--if you want to call it pressure--pressure them as much as possible to research all of this.

Dr. Amaral.

Dr. Amaral. Mr. Chairman and members, my name is David Amaral and I am a professor of psychiatry and neuroscience at the University of California, Davis.

The last 3 years, it has been my great privilege to be the research director of a new clinical research experiment called the MIND Institute. MIND stands for Medical Investigation of Neurodevelopmental Disorders. I deliberately referred to the Institute as an experiment because of the unique way in which it came into being, the unique way in which it governs its research, clinical, and educational programs, and the unique focus on understanding the biological basis of autism and other neurodevelopmental disorders in order to discover treatments and ultimately cures.

Historically, parents of children with autism have been given little hope and frequently advised to institutionalize their child and move on with their lives. This option was

unacceptable to four Sacramento-area fathers, all of whom had sons diagnosed with autism in the 1990's. Chuck Gardner, a general contractor, Rick Hayes, an investment management, Rick Rollens, former secretary of the California State Senate, and Lou Vismara, a cardiologist, joined forces to create the concept of developing a world-class research and treatment center devoted to understanding the biology of autism in order to find treatments for theirs and other's children.

These four dads approached the UC Davis health system with the idea of forging a unique partnership between a University medical center and parents of autistic children to develop an institute where families could bring their children for state-of-the-art one-stop diagnosis. Those children diagnosed with autism or other neurodevelopmental disorders would then become subjects for multidisciplinary research aimed at understanding the causes and medical ramifications of their disorders. Once the biology of autism was better understood, then the clinic would become the proving ground for new treatments that would be developed based on the new research findings.

The MIND Institute research program, since that time, has followed a number of parallel paths of development. It is important to point out that the Research Committee, which is charged with all decisions about research direction at the Institute, is made up equally of parents and senior scientists at UC Davis. The committee has agreed that the prime directives of MIND Institute research are to remain open to all possibilities of causality, to carry out rigorous research in a collaborative multi-disciplinary fashion, to carry out innovative and even highly risky research if there are potentially large payoffs, and to try and determine the critical path to understanding the biology of autism in order to develop treatments as quickly as possible.

The MIND Institute research program currently has four components. It has a UC Davis intermural program, and we are attempting to develop a critical mass of researchers and facilities at UC Davis in order to carry out state-of-the-art multi-disciplinary research on autism and other neurodevelopmental disorders.

It is clear that certain forms of research and therapy will only be accomplished when an intimate relationship is established between the clinic and basic science. This is really the guiding vision of the MIND Institute.

We have an investigator-initiated grant program. It is important to note that more than half of all the research funds allocated to the MIND Institute have actually been distributed to researchers at other UC campuses and other research facilities internationally to carry out research on autism and neurodevelopmental disorders. This extramural program is guided, again, by the parent-oriented philosophy that it is more important to get the critical research accomplished

quickly than get the credit for accomplishing it at a particular institution.

We also have targeted research initiatives. Funds have been allocated to carry out research in areas that are currently underrepresented or in need of immediate attention. The MIND Institute, for example, has launched a nationwide effort to investigate the potential relationship between vaccines and autism. I will say more about that in a moment.

Finally, we have a MIND Institute scholars program. A major impediment--and we have heard this today--to rapid progress to research on autism is the relatively small number of scientists and clinicians who have autism as their primary area of interest. To encourage young scientists to enter the field, the MIND Institute has funded pre-doctoral students and post-doctoral fellows throughout the University of California system. It is hoped that these MIND Institute scholars will be the future leaders of autism research.

Let me briefly highlight some areas of current and future MIND Institute research. The first I would like to mention is the biomarkers program.

One of the first grants funded by the MIND Institute was awarded to a team from the California Birth Defects Monitoring Program, who collaborated with Dr. Karen Nelson from the NIH and with investigators from the MIND Institute. We heard a little bit about this this morning.

The so-called blood spot study sampled the blood spots that are taken from all children born in California. The investigators sought to determine whether there might be abnormal levels of certain peptides in the blood spots of children who were later diagnosed with autism.

This highly risky--what some would call a fishing expedition--made the striking discovery that several peptides were elevated in children who later became autistic or mentally retarded, but were not elevated in children with cerebral palsy or normal control subjects. This has led to the suspicion that more sophisticated techniques might provide a diagnostic marker for those children who are susceptible to autism. Of course, the significance of this finding is that there is substantial suspicion that while autism has a genetic component which makes children susceptible to the disorder, they must encounter another factor--a so-called second hit--that brings on the autistic symptomatology.

While it is not clear what the second hit may be--we have heard that many parents and others are concerned that it might be childhood vaccination or environmental contaminants--regardless of the precise identity of the second hit, if susceptible children could be detected at birth or before, once the causative agents are determined, these children could be protected from exposure. Therefore, finding a biomarker of autism is the highest priority of the MIND Institute research

program.

One strategy is to employ the power of the Human Genome Project. In January 2001, the MIND Institute announced that it was allocating $1 million to develop a new neurodevelopmental genomics laboratory. The laboratory aims to identify a genetic profile or fingerprint of those children who may be vulnerable to autism. The goal of this program is to have an accurate diagnostic test that will be used to evaluate all children at birth, like the children are currently tested for Phenylketonuria.

A second initiative has been our vaccine-autism link research. As initially described by Mr. Rick Rollens in testimony to this committee on August 3, 1999--and we have heard much about this today--there is strong suspicion among parents that one ideology of autism of a child is associated with child vaccinations. While many organizations have been hesitant to take on this issue, the MIND Institute considered this to be a fundamental area for immediate action. If there is an identifiable culprit in existing vaccines that cause autism, then the removal of the agent or changes in vaccination policy could reduce future cases of autism.

In August 2000, the MIND Institute issued a request for proposal for research leading to precise scientific data on the potential links between vaccines and autism. With a private donation of $1.2 million and additional funds from the State of California, the RFP was advertised nationally and throughout the UC system and several grants have already been funded to carry on this research.

Another area of research is on the epidemiology of autism. The California State Legislature commissioned the UC Davis MIND Institute to carry out an evaluation of the factors that have led to the nearly 300 percent increase in the number of clients with autism in the regional center system and allocated $1 million for this effort. The principal investigator of this study is Dr. Robert Byrd in our Department of Pediatrics.

The overarching goal of this study is to determine whether factors such as in-migration or diagnostic shift can account for some of the increase in clients with autism. If you can discount some of these factors, then it has to be something else and we will look at those factors as well. The study team has been assembled. The field work is planned for September through December of this year. The analysis and reporting of results are slated for June 2002.

Another important area of work is what we call the autism tissue program. Much of the progress that has been made in the understanding of Alzheimer's Disease has come from the neuropathological and molecular biological analysis of post-mortem brain tissue. Literally hundreds of thousands of brains have been evaluated through recruitment at Alzheimer's research centers throughout the United States. In contrast, fewer than

40 autistic brains have been subjected to post-mortem analysis.

While it is clearly a very difficult issue that requires utmost sensitivity and compassion, progress in the understanding of the biology of autism will rely on the acquisition of well-preserved brain tissue from autistic patients. So to facilitate the goal of acquiring and distributing this resource, the MIND Institute has joined forces with the autism tissue program, sponsored by the National Alliance for Autism Research and Autism Society of America Foundation, to carry out the nationwide campaign to make parents and families aware of the need for tissue donations and to develop an efficient acquisition network that will allow optimal use of this precious resource.

And the last area I wanted to mention is a recently announced international meeting for autism research. There is currently no national or international meeting that brings together all scientists carrying out research in autism. The MIND Institute has joined with Cure Autism Now and the National Alliance for Autism Research to launch the first international meeting for autism research in San Diego on November 9 and 10 of this year. This meeting will encourage presentations of all types of research dealing with any aspect of biological basis of autism or experimental approaches to treatment.

It is expected that this meeting will contribute to increasing the awareness of new research findings and should foster new areas of research as well as new collaborative efforts.

So to summarize, the MIND Institute has quickly established a multi-component research program that is designed not only to help the children of today but those of the future. First, we are building a strong local infrastructure that will be uniquely capable of carrying out translational research on autism. Patients will not only be diagnosed in the clinic, but will become subjects for research. Once new findings lead to new treatments, the clinic will be the proving ground for these approaches. And once a new treatment is proven, it will be distributed to institutions worldwide for implementation.

Second, at the same time as research is carried out in Sacramento, the MIND Institute will support innovative research throughout California and eventually, with adequate fundraising, throughout the world.

Third, in addition to our own efforts, we will partner with other advocacy and research groups, including the NIH, to foster efforts that must be carried out through a concerted effort.

Through building a strong research team and collaborating nationally and internationally, it is my hope that we will ultimately understand and defeat autism. In the meantime, the MIND Institute will do everything in our power to treat children who are currently afflicted and strive to prevent new

cases in the future.

Thank you very much.

[The prepared statement of Dr. Amaral follows:]

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Mr. Burton. Thank you, Dr. Amaral.

Dr. Miller.

Dr. Miller. Thank you, Mr. Chairman.

Thank you for inviting me to this congressional hearing. I do so in my capacity as an epidemiologist who has worked for 22 years in the Public Health Laboratory Service in the United Kingdom on vaccine-related issues, with specific expertise in studies relating to vaccine safety.

For clarification, I should say that the PHLS in a non-governmental public body whose role is to provide a national capability for the diagnosis, surveillance, and prevention of communicable disease and the provision of independent advice about the control of communicable disease to help professionals and the Department of Health. The remit of the Immunization Division--which is part of the PHLS--of which I am head, is the national surveillance of immunization programs, including the safety and efficacy of vaccines that are in routine use.

Together with statistical colleagues in the PHLS and other academic institutions, over the years I have conducted a number of epidemiological studies designed to investigate various putative adverse events after different vaccines, including MMR, DPT, and more recently oral polio virus vaccine. These are referenced in my CV.

In some of these studies, evidence of a causal link between a specific adverse event and a vaccine has been found, and risks as rare as 1 in 10,000, 1 in 22,000, and even 1 in 143,000 doses have been detected. In other studies of possible adverse events, the results have been entirely negative. This is the case with the epidemiological studies I have conducted related to the postulated link between MMR and autism. Similar negative findings have been found in other work conducted elsewhere on the potential epidemiological link between MMR and autism.

These epidemiological studies have been designed to test the hypotheses implicit in the case reports and population trends in autism that Wakefield and others have interpreted as evidence of a causal link with MMR vaccine. The published evidence cited--some parents of autistic children say that the onset of symptoms in their child first occurred shortly after MMR, that prior to MMR their child was developing normally, that the onset of behavioral regression associated with MMR is typically accompanying by bowel symptoms, and that there has been an epidemic increase in the prevalence of autism which coincides with the introduction of MMR vaccine.

The studies I shall describe have been designed

specifically to test the hypotheses that are implicit in these observations. I think it is disingenuous of Dr. Wakefield to say that he has inferred no hypotheses. I think it is also disingenuous of Dr. Spitzer to say that the study I was involved with was essentially a hypothesis-generating study. It was specifically testing a prior hypothesis that was derived from Wakefield's paper in the Lancet where the evidence that is put forward for an association between MMR and autism is the onset of regressive features or other behavioral disturbance shortly after MMR.

In brief, the summary of the findings of the various epidemiological studies--which are described in detail in my written submission to this committee with full references--are as follows.

There is no evidence that the onset of autistic symptoms is more likely shortly after MMR vaccine than at any other time. Indeed, new evidence which is shortly to appear from my colleagues and myself in a vaccine journal shows that there is no evidence that MMR vaccine increases the likelihood of autism at any time after vaccination.

Children with autism are no more likely to have received MMR vaccine than normal children. The introduction of MMR as a routine immunization for children in the second year of life has not been associated with a step-up increase in the incidence of autism.

When analyzed by birth cohort, there is no correlation between MMR uptake and prevalence of autism. I recognize that the Wakefield hypothesis has now moved on and has evolved--possibly under pressure of these epidemiological findings--but it is important to remember that the published work of Wakefield and others in relation to the putative link has been tested in the studies I have just described the findings of.

Most importantly, the final finding I will describe and show you the data from the study which is not yet published, there is no epidemiological evidence to suggest the emergence of a new syndrome of autistic enterocolitis associated with the use of MMR vaccine.

As I said, this latest finding, which I think is most pertinent here in relation to the postulated existence of this characteristic regressive autism with autistic enterocolitis--I would like to present the results of this later study here.

If it is true that vaccine-attributable cases typically present with developmental regression and bowel symptoms, then the proportion of such cases should have increased since the introduction of MMR. That is a logical conclusion and a logical inference from the hypothesis that is implicit in the data Dr. Wakefield has shown.

To test this hypothesis, my colleagues and I have updated our 1998 study of prevalent autistic cases in the North Thames Region of England by carrying out a further survey in 2000,

2\1/2\ years later. The prevalence data of the more recent birth cohorts shows that the rise in the early 1980's and early 1990's has now levelled off with no significant increase in prevalence in birth cohorts from 1993 onward.

The current prevalence rate is about 1 in 350 to 1 in 400 children. That is a high rate. And I would like to make it clear at this point that I do not in any way believe that this is a condition which should not attract substantial amounts of funding. We need to find the etiology and we need to find effective treatments.

However, the question of whether there has been an epidemic increase or whether that prevalence was there all the time but has only been recognized with appropriate diagnosis and referral mechanism I think is open to question. Certainly, my colleague, Professor Brent Taylor, who is a consultant community pediatrician, is of the opinion that the rise we had seen prior to 1993 was due to improve recognition and referral of cases rather than a real rise. I think the fact that it has flattened off since 1993 is consistent with that interpretation of the data.

However, the main purpose of this updated study was to test whether there has been an increase in the proportion of cases with regressive features and bowel symptoms associated with MMR.

[Slide presentation.]

Dr. Miller. This shows that amongst children--there were 500 children in this survey--of children with regression--we concentrated specifically on children with regression and bowel symptoms. You can see there the portion of children with regression categorized by whether they had ever had MMR or indeed any measles-containing vaccine, whether they had that vaccine prior to parental concern--those are the cases that could possibly be caused by the vaccine, they were normal until they had thee vaccine--or whether they had the vaccine after parental concern. You can see that there is no significant difference in the percentage of cases with regression by MMR status.

A similar analysis done of the percentage of cases with bowel symptoms by MMR status again shows no significant difference between those three categories of autistic children--no MMR, MMR before onset, or MMR after onset.

Looked at another way, if we look at the percentage of cases with regression by year of birth, going from 1979 up to 1998--and remember that we introduced MMR in the UK in 1998, so in the middle there--you can see there has been no change in the proportion of cases with regression by year of birth.

Similarly, there has been no change in the cases of bowel symptoms by year of birth. Neither did we find that there was any characteristic bowel features in association with the use of MMR vaccine, constipation and diarrhea. These results are

currently being submitted for publication.

In conclusion, in my view, the available epidemiological evidence, both from the United Kingdom and elsewhere, does not support a link between MMR and autism of the nature and frequency implicitly postulated by Wakefield and others and the basis of their published work so far. I recognize that the hypothesis has now evolved and moved on. Indeed, it provides strong grounds for rejection of the hypothesis that MMR is responsible for the reported rise in autism and that such cases are characterized by behavioral regression accompanied by bowel symptoms.

Clearly, no epidemiological study could prove that MMR vaccine never causes autism, however rarely. In this regard, epidemiologists are no different from any other scientist in that proof of a negative is impossible.

As with all epidemiological studies of any putative adverse event, the existence of a rare, idiosyncratic causal association cannot be entirely excluded. However, the existence of such a putative association between MMR vaccine and autism is at present entirely speculative.

Thank you.

[The prepared statement of Dr. Miller follows:]

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[GRAPHIC] [TIFF OMITTED] T6856.104

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Mr. Burton. Thank you, Dr. Miller.

Dr. Gershon.

Dr. Gershon. Thank you, Mr. Chairman.

I am Dr. Michael Gershon, professor of anatomy and cell biology at Columbia University in New York.

Life is often unfair. The unfairness of the life dealt to autistic children, however, is so unfair that it defies comprehension. The mental elements of autism, which may

sentence an innocent child to a life in virtual solitary confinement, are bad enough. To have to endure that sentence in gastrointestinal misery outdoes the trials of Job. The withdrawal from social contact that characterizes autism is so striking, moreover, that the abnormal behavior of afflicted children has historically tended to blind non-parental observers to symptoms from their gut, which in comparison, seem trivial.

Historically also, the possibility that there might be a pathophysiological link between the gut and the brain has not been considered, even by scientists who should have known enough to do so. Help to alleviate the gastrointestinal accompaniments of autism, therefore, has only recently been sought and investigation of the involvement of the bowel in autism begun.

Given that the involvement of the bowel in autism has not previously been studied, there is little that one can say right now about the causes of that involvement except that it is a topic worth considering. Certainly, the incidence of gastrointestinal problems in children with autism appears to be high and if one really looks for these conditions even higher. Professors Wakefield, Horvath, and their colleagues, therefore, have done a real service for patients and the biomedical community in publicizing the association of gastrointestinal abnormalities in autism.

At the start of a new field of research, such as the role of the gut in autism, one naturally formulates hypotheses that one can test. Hypotheses are very much a part of the scientific method. Unfortunately, it is relatively easy to construct an argument in support of a favored hypothesis, but an argument differs from evidence and should not be confused with it. An argument can serve to motivate hypothesis testing, but evidence is required for hypothesis confirmation.

The hypothesis that MMR vaccine is a cause of autism is supported at the moment by a well-crafted argument. There is, however, little or no hard evidence available to support that hypothesis. Furthermore, based on my understanding of gastrointestinal function and the nature of the blood brain barrier, I believe that it is unlikely that the hypothesis, as originally formulated by Wakefield and others, that MMR causes autism is correct.

The hypothesis that MMR is causally related to autism, which has been associated with Dr. Wakefield, postulates that the attenuated measles virus component of the vaccine persists in the bowel of those vaccine recipients destined to manifest autism as a result of their vaccination. The persistent measles virus is thought to elicit an immune response that is then postulated to increase the permeability of the intestinal epithelium, giving rise to a ``leak.''

This leak enables toxic materials--in particular, opioid

peptides--to be absorbed from the intestinal lumen. These toxins then enter the bloodstream and are carried to the developing brain. The so-called rogue peptides, which are derived from the gut, cross the blood-brain barrier and damage the developing brain, giving rise to autism.

The evidence that measles virus actually persists in the bowel is controversial. The idea that measles virus persists has been recently been supported by Drs. Wakefield and his collaborator, Dr. O'Leary, with data derived from sensitive molecular biological techniques, which suggest that the virus is present in the bowel, but in very low copy numbers.

These data are still largely unpublished, and the findings have not yet, to my knowledge, appeared in a peer-reviewed journal. Other investigators have not been able to reproduce the molecular observations. Furthermore, test samples containing coded amount of measles RNA from cultured cells and from transgenic mice--which express the human measles virus--that were sent to Dr. O'Leary by Dr. Michael Oldstone were not read with the effectiveness needed to support the claims of low copy numbers of virus persisting in the gut of vaccinated individuals with autism.

Oldstone has concluded that the record of performance would not be acceptable for certifying a clinical laboratory. The virological support for the hypothesis of measles virus persistence, therefore, is not established and cannot be considered so until it is independently confirmed.

The data supporting the next step--the leak of toxic opioid peptides into the body from the lumen of the bowel--is scanty at best. Urinary observations of such are unreliable.

The thought that inflammation damages the epithelial lining of the bowel, causing its permeability to increase, is plausible. On the other hand, there is no reason that a leak in the gut should be a one-way leak. Nor is there any explanation as to how a leak could be specific so as to let only some molecules through and not others of the same size and shape pass through.

No movement of peptides or proteins from the tissue fluid to the intestine has been detected in autism or as a result of MMR vaccination. Protein-losing enteropathy has not been reported to be associated with autism, nor has it been reported to be a sequela of MMR vaccination in any significant number of people.

On the other hand, if the bowel were to be permeable in a size manner so that the large molecules of the body do not get out, then small molecules from the gut would go both ways through the proposed hole. That would cause massive malnutrition and malabsorption in the patients, which has not been reported.

So the absence of a telltale protein-losing loss or a failure of absorption in patients en masse with autism and in

recipients of MMR vaccine thus suggests that the postulated leak of the gut admitting opioid peptides does not indeed occur. To paraphrase Sir Arthur Conan Doyle in Sherlock Holmes, the failure of these things to occur and the failure of absorption is the dog that did not bark. The postulated leak of the bowel is thus unlikely to occur or to be significant.

The idea that opioid peptides or other toxins enter the body from the bowel and cause autism overlooks another filter that is in place to remove them, and that filter is the liver. Everything the gut absorbs goes first to the liver as a consequence of the circulation. There is no evidence that MMR damages the liver. The postulated opioid peptides, therefore, would have to be absorbed in overwhelming amounts to overcome the ability of the liver to remove them. The liver is exceedingly good at removing opioids. There is no other toxicity noted in organs and the fact that the liver is there and is normal in patients with autism suggests that this postulated barrier is not overcome.

Finally, once the presumptively toxic peptides--if they ever could--overcome the barriers of the intestinal epithelium and the liver, which does not seem likely, the blood-brain barrier remains. That barrier is constituted by special vessels in the brain and it ought to be impenetrable to opioid peptides or other toxins. How these so-called toxins get across is unknown. One molecule that is large that does get across is leptin, which is a natural hormone, but it has its own transporter. No such molecules are known. So for a gut-derived peptide to be a cause of autism, one has to assume that a miracle occurs to cause the blood-brain barrier to open, like the Red Sea did for Moses and the Israelites during the exodus from Egypt.

Finally, there is no reason to assume that MMR is the only--or even the most likely--reason for an association between gastrointestinal disease to be associated with autism. The nervous system of the gut, the enteric nervous system, resembles the brain both structurally and chemically, and is known to share its fate in other conditions, including Alzheimer's and Parkinson's diseases.

It seems reasonable, therefore, to postulate that the incidence of gastrointestinal symptoms in children with autism is high because autism is a disease with manifestations in the gut as well as in the brain. Alternatively, a brain that functions abnormally because of autism may cause the bowel to function abnormally. Similarly, if there is a problem in the bowel, it can disturb the brain.

Let me tell you, Mr. Chairman, as I prepared for this talk, I became painfully aware of the kinds of problems that can happen in the bowel as the brain is disturbed. [Laughter.]

In summary, therefore, I think that there are alternative explanations for much of this and that the preponderance of

evidence and the nature of the function of the gut, liver, and blood-brain barrier combine to indicate that it is unlikely that the hypothesis associated with Dr. Wakefield that MMR vaccine causes autism is correct. The idea that the measles virus persists in the gut of vaccinated individuals is supported only by data that is controversial and has not been confirmed.

The proposal that the bowel leaks due to measles virus persistence and absorbs opioid peptides or other toxins assumes a one-way leak. Since leaks are intrinsically not one-way, but holes in a barrier, body proteins or ions would be expected to flow out and no such movement has been detected in MMR or autism.

The hypothesis that toxins are absorbed does not take filtration by the liver into account or explain why gut-derived peptides are not removed.

Finally, it does not explain why peptides can get through the blood-brain barrier to cause autism and there are alternatives which are more plausible that can explain the association of GI malfunction in autism that have nothing to do with MMR.

In closing, I would just like to say that I sympathize tremendously and empathize with patients with autism and their parents. But it may be counterproductive for patients with autism, their parents, and for the whole population to devote energy and resources single-mindedly to the pursuit of a single theory of autism, when that theory might be false. The effort diverts scarce resources from avenues that might be needed and productive and should be devoted to this terrible condition.

Thank you.

[The prepared statement of Dr. Gershon follows:]

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[GRAPHIC] [TIFF OMITTED] T6856.114

[GRAPHIC] [TIFF OMITTED] T6856.115

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Mr. Burton. Let me just start off by saying that I know just a couple of things. No. 1, there is an epidemic. There is a huge quantum leap in the number of children that are autistic. That is irrefutable. That is No. 1.

No. 2, I know that my grandson, Christian, was a normal child starting to speak and doing everything that was normal and 1 day he got the DPT shot, he got the MMR shot, he got the Hepatitis B shot, the Polio shot, and the Marcus Influenza shot, and 10 days later he had those bowel problems, had chronic diarrhea, ran around hitting his head against the wall, flapping his arms, and he could not talk anymore.

That may be just a coincidence, but it happened. I saw it with my own eyes, so something happened. Whether it was the MMR shot or the mercury that was in these other vaccines or a combination of the two, I do not know. But I do know that hundreds of thousands of children in this country and around the world are suffering because of autism, and many of them are suffering from autism shortly after having received one or more of these vaccines.

Dr. Haley, you said that there was about a 10-fold occurrence of autism in children who had the mercury vaccines and the MMR. I am not sure exactly how you said it.

Dr. Haley. I was not making any mention of the rate of autism.

Mr. Burton. What were you saying?

Dr. Haley. It is on the back page of the handout.

When you compare the toxicity against the bank of enzymes or against enzymes in a brain tissue, if you add the vaccines that do not contain thimerosal, they show the least amount of toxicity, essentially, very little at all.

Mr. Burton. Right.

Dr. Haley. If you use the same vaccine, only with thimerosal added as a preservative, they are tremendously much more toxic.

Mr. Burton. You said about 10 times, did you not?

Dr. Haley. I am being very conservative; 1 microliter of these vaccines will totally inhibit these enzymes. You can sometimes add 10 microliters of the non-thimerosal-containing vaccines and see just a few percent----

Mr. Burton. You also said that similar things occurred with the MMR vaccine.

Dr. Haley. We also measured the mercury level because some of the vaccines we received had been used a bit. We looked at the level of mercury. It fit what you would expect. There are low levels of mercury in the non-thimerosal-containing

vaccines. There is some in all of them. The ones that had thimerosal added were quite high.

The MMR came across as if it had no thimerosal added. There was a small amount in there. I think it would be similar to those that had no thimerosal added. There was mercury in there, but not very much.

Mr. Burton. There was mercury in the MMR vaccine?

Dr. Haley. Yes, but a very small amount.

Mr. Burton. But there was mercury in the vaccine?

Dr. Haley. Yes, but the toxicity----

Mr. Burton. Merck, when we called awhile ago, said that there was no mercury in the MMR vaccine. You are saying that there was a very small amount.

Dr. Haley. Yes, we found it. I would want to do 20 of them before I came up with an average, but we did find a small amount of mercury. It was very tiny, though.

The MMR vaccine, unlike those vaccines without thimerosal, was very toxic. It was as toxic as if it had thimerosal in it.

Mr. Burton. So would you say it was 10 times more toxic than a vaccine without thimerosal?

Dr. Haley. I would say so, yes.

Mr. Burton. Dr. Spitzer and Dr. Wakefield, I am sure you are squirming there. Would you like to make any kind of comment about what you just heard? [Laughter.]

Dr. Wakefield. Generally, Mr. Chairman, or in specific relation? [Laughter.]

Mr. Burton. The whole hypothesis of your research was pretty much trashed by the last two witnesses.

Dr. Wakefield. I think Dr. Miller confuses inference with implication. She says that implicit in what we had written was a hypothesis. That, unfortunately, was her inference rather than our implication.

What we have written--and this is one of the earliest articles where we articulated a hypothesis--I am afraid this is in scientific jargon--the hypothesis hypothesized that autistic enterocolitis is an emergent, inflammatory bowel disease that follows a low-dose compound viral exposure. Basically, that this subset of autism with an inflammatory disease is an emergent form of inflammatory bowel disease that follows a very atypical pattern of viral exposure that requires not one virus but an interaction between viruses and possibly other things as well.

And we go on in that same paper--and I will not go into the details because it is too much scientific jargon--but it comes back very much to what Dr. Bradstreet was talking about. If the developing immune system is impaired in some way from developing an appropriate anti-viral response to exposure to mercury or other vaccines, if it is skewed in the wrong direction, then it may behave aberrantly in the face of a virus.

I am very happy to provide Dr. Miller with a copy of this paper and I will include one for your records.

Mr. Burton. Thank you.

Dr. Spitzer.

Dr. Spitzer. I would first like to make a comment.

There has been implication about comparing benefits and costs or good and harm in this situation. The understandable zeal, as indicating in the Institute of Medicine report, of coming close to wiping out a disease and the sequela of measles through the measures that are being taken is a very laudable goal.

If we think, on the other hand, that say 10 percent only of autistic children are those in which we eventually find a link between the disease and that vaccine were the case, a conservative estimate is 150 children per 100,000 with autism--reducing it by 10 percent is reducing 15 near deaths, if you wish, in the community.

With respect to the other side of the coin, comparisons are almost always made, as I have read them recently in the literature, with no immunization at all as opposed to making the reference the best acceptable alternative, which is univalent measles vaccine. The grandchildren I have I want to have vaccinated, but with univalent unless it is clarified.

That would reduce in UK statistics, which I only give in a preliminary way--I was just looking at them last Friday for the first time--going from second to MMR meant a reduction of about 16 per 100,000 to usually zero or close to zero in developed countries like the UK. It really is about the same, even if only 10 percent of autistic children are affected.

That means it is important that we look at subsets, even small subsets. If we can prevent 10 percent of autism by a more judicious strategy of immunization, to that extent we will have balanced the ledger of harm.

Last, I would like to stress in my case, I call myself a worried agnostic. I do not know whether there is an association. I think the evidence leans slightly in the direction of supporting an association. Perhaps causation, but at least association. I only feel that I am involved in one cause, and that is the pursuit of truth through scientific, admissible science, even if it takes 4 or 5 years to get to the first step.

Mr. Burton. Thank you, Dr. Spitzer.

Mr. Waxman, do you have some questions?

Mr. Waxman. Yes, I do.

Thank you, Mr. Chairman.

Dr. Wakefield, Marie McCormick is the Chair of the Institute of Medicine's Committee on Immunization Safety Review. She said at the press conference at the release of the report that the MMR vaccine is as safe as a vaccine can get.

How do you respond?

Dr. Wakefield. That is a very interesting comment. It is rhetorical inasmuch--let me put it this way. When the vaccine was first put together in 1969, one of the concerns I had in particular was that of interaction of viruses one with another. It is called viral interference.

Mr. Waxman. Dr. Wakefield, we are limited to 5 minutes each, so I would really like a very terse and clear response.

Dr. Wakefield. When the MMR was first put together, it was evident that the viruses interacted one with another. That was assumed to be a benign process. That was a major mistake, in my impression. I do not believe that when you put them together it is a benign process. It alters the outcome from the vaccine, it alters the immune response.

Mr. Waxman. Do you think the MMR vaccine is as safe as a vaccine can get?

Dr. Wakefield. No, absolutely not.

Mr. Waxman. That is your view, but the Institute of Medicine is not the only organization that disagrees with you. Your work has also been scrutinized by the Medical Research Council and the American Academy of Pediatrics and none of them has found any evidence to support your hypothesis.

Dr. Miller, in your testimony, you demonstrate that the proportion of autistic children with regression or bowel symptoms has not changed over the period in which the MMR has been used in the UK and is also no different for children who have never had an MMR vaccination or those who developed autism after the vaccine.

What does that suggest about Dr. Wakefield's theory?

Dr. Miller. I obviously do not want to put hypotheses into Dr. Wakefield's mouth. The hypothesis I would infer that should be tested on the basis of his suggestion of an autistic enterocolitis syndrome is that there should have been an increase in the proportion of such cases with regression and bowel symptoms associated with the use of MMR vaccine. I cannot find that in a large sample. I find that at variance with any inferences I might make about what I would expect to have happened on the basis of Dr. Wakefield's theories.

I therefore have to come to what I believe is a reasonable conclusion that my observation does not support his hypothesis.

Mr. Waxman. In other words, your new findings show that MMR is not linked to bowel syndrome and is not linked to autism. And this research, combined with the IOM report, really show that there is no evidence to support a causal connection between autism and MMR.

We have limited resources to devote to this cause. As a public health official and an epidemiologist, do you think that more resources should be devoted to investigating the MMR-autism connection? Or are there better places to devote our resources?

Dr. Miller. As I said in my testimony, I think the question

of what is the cause of autism--it is a common condition and we need effective treatments--is extremely important to answer. I think that there have already been quite a number of resources devoted to the question of MMR and autism, both looking at the evidence by expert committees plus individuals like myself doing as best we can with epidemiological studies. These have been uniformly negative.

As I said in my oral testimony, one cannot rule out a rare idiosyncratic response. However, in relation to what is the major cause of autism, I am firmly of the view that MMR has been excluded as a major cause of autism. Therefore, I do not think it would be profitable to--if you like--hijack the research agenda to concentrate on answering this question, which is derived basically from speculation and unsubstantiated and, as yet, still unpublished evidence in relation to MMR and autism.

Mr. Waxman. Thank you.

Dr. Gershon, an important part of Dr. Wakefield's theory, as I understand it, is that the measles virus persists in the gut. Yet from what I understand, no other scientist has been able to replicate Dr. Wakefield's findings of the persistence of measles virus in the gut. Moreover, I also understand that Dr. O'Leary, Wakefield's associate who does the looking for the measles virus, was tested to see if he could correctly identify measles virus in infected samples and he failed that test.

Do you know if that is correct? If so, can you explain the significance of this?

Dr. Gershon. It is correct. And the significance of it is that the evidence we have heard--which is largely unpublished and is not supported or duplicated by other laboratories--is not adequate to support Dr. Wakefield's hypothesis. So the evidence that the persistence of measles virus goes on in the gut is simply unfounded at the moment.

Mr. Waxman. Mr. Chairman, I would like to ask unanimous consent if I could have another 5 minutes to pursue questions because I have a conflict and have to run to another meeting.

Mr. Burton. Go ahead.

Mr. Waxman. Dr. Haley, your research demonstrates thimerosal inhibits enzyme activity and that demonstrates that the thimerosal, in your experience, is dangerous to the enzyme in the petri dish.

Don't we need to know how much thimerosal is in the vaccine before we know whether it is dangerous to a human being?

Dr. Haley. Toxicity is always related to dose, but also size, the ability to clear it, the health of the patient, the metabolic status, if they were suffering from a spurious ailment it would be more toxic.

Mr. Waxman. So the research you are presenting today does not definitively answer the question of whether the amount of thimerosal in childhood immunizations is dangerous or not, does

it?
Dr. Haley. That it is dangerous?
Mr. Waxman. Yes.
Dr. Haley. I think if you consider the aspect that we are dealing with multiple toxicities and exposures to mercury from a lot of different sources that adding an abundance of mercury to a child----
Mr. Waxman. My question, though, is whether the amount of thimerosal in the childhood immunizations is dangerous, the amount that is in there. There may be other exposures.
Dr. Haley. The amount from the vaccine alone would probably be not enough by the data we have seen. But again, that would depend upon the health of the patient you are giving it to.
Mr. Burton. Would the gentleman yield?
Mr. Waxman. Sure.
Mr. Burton. Is there a cumulative effect of mercury----
Dr. Haley. Yes.
Mr. Burton. In other words, my grandson--and I appreciate you yielding--got nine shots. I think four or five of those shots he got on that 1 day contained mercury. They said that was 41 times what was normal.
Would that cumulative effect have an adverse impact?
Dr. Haley. Absolutely.
Mr. Burton. Did you hear that, Henry?
Mr. Waxman. What was that answer? [Laughter.]
Dr. Haley. There are a lot of reports out there with infants that have been exposed to excess ethyl mercury generating compounds.
Mr. Waxman. Are you aware of an abstract study funded by NIH that looked at the blood mercury levels of full-term infants following the administration of thimerosal-containing vaccines?
Dr. Haley. Yes, I am. My opinion on that is that blood mercury levels have been considered by many people not to be worth very much to the extent of mercury toxicity. It is a retention toxicity.
Mr. Waxman. I would like to read the conclusion of that abstract. ``Low levels of mercury can be detected in the blood of some full-term infants following the administration of vaccines containing thimerosal. None of the blood mercury levels observed in the studied infants exceeded the most recently revised lowest level of maternal blood mercury considered to represent a potentially significant exposure to the developing fetus.''
That seems to disagree with your testimony. That seems to be at odds with what you are saying.
Dr. Haley. If anybody is saying they can look at the level of mercury in blood after a vaccination and then come to the assumption that this did no harm to that patient, I sincerely disagree with them.

Mr. Waxman. Does the research you have represented today prove that the mercury in vaccines causes autism?

Dr. Haley. Absolutely not.

Mr. Waxman. In your testimony, you stated that infants cannot clear mercury from their bodies. But a recent study conducted by the University of Rochester testing mercury in infants found that mercury was detected in the infants' feces.

Don't these findings prove that infants can clear mercury from their bodies?

Dr. Haley. I did not say they could not, I said that they could not do it as well. They have reduced bilary transport. It takes a while for that to develop. And from what I understand, they get the vaccination on the day they are born.

Mr. Waxman. Dr. McDougle, first I want to begin by commending you for the excellent work you are doing to advance our understanding of how to treat autism. Much of your attention is focused on determining the causes of autism, and that is important, but it is also important to help individuals and families who are suffering now.

I understand you are in the middle of a 5-year grant to develop medications to treat the symptoms of autism. Can you give us a preliminary assessment of the effectiveness of some of the medications you are studying?

Dr. McDougle. Yes. I would say that the first study we completed was with a medication called Risparidone. Although the blind has not been broken yet and we are not aware of who was on which placebo or drug, certainly a number of children have improved and benefited with particular improvements in the areas of aggression, self-injury, irritability, and I think has ultimately improved their quality of life.

Mr. Waxman. So some of them are working?

Dr. McDougle. Yes.

Mr. Waxman. Thank you very much, Mr. Chairman and my colleagues.

Mr. Burton. I hope you did not miss the response from Dr. Haley on that one thing because we have asked this question of others when you were not in attendance, and that is that the mercury in the vaccines has a cumulative effect. If the child gets eight or nine shots in 1 day, as my grandson did, he is getting an exorbitant amount of mercury in one dose. In my grandson's case, 10 days later he was autistic.

Dr. Weldon.

Mr. Weldon. I want to thank all the witnesses. For me, personally, I am just trying to find out how we can direct our research funding better to try to get some answers to some of these questions.

Dr. Miller, you described the Public Health Lab as being a non-governmental public body. Do you get funding from the British Government, though?

Dr. Miller. Yes, in the same way the National Health

Service is funded by the British Government, but we are not an arm of government. Our relationship to the Department of Health and Government is the same as the UK National Health Service.

Mr. Weldon. Is all your funding from the government? Or does some of it come from other entities? Specifically, does any of it come from the pharmaceutical industry?

Dr. Miller. Our core funding comes from the government. As with the National Health Service, researchers like myself apply for funding from research agencies, research funds from the Department of Health. I have no commercial interests in any vaccine company. I do not act as a consultant or an advisor to a vaccine company. I do, along with other individuals, have research funds for specific studies, largely clinical trials, from vaccine companies. I have not been sponsored from any of the work that I do on autism from vaccine companies.

I should say that in relation to the circumstances under which any funding comes from such commercial sources, the legal department of the Public Health Laboratory Service draws up a very stringent contract with the commercial company to ensure that there is total scientific independence of the PHLS in publication and interpretation of those results. This is a standard procedure for organizations such as the PHLS.

Mr. Weldon. So you are saying that the funding comes from the British Government and some of it does come from pharmaceutical companies, but you have these----

Dr. Miller. A small amount for specific research projects.

I am also an advisor to the Medicine Control Agency, that is similar to the FDA. And as a requirement for that, we have a declaration of interest. Should members of the committee wish to see the funding I have received and for what purposes, then they are free to view that. I am not sure if it is on the MCA Web site.

So there is a full declaration of interest. The ability to provide independent scientific advice is scrutinized by the MCA in relation to the type of financial benefit that is received for research studies from companies. I have not been prevented from having any input over advisory matters in relation to the research funding that I have received.

I should say, it is a very small proportion of the total amount I have received for research studies.

Mr. Weldon. It would be very comforting to me if the PHLS would just spend $500,000 and try to recruit 50 kids with autistic spectrum disorder and gastrointestinal symptoms and just scope them and try to duplicate his findings. It is very little comfort to me, all these epidemiologic studies, because the hypothesis is not that MMR causes all forms of autism. If you are operating under the assumption that MMR causes a small percentage of the cases of autism, then that may be very, very difficult to detect in an epidemiologic study.

If the British Government is all concerned about

vaccination rates declining because of Wakefield's findings, why don't they just scope 50 kids? What is the problem?

Dr. Miller. I would like to say first of all that you have put your finger on the nub of the question here. I think you have accepted that the epidemiological evidence has already excluded MMR as a common cause of autism. I said in my testimony that it is impossible epidemiologically to prove that it could never cause it.

So the question is, for how rare an event would you like a study to be set up to exclude or to find that sort of risk?

For the purposes of spending public money, if one has excluded MMR as a frequent cause of autism----

Mr. Weldon. I would like to interrupt you, because I have a limited amount of time.

He came in my office and showed me the pictures. I have spoken to people. I am an internist. These kids have florid inflammatory bowel disease. Why can't somebody duplicate this study?

We have this poor, lone guy coming here constantly, year in and year out. [Laughter.]

And Dr. O'Leary, might I say, is the guy who identified Herpes Simplex Type A. He came here to the NIH and all of the people at NIH supposedly dismissed it as being invalid and ultimately it was found to be true that Herpes Simplex Type A causes carposisarcoma. O'Leary is a very, very reputable scientist.

Why can't we repeat O'Leary's data?

Dr. Miller. First of all, we have to wait to see the virological findings published in a peer-review journal. As Dr. Gershon said, we have not yet seen those.

The Public Health Laboratory Service, as I mentioned, its remit is the national diagnosis, surveillance, and prevention of communicable disease. Autistic enterocolitis, as far as I am aware, is not demonstrated to be a communicable disease, nor indeed to result from vaccination.

Now whether there is a syndrome called autistic enterocolitis which has distinctive pathological features, fenotific presentation is another question. And maybe gastroenterologists, in combination with autism experts should be looking at that. It is not a question for PHLS.

Mr. Weldon. The responsibility to duplicate his work is not something that your department would----

Dr. Miller. Our responsibility would relate to the question, if there is such a syndrome, Is there evidence that it is associated with MMR?

Analyses of that has come to the conclusion that no--whether or not there is such a syndrome, whether or not it has relevance to the current prevalence of autism is another question, and academic institutions with expert gastroenterologists and autism experts may indeed be looking at

this.

I would say the Medical Research Council has funded a large study to look at the question of etiology of autism and what the risk facts are to try to throw some light on it, but it is not a question related to vaccines or communicable disease.

Mr. Weldon. I have some questions for Dr. Gershon.

This is not published, but I have been told by some of the people doing research in treating children with autism that a substantial percentage of them do have elevation in their liver function tests.

If that were published and proved to be true, would that affect your opinion regarding this theory of these neuroactive peptides?

Dr. Gershon. It would affect my opinion if the elevation of liver function tests were such that it would affect the ability of the liver to act as a filter.

Mr. Weldon. So you would want to see very significant elevations, not very mild elevations.

Dr. Gershon. For example, jaundice.

Mr. Weldon. You would want to see jaundice?

Dr. Gershon. I would like to see some evidence that the liver is failing in its job as a filter. I would also like to have some evidence that material is moving from into the gut from the body. I would like to see some evidence that the intestinal epithelial barrier is failing. And I would like to see some mechanism to get whatever toxins are so-called absorbed through the blood-brain barrier.

Mr. Weldon. Regarding the blood-brain barrier, it was brought to my attention that a Dr. Connolly published in the Journal of Pediatrics in May 1999. Maybe you might be familiar with this study. The title of the article was ``Serum Autoantibodies to Brain in Landau-Klefner Variant, Autism, and Other Neurologic Disorders.'' It was basically showing antibodies to brain endothelium.

Are you familiar with that study at all?

Dr. Gershon. I have seen the study.

Mr. Weldon. That does not affect your opinion at all about this theory? That study has no impact?

To me, that study suggests that there could be a possible link and explanation here. I am not saying there is, as a scientist myself. I think I would want to see more research. But you dismiss the theory outright, and that study suggested to me that in some of these kids there may actually be a breakdown in the blood-brain barrier.

Dr. Gershon. That study did not demonstrate a breakdown in the blood-brain barrier. It showed autoantibodies. That is a different issue.

The existence of antibodies--it could be an autoimmune mechanism, I guess, is what you are implying--that helps to break the blood-brain barrier down. There could be a lot of

things.

Every step along the way, an improbable event could happen. But there are a lot of steps along the way.

I would like to direct your attention to two other points. One part of my testimony and one further one.

I pointed out that there are alternative mechanisms by which to explain the association between bowel disease and autism. One need not postulate a set of improbable mechanisms to get toxins into the brain. The bowel and the brain communicate by other means. The fact that both are involved in autism is, to me, established. As I said at the outset, Professor Wakefield is to be commended for publicizing that.

On the other hand, I do not think it is established that the reason for the link is MMR. The bowel has many mechanisms of affecting the brain and the brain the bowel. The same disease, autism, can give rise to symptoms in both places.

The other thing, in regard to what you said about scoping--if the British Government or our Government were to scope a lot of children and find inflammation in the bowel, I would expect that they would in fact find that. Nobody, to my knowledge, is quarrelling with the aspect of what Dr. Wakefield has published, which is that some children with autism have in fact inflammatory bowel disease. That is not in contention. What is in contention is that resulted from MMR and that there is persistent measles virus in it, that what they detect is not just passenger leftover from the vaccine that is not real virus.

It is very hard to show that. And Professor O'Leary--I am not saying he is not a good molecular biologist. I think he is an excellent molecular biologist. But when asked with coded samples that were sent to him by Michael Oldstone to show that he could detect these low copy numbers which are postulated, he did not pass the test. He identified successive samples differently on different occasions. He missed some diagnoses. When there were very large amounts of measles virus, he could detect it, as could everybody else.

And here we have a situation where other laboratories are trying to duplicate this finding of measles virus, and they are not doing it. Yet this laboratory has failed the test of coded samples to do it.

Mr. Weldon. Mr. Chairman, could we have Dr. Wakefield?

Mr. Burton. Dr. Wakefield.

Dr. Wakefield. I am sorry, I have to take issue with that. That is a complete misrepresentation of the data.

First, Dr. Gershon suggests that other people have looked in the intestine of these children for the detection of measles virus. No one has done that, to my knowledge. So the only laboratory that has looked in the intestinal biopsies of these children is Dr. O'Leary's laboratory. Other people have looked in the intestines of children with Crohn's Disease for evidence

of measles virus, which we have suggested. Indeed, one of the people on the panel of the IOM presented data at the American Academy of Pediatrics last June showing that they had could identify measles virus genetic material in children with Crohn's Disease and some controls.

I want that to go on record. That has been presented.

So independently groups from Canada and from Japan have found measles virus in the intestines of children with inflammatory bowel disease.

The issue of the study with Michael Oldstone was not as it was portrayed. I am very, very concerned that Michael Oldstone should breach confidence of data that has not been presented in any forum, and has not even actually been finally analyzed. But in fact when they did analyze them, the only discrepancy was that there was no contamination at all, but a very, very, very low copy number of the virus, which the tacman PCR system--which Dr. O'Leary helped develop--detects the virus found that they might be able to detect it in two out of three samples.

This is merely a function of low copy viral detection. It is now a function of the ability of us to find viruses in vanishing small amounts with technology that is not available in Dr. Oldstone's lab. So the data have not been presented fairly, and I want that to go on record.

Mr. Burton. Dr. Weldon, you can keep the time, but I want to make a comment or two because I have no more questions for the panel. Then I will let you conclude the questioning.

A lot of kids are ruined for life. I detect a close-minded attitude on something that is so important--not to one child, my grandson, but to hundreds of thousands of kids. Every 3 hours in California--it was every 6 hours just about a year ago--but every 3 hours in California, there is a new child with autism. Every 3 hours.

It is a horrible, horrible thing to have to live with, not just for the child but for the parents, the grandparents, and everybody else, not to mention the cost.

So we have some people that have a closed mind about various theories about this. I think this is a time for everybody to be open to almost any theory, if it is cost-effective, to look at it to see if it can be proved or disproved.

I want to tell you a story. Louis Pasteur was kicked out of the medical profession and ostracized for 17 years and then he was knighted. And it was because everybody had a closed mind.

I have a very good friend who lives in Australia. His name is Dr. Barry Marshall. I do not know if you have ever heard of him or not. But I went to Africa and I was in the jungles of Angola and I came down with a bug, I thought, because I could not eat anything or keep it down for 2 years. It was awful. So I went to gastroenterologists. I went to several of them. And they all said it was my nerves and strain on my body. They gave

me Zantac and Prilosec and everything else under the sun.

Then I read this article about this guy named Barry Marshall. I think it was in one of the major publications. He was a scientist doctor from Australia. He said that the stomach problems in 90 percent of the people in the world was caused by a bacteria. Everybody said that a bacteria cannot live in the stomach.

He went and gave a speech to a symposium in Belgium. After he gave the speech--or right near the end--they literally started laughing at him because it was impossible for a bacteria to live in the lining of the stomach and he was crazy. So he went home and drank the bacteria--not unlike what Louis Pasteur did. He went home and drank it and got deathly ill and cured himself with the combination that he gave me.

I went down to see him after 2 years of suffering and he tested me. My doctor said I didn't have that. But I went to see him and he gave me this concoction of bismuth and antibiotics and something else. I took it for 2 weeks and I have not had a problem since.

But the close-minded doctors who were experts, who had all the answers, told me that I could not be cured, that I had to take these stomach pills for the rest of my life. All I can tell you is that we have a problem with kids that is humongous. It is going to affect the whole world if we do not do something because we are vaccinating kids all over the world. If mercury or the MMR vaccine or whatever it is is causing it, we need to find out and we need to find out pretty darn quickly.

For people to have closed minds when 1 out of 150 or 200 kids in Oregon or 1 out of 400 in the United States or 1 in 500 in the United Kingdom are coming down with autism is almost criminal. You ought to explore everything to find out what the answer is.

With that, I will shut up.

[Applause.]

Mr. Burton. Dr. Weldon.

Mr. Weldon. I just have a couple of quick followup questions.

Dr. Wakefield, Dr. O'Leary came in my office and showed me his PCR data, all the different versions of that. I think he ran eight different types of tests. Why hasn't that been published yet? We have had Dr. Gershon point that out repeatedly that it has not been published. What is the problem?

Dr. Wakefield. There is no problem. It is being presented for the first time at the American Gastroenterological Association in Atlanta in May. It has been peer-reviewed and we will see how that goes. But it is awaiting publication at the moment.

We have been asked to provide strain-specific sequencing. In other words, the acceptance is that the virus may well be there. I sat down with Michael Oldstone himself who said that

he accepted that we found the virus. NIH's measles expert who came to troubleshoot this said that the virus is there. But the reviewers have asked for strain-specific sequencing. Those studies are being conducted at the moment and we will put those into the papers. It is an entirely reasonable question and one that we are answering.

Mr. Weldon. So you expect publication after that issue is decided?

Dr. Wakefield. Once we have addressed that issue, yes.

Mr. Weldon. Just one more question for you, Dr. Miller.

Were you on the original panel that approved the MMR in England?

Dr. Miller. No, I had no role in that at all.

Mr. Weldon. That is all I have, Mr. Chairman. Thank you.

Mr. Burton. I want to thank you all very much. You have been very patient. You have been sitting for a long time. You have been very helpful.

We will submit all your statements and all your comments to the health agencies here. We will continue to fight on to try to find a solution to this problem, with your help.

Thank you.

We have one more witness who could not be with us tomorrow, Dr. McCormick from the Institute of Medicine. She is the chairman who did the report that we had heard about.

Dr. Weldon, you can stay for Dr. McCormick, I hope. She was the chairman of the committee that did the report that was recently released. I need you.

[Witnesses sworn.]

Mr. Burton. Do you have an opening statement, Dr. McCormick?

Dr. McCormick. Yes, I do.

Mr. Burton. You are recognized.

STATEMENT OF MARIE MCCORMICK, MDSCD, CHAIR, COMMITTEE ON IMMUNIZATION SAFETY REVIEW, INSTITUTE OF MEDICINE, ACCOMPANIED BY WILLIAM COLGLAZIER, EXECUTIVE OFFICER, NATIONAL ACADEMY OF SCIENCES; AND SUSANNE STOIBER, EXECUTIVE OFFICER

Dr. McCormick. Good afternoon, Mr. Chairman and members of the committee.

My name is Marie McCormick. I am a professor and Chair of the Department of Maternal and Child Health at Harvard School of Public Health and I Chair the Institute of Medicine's Committee on Immunization Safety Review, which released its report on MMR Vaccine and Autism on Monday, April 23rd. I appreciate the opportunity to provide testimony to you based on the findings of this report. A copy of my testimony and the executive summary has been submitted for the record.

Dr. William Colglazier, executive officer of the National Academy of Sciences, and Ms. Susanne Stoiber, executive officer

of the Institute of Medicine accompany me.

As I mentioned, two committee members are here, Dr. Steve Goodman and Dr. Constantine Gatsonis.

The genesis of this report was a December 1999 discussion between the CDC and the IOM regarding the need for an independent group to examine vaccine safety concerns. The CDC and NIH formally engaged the services of the Institute of Medicine in September 2000, which in turn appointed the committee in November 2000.

The committee is comprised of 15 members with expertise in pediatrics, immunology, neurology, infectious disease, epidemiology, biostatistics, public health, genetics, ethics, risk perception, and communication. To preclude any real or perceived conflicts of interest, committee members were subject to strict selection criteria that excluded anyone who had participated in research on vaccine safety, received funding from vaccine manufacturers or their parent companies, or served on vaccine advisory committees.

The committee is charged with examining three vaccine safety issues each year for 3 years. The committee was asked to assess the scientific plausibility of the safety concern, the significance of the issue in a broader social context, and to suggest appropriate actions. The first hypothesis the committee was asked to consider is the linkage between MMR vaccine and autism.

The MMR vaccine has been extremely successful in virtually eliminating measles, mumps, and rubella in the United States. Measles cases, for example, dropped from over 400,000 per year in the pre-vaccine era to only 100 in 1999.

Some are concerned, though, that the MMR vaccine might cause autistic spectrum disorders. These are incurable, permanent, and serious developmental problems in children and adults. Scientists generally agree that most cases of autistic spectrum disorders result from events that occur in the prenatal period or shortly after birth. However, concern arises about the MMR vaccine because autistic symptoms typically become more evident in the child's second year, about the same time the MMR vaccine is first administered.

A growing body of work has examined this subject. In a study published in the Lancet in 1998, researchers describe 12 children who developed behavioral problems, including autism, shortly after receiving the MMR vaccine. Since then, this group and others have further examined this potential relationship.

To evaluate the hypothesis on MMR vaccine and autistic spectrum disorders, the committee conducted an extensive review of the published, peer-reviewed scientific and medical literature. We held an open scientific meeting including a broad group of researchers and vaccine safety advocates. Finally, a working group of the committee conferred with parents of autistic children and vaccine safety advocates to

discuss their concerns.

The committee concludes that the evidence favors rejection of a causal relationship at the population level between MMR vaccine and autistic spectrum disorders. The committee bases this conclusion on the following evidence: a consistent body of epidemiological evidence shows no association at a population level between MMR vaccine and autistic spectrum disorders; the original case series of children with autistic spectrum disorders and bowel symptoms and other available case reports are uninformative with respect to causality; biologic models are fragmentary; and there is no relevant animal model.

However, the committee notes that its conclusion does not exclude the possibility that MMR vaccine could in rare cases contribute to autistic spectrum disorders resulting in a very small number of affected children. This possibility arises because the epidemiological evidence lacks the precision to assess rare occurrences and the proposed biological models, although far from established, are nevertheless not disproved.

In its significance assessment, the committee considered the burden of measles, mumps, and rubella infections, the burden of autistic spectrum disorders, and the level of public concern. Measles, mumps, and rubella can lead to significant morbidity and mortality and treatment of these diseases is limited.

Outbreaks of measles, mumps, or rubella disease could easily occur now were MMR immunization rates to decline as a result of fears about MMR. Yet, because MMR vaccine is a mandatory vaccine that is administered to healthy children--in part, as a public health measure to protect others--the responsibility of the Government to ensure the safety of the vaccine is high. The burden of autism, an incurable and serious disorder, requires consideration of all possible etiologies. In addition, the level of public concern about MMR vaccine safety is high.

Because of the limitations of the evidence, the significant public concern surrounding the issue, the risk of disease outbreaks if immunization rates fall, and the burden of autism, the committee recommends that further attention be given to this matter.

Specific recommendations regarding policy review, research and surveillance, and communication follow.

In terms of policy review, the committee does not recommend a policy review at this time of the licensure of the MMR vaccine or of the current schedule and recommendations for administration of MMR.

The committee concludes that further targeted research on the possible contribution of MMR vaccine to autistic spectrum disorders in some children is warranted. For example: use accepted case definitions and assessment protocols for autistic spectrum disorders to enhance the precision and comparability

of research results; explore whether exposure to MMR vaccine is a risk factor for autistic spectrum disorders in some children; explore whether measles vaccine-strain virus is present in the intestines of some autistic children; and encourage all who submit reports tot he Vaccine Adverse Event Reporting System about MMR vaccine and autism to provide as much detail and documentation as possible.

The committee heard from parents that obtaining unbiased and accurate information on the possible relationship between MMR vaccine and autistic spectrum disorder has been difficult. The committee recommends that governmental and professional organizations, CDC and the FDA in particular, review some of the most prominent forms of communication regarding the relationship between MMR vaccine and autism spectrum disorder. Direct input from parents and other stakeholders would be invaluable in conducting an evaluation of communication tools.

In its discussion of recommendations, the committee identified more general concerns that it could not adequately address in this report. It intends to address these in the future.

This concludes my oral statement and I would be happy to answer any questions.

[Note.--A copy of the Institute of Medicine publication entitled, ``Immunization Safety Review,'' may be found in committee files, or obtained by calling the National Academy Press at 1-800-624-6242.]

[The prepared statement of Dr. McCormick follows:]

[GRAPHIC] [TIFF OMITTED] T6856.125

[GRAPHIC] [TIFF OMITTED] T6856.126

[GRAPHIC] [TIFF OMITTED] T6856.127

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[GRAPHIC] [TIFF OMITTED] T6856.131

[GRAPHIC] [TIFF OMITTED] T6856.132

[GRAPHIC] [TIFF OMITTED] T6856.133

Mr. Burton. Thank you, Dr. McCormick.

What does this mean? ``However, the committee notes that its conclusion does not exclude the possibility that MMR vaccine could contribute to ASD in a small number of children because the epidemiological evidence lacks the precision to

assess rare occurrences of a response to MMR vaccine leading to ASD and the proposed biological models linking MMR vaccine to ASD, although far from established, are nevertheless not disproved.''

What does that mean?

Dr. McCormick. What that means, I think is what Dr. Miller said, that the level of analysis you are able to do could not rule out rare occurrences.

In terms of the biological model, we were talking specifically about the type of evidence Dr. Wakefield had presented. Unfortunately, because it was an open meeting, Dr. Wakefield was reluctant to present his full range of data because it would also have to be put out on the Web and it was considered pre-published.

Mr. Burton. I understand, and I do not want to cut you off, I just want to bear on this question.

On television all across the country, we saw yesterday that our health agencies and your committee said that the MMR vaccine was not going to be a contributing factor and could not cause autism.

Dr. McCormick. Based on the evidence that we got to the committee, that is true.

Mr. Burton. What does this mean, that you just said?

Dr. McCormick. We are leaving the door open for additional evidence because we could not hear the evidence that was being presented. We were not provided the evidence on the presence of measles vaccine. It does not mean that that whole theory is going to be proven, we are just saying----

Mr. Burton. Let me read this to you again, ``although far from established, are nevertheless not disproved.''

So what you are saying is that the causal link is not disproved. Is that right?

Dr. McCormick. No, we are saying it is not established.

Mr. Burton. But you are saying that it is not disproved.

Dr. McCormick. It is not established, either.

Mr. Burton. So you do not know, do you? Can you say categorically, 100 percent, that the MMR vaccine is not a contributing factor to autism? Can you say that?

Dr. McCormick. No, because we said in rare cases.

Mr. Burton. That is the point. You put out a report to the people of this country saying that it does not cause autism, there is no causal link, and then you have an out in the back of the thing. You cannot tell me, the committee chairman, under oath, that there is no causal link because you just do not know, do you?

Dr. McCormick. Because in part we were not provided the evidence----

Mr. Burton. Do you know?

Dr. McCormick. I do not know.

Mr. Burton. Then why did you say so in the report?

Dr. McCormick. Because the bulk of the evidence----

Mr. Burton. Because the bulk of the evidence? But you do not know. You just said that.

Dr. McCormick. In fact, most of the reports I saw indicated that.

Mr. Burton. Do you know what it is like to have an autistic child?

Dr. McCormick. I do.

Mr. Burton. You have an autistic child?

Dr. McCormick. No. My brother has two.

Mr. Burton. Your brother has two?

Dr. McCormick. Yes.

Mr. Burton. Then you know what he goes through?

Dr. McCormick. Yes.

Mr. Burton. Do you know how many kids are getting autism? Every 3 hours in California, there is a new child with autism. It used to be every 6 hours. You used to have 1 out of every 10,000 kids who were autistic.

We do not know all the answers. We do not know if the mercury, the thimerosal in the vaccinations are causing autism. You do not know for sure whether the MMR vaccine is causing autism.

Dr. McCormick. I know it is not causing most of the cases of autism.

Mr. Burton. But the point is, if you are the one that it does cause--if your child is the one that does get it and we find out there is a causal link, isn't that awful? Isn't that awful?

I just have to tell you, as I said to the last panel--and you heard what I said about Louis Pasteur and Dr. Barry Marshall, didn't you?

Dr. McCormick. Yes.

Mr. Burton. This is such a serious thing with hundreds of thousands of people that are going to be autistic and be a burden on society for the rest of their lives, it is going to cost us trillions of dollars--when you talk about 1 in 250 or 500 kids--they are going to grow up and they are going to be a burden on society. We should not close the door to any avenue of research to find out what is causing that.

It is not being caused just by genetics, I do not believe, because you are having a huge quantum increase in it. Something is causing it and we ought to be open to everything.

Dr. McCormick. In fact, the report, sir, does recommend continued attention to this linkage.

Mr. Burton. I know, but that is not the point.

Of course, I read that. But most people in this country did not. All they heard on television was that there is no causal link, none. I heard doctors saying that this has been studied by experts not connected to the pharmaceutical industry.

Now let me ask another question, because this is pretty

important, too.

You sent this report out to a group of people to look at, didn't you?

Dr. McCormick. I did not send out the report.

Mr. Burton. Somebody sent it out, did they not?

Ms. Stoiber. I am sorry. I would answer those questions because the committee is not responsible, the Institution is.

Mr. Burton. Stand up and be sworn.

[Witness sworn.]

Mr. Burton. Did you send out the report to be reviewed?

Ms. Stoiber. Not personally, but institutionally, we sent out the report.

Mr. Burton. And you sent it to Linda Cowan, Eric Fombonne, Neal Halsey, Samuel Katz, among others, right?

Ms. Stoiber. That is correct.

Mr. Burton. Neal Halsey and Samuel Katz are people that do not subscribe to the theory that the MMR vaccine might be a contributing factor, right?

Ms. Stoiber. I have no idea, sir, what they subscribe to.

Mr. Burton. Well, let me tell you they do. Those two people do not believe that the MMR vaccine is a contributing factor to autism.

You sent it to them for review, and I presume they went through it and might have made some modifications--I do not know--but you did not send it to Dr. Wakefield who is on the other side of the issue. Why?

Ms. Stoiber. When we select a review panel--and there are 15 reviewers to this report--we try to select people from all sides of an issue, those who believe there are connections and those who believe there may not be connections. I think in fact there are three reviewers that were specifically selected because they have the confidence and have been engaged in the research that would in fact be supported by the advocates of this connection.

We take into account all of the reviews carefully. The reviewer's comments are blinded. We do not know who they are when we receive them. And no reviewer ever has the power to change a word in our report.

Mr. Burton. Were any of these people presenters at the conference?

Ms. Stoiber. Yes, two of the people were.

Mr. Burton. Who were they?

Ms. Stoiber. Dr. Fombonne and Dr. Miller.

Mr. Burton. Did Dr. Halsey or Katz, either one, present?

Ms. Stoiber. They did not.

Mr. Burton. They did not?

Ms. Stoiber. No.

Mr. Burton. Halsey and Katz have financial interests in pharmaceutical companies. Fombonne and Miller did present?

Ms. Stoiber. That is correct.

Mr. Burton. And they did not agree with the thesis----

Ms. Stoiber. I am sorry. Dr. Miller did not present. It was Dr. Volkmar, Ward, and Fombonne.

Mr. Burton. Dr. Fombonne was one of the people who reviewed it and he was a presenter on the other side of the issue, as I recall. He believed the MMR vaccine was not in any way associated with the autism.

Ms. Stoiber. He reported the results of his study, which showed no association.

Mr. Burton. And Dr. Wakefield was on the other side of the issue. He was a presenter, as well, but he was not given a copy of this to review.

Ms. Stoiber. The reviewers, sir, were not selected because they were presenters, but were selected because they represented a wide spectrum of views on the subject. The fact that two of them also presented was totally coincidental and they were selected for their ability to provide a broad assessment of the evidence.

Again, we tried to balance, always, the reviewers selected so that those who have opposing views are equally and well represented among the reviewers.

Mr. Burton. Do you know if any of the people that reviewed it--other than the ones I mentioned--had financial interests or connections with any pharmaceutical companies that produced the MMR vaccine?

Ms. Stoiber. To the best of our knowledge, they do not. In fact, we do not do the same kind of extensive review of the financial holdings of reviewers that we do of committee members. But to the best of our knowledge, aside from the fact that they may own mutual funds that hold pharmaceutical stocks, there is no reason to believe there are any financial ties.

Mr. Burton. In the past, we have subpoenaed from the health agencies--and we are still going through them--the financial disclosure forms of people in the decisionmaking process who make decisions on these vaccines. So therefore I would like to know--and we would like for the Institute of Medicine to contact the people on the review committee and ask them to submit to us any holdings they have in pharmaceutical companies. If I have to, I will subpoena that.

Would you tell them? And any that are connected with an institution that gets grants from the pharmaceutical companies.

Ms. Stoiber. I will first say, sir, that they are not in a decisionmaking process.

Mr. Burton. I understand. They were in the review process.

Ms. Stoiber. They solely reviewed. And after their reviews were received, the committee had the ability to assess whether or not to accept any of that advice. Some was accepted and some was rejected.

Mr. Burton. When it was accepted, did it involve any changes?

Ms. Stoiber. Very few.

Mr. Burton. Were any changes made after----

Ms. Stoiber. Always changes are made in response to review because reviewers point out weaknesses in the analysis, they point out lack of clarity in the expression, but I can say to you that no central conclusions changed during the course of review.

Mr. Burton. We will take a look at that and I will make the decision on that after I review all this. But I want to know about the reviewers and what recommendations they made and changes. I would like to have that. I would also like to know whether or not they had any interest or got any grants of any kind from any pharmaceutical companies. I would also like to have that information from any of the people on the original report panel.

According to our request, we wanted to make sure that these people are insulted who are working on this report from any influence being exerted by any pharmaceutical company. I would like to find out if any of the people who were on that panel who wrote the report if they have any financial interest or ties and whether they got any grants from any pharmaceutical companies.

I wish you would take that request back to the agency and tell them that, if necessary, we will be glad to send them a subpoena to get this information.

Ms. Stoiber. I can assure you that no member of the committee has any financial ties to the pharmaceutical industry.

Mr. Burton. How about grants?

Ms. Stoiber. Or grants. I do not have the authority to tell you that we can deliver the financial background of reviewers, but I will certainly take that back the Academy and assess it and get back to you.

Mr. Burton. You can tell them that I would like to have it and if they choose not to send it, I will send them a subpoena and I will get it.

Ms. Stoiber. I think we do not have the detailed financial statements of the reviewers.

Mr. Burton. Then how can you tell me right now that they do not have any financial interests?

Ms. Stoiber. Of the reviewers.

Mr. Burton. How about the people on the panel?

Ms. Stoiber. For those on the panel, we have extensive financial disclosure.

Mr. Burton. Then I want it.

Ms. Stoiber. What we do not have is the same kind of information for people who served as reviewers.

Mr. Burton. We want that and we want to know if they got any grants of any kind from any of the pharmaceutical companies.

Dr. Weldon, sorry to take so much time.

Mr. Weldon. Mr. Chairman, I ask unanimous consent to introduce for the record a statement from the Middlebrook Family of Indialantic, FL, in my congressional district, who have struggled with autism.

Mr. Burton. Without objection, that prepared statement will appear in the record.

[The prepared statement of Mr. and Mrs. Middlebrook follows:]

[GRAPHIC] [TIFF OMITTED] T6856.134

Mr. Weldon. Dr. McCormick, you were quoted on CNN as saying that the MMR vaccine is as safe as a vaccine can get. Is that correct?

Dr. McCormick. Yes.

Mr. Weldon. If you were to find that the data, that the epidemiologic studies that have been quoted today--which I assume you reviewed and that played a key role in your decisionmaking process--correct me if I am wrong.

Dr. McCormick. We were not aware of Dr. Miller's study at the time of the decision.

Mr. Weldon. How about the Taylor study?

Dr. McCormick. Taylor, yes.

Mr. Weldon. If you were to find that any of that data was defective, would that affect your opinion on the safety of the MMR vaccine?

Dr. McCormick. First, I think in terms of the statement that it is as safe as any vaccine can be, it is made with the understanding that all vaccines carry some degree of risk and side effects.

Mr. Weldon. Right.

Dr. McCormick. We carefully looked over that epidemiologic data twice. Not only did we have a prepared review, but both Dr. Goodman and Dr. Gatsonis looked at that information again separately to look at the quality of that information.

I think any single study can be critiqued. It was the fact that there were multiple studies with different kinds of designs, looking at different populations, addressing different parts of the pie, and all the results came out the same way. It was the consistency of cross-studies that was impressive, not that any single study could not have been critiqued as not having addressed all issues.

Mr. Weldon. Were you looking at their studies or their raw data?

Dr. McCormick. We were looking at the studies.

Mr. Weldon. Did you have access to the data?

Dr. McCormick. No.

Mr. Weldon. The committee has asked for the data and it has not been made available to us.

Dr. McCormick. We did not have the data.

Mr. Weldon. Mr. Chairman, that is the only question I have.

Mr. Burton. Let me just ask one or two more questions.

I have here a list of the people that were on the committee. The University of Washington School of Medicine, Christopher Wilson--he is a professor there. Does the University of Washington School of Medicine get any grants from any pharmaceutical companies?

Or how about Alfred Berg, University of Washington? Or Bennet Shaywitz, Yale University? Or Gerald Medoff, professor of medicine and microbiology at Washington University School of Medicine? Or Columbia? Or Michigan? Or George Washington?

All those schools get grants from pharmaceutical companies, don't they? And don't those people who work for those universities that get those grants know those grants are paying for a lot of the research they are doing?

Ms. Stoiber. Our bias and conflict of interest excludes only the personal situation of the individual serving on the committee, their grant support or grant support in their immediate labs. Clearly, it would be very difficult to compose a committee of experts if you excluded every University in the country because they receive some grant somewhere in the university from the pharmaceutical industry.

Mr. Burton. I understand that. But the problem is, if you are getting a large grant from a pharmaceutical company, and you know that your laboratory at whatever facility you are working at or employed by is getting that grant, and you know that they have an interest in the decision being made, don't you think that would wear a little bit on the processes on the people on the commission?

Ms. Stoiber. I genuinely do not. I think these individuals took this as the very highest level of responsibility to look at the science on its face and were not influenced by external factors of that nature. But clearly opinions could differ on that.

Mr. Burton. Thank you.

Mr. Waxman.

Mr. Waxman. Dr. McCormick, a number of times during this hearing Mr. Burton has impugned the integrity of the Institute of Medicine's committee. As I understand it, the committee established strict criteria for committee membership. No one with any ties to vaccine manufacturers or their parent companies was allowed to be on the committee. No one who had ever served on a vaccine advisory committee was allowed to be on the committee. Even people who had provided expert testimony or had published about vaccine safety were excluded from the committee.

Yet the chairman insists that the report is tainted by bias. He says that after the committee wrote the report the Institute sent it out to a panel of reviewers that contained individuals with conflicts of interest and that those

individuals have biased this report.

My understanding is that reputable, published scientific findings need to go through a review process. Is that correct?

Dr. McCormick. I would defer to Ms. Stoiber, who has been answering these questions on institutional policy.

Ms. Stoiber. But I think he was asking about peer review generally.

Mr. Waxman. If you have a reputable, published scientific finding, doesn't that need to go through a review process?

Dr. McCormick. Absolutely.

Mr. Waxman. In fact, it would have been irresponsible not to have the report reviewed. Isn't that correct?

Dr. Amaral. I think that is one of the safeguards of the Institute of Medicine, that there is such an extensive review of reports.

Mr. Waxman. Was this review process any different from the process of publishing an article in a peer-reviewed journal?

Dr. McCormick. It is much more extensive. It is much more critical.

Mr. Waxman. The chairman also continues to say that the report changed after this review process. Is this true?

Dr. McCormick. There were changes of fact, there were some changes of wording to more appropriate wording. There was no change in the overarching conclusions of the report.

Mr. Waxman. Did the committee's recommendation change after it received the reviewer's comments?

Dr. McCormick. No.

Mr. Waxman. If a parent came to you with concerns about the safety of the MMR vaccine, after hearing all the evidence presented to the panel and after hearing the deliberations of the panel, what advice would you give to that parent about whether to vaccinate their child?

Dr. McCormick. I would give the advice that the child should be vaccinated. The risks of measles far outweigh the risks for autism. We are talking about risks of death, risks of severe chronic dementia called SSPE. These risks are real and documented as a result of wild-type virus.

I think the risks of MMR and autism should continue to be explored, but I do not think that MMR causes even the bulk of autism. The committee did not feel they had enough information themselves to make that kind of assessment, but that is my personal view. The risks of wild-type measles are real.

Mr. Waxman. I said in my opening statement that the committee concluded that there is ``no credible scientific evidence establishing a link between the MMR vaccine and autism.'' Is that a correct characterization of the committee's conclusions?

Dr. McCormick. Yes.

Mr. Waxman. In Chairman Burton's opening statement, he stated that ``the committee found that there was insufficient

evidence to prove conclusively or disprove a connection between the MMR vaccine and acquired autism.''

That seems to me to be a gross mischaracterization of the committee's findings. The committee could have chosen to say that there was inadequate evidence, but you did not say that. You said that the evidence favors a rejection of a causal connection between the MMR vaccine and autism.

Why did the committee say that the evidence conflicts with the theory that the MMR vaccine causes autism?

Dr. McCormick. The theory really has not been substantiated with a full chain of evidence. As I mentioned earlier when you were not present, Dr. Wakefield was unable to present his full data because he was reluctant to present it in a public setting before it was peer-reviewed. We left the door open that should such data come in and look more solid and that there was a causal chain we would clearly relook at the results. But it seemed to be a long way away before that kind of causal linkage was not only established but replicated in other laboratories.

Mr. Waxman. The Institute of Medicine report also states ``its conclusion does not exclude the possibility that MMR vaccine could contribute to ASD in a small number of children.''

Mr. Burton reads this and draws the conclusion that there is a lot of uncertainty about the safety of the MMR vaccine. Do you agree with this? Do you think the science raises serious questions about the safety of MMR?

Dr. McCormick. No.

Mr. Waxman. When I read the report, I draw a different conclusion than the chairman. We all know that it is very hard to prove a negative. My understanding is that the Institute is saying that it could not prove a negative. Is that correct?

Dr. McCormick. That is correct.

Mr. Waxman. This does not make MMR a likely cause of autism. It does not even make the MMR theory an untested hypothesis. Rather, the theory has been examined and all the epidemiological evidence points toward rejection. Is that correct?

Dr. McCormick. That is correct.

Mr. Waxman. My time is up. Thank you, Mr. Chairman.

Mr. Burton. But you cannot say categorically that the MMR vaccine does not cause, in any causes, autism, can you?

Dr. McCormick. No, that is what the statement says.

Mr. Burton. Thank you.

Let me just ask you two more questions.

If it is true that autistic children do not get proper medical evaluations to assess if they have gastrointestinal and immune system disregulation, as pointed out by Dr. Wakefield, how can the IOM committee conclude that the percentage of children with autism caused by MMR is small?

Dr. McCormick. Because the bulk of the epidemiological

evidence shows no causal connection on a population basis.

In terms of the investigations Dr. Wakefield has recommended, we, too, like Dr. Gershon, really applauded Dr. Wakefield for expanding the notions of what the problems are that these children have.

Mr. Burton. Dr. Weldon said to the people from England, why don't you just take a look at 50 or 100 or 500 kids that have autism and gastrointestinal problems and check to see if the thesis is correct? Why not do that?

Dr. McCormick. We recommended continue attention to that and for duplication of the results in the report. That was one of the recommendations.

Mr. Burton. If that is one of the recommendations, that research is necessary, why would you put out a report that everybody in the country that was interested in this heard on television saying that there was no causal link, period. That is all we heard. I watched every channel and they all said the same thing, that there is no causal link.

Yet you just said that you cannot make a categorical statement like that.

That confuses a lot of people and it raises uncertainty even to a higher level because people want to trust the Government and this creates doubt.

I have one more question for you.

Since there has been a published report of vaccine-strain measles causing encephalitis in a healthy child, why was it stated in the IOM report that no such data existed?

Dr. McCormick. We did cite it. It was found that after the primary hospitalization these children were found to have a primary immune deficiency so that they were not previously healthy children.

Mr. Burton. Would you give me that one more time?

Dr. McCormick. After hospitalization, the patient that had this measles-strain encephalitis was found to have a primary immune deficiency with a decreased CD-8 count and hypogammaglobulin. So the inflammation was thought to be due to immune deficiency.

Mr. Burton. So if a child has an immune deficiency, then they are at risk for an adverse event?

Dr. McCormick. Children with immune deficiency are at risk of a wide variety of adverse effects.

Mr. Burton. From the MMR vaccine?

Dr. McCormick. Not necessarily. It depends on the nature of the immune deficiency.

Mr. Burton. Well, I want to thank you very much for being here. I do want to say, though, that because this is such an epidemic, I think our health agencies ought to look at every possible avenue, and follow every possible avenue, to find out if this is why we have this fantastic increase.

In Mr. Waxman's district in California, every 3 hours there

is a new case of autism. It used to be one in every 6 hours, as you heard earlier. Nobody seems to have any idea why.

To rule out anything and then say at the end that in some cases it may not be conclusive when you do not have all the facts yet--you have not done a study on kid's guts that have autism to see if that measles vaccine is in there. It seems to me that is giving information that is not completely factual and closing a door that probably should not yet be closed.

Also, on the mercury vaccine--which you do not have anything to do with----

Dr. McCormick. Oh, yes, we do.

Mr. Burton. You will be working on the thimerosal issue?

Dr. McCormick. That is our next report.

Mr. Burton. Well, I hope you will be very, very thorough and careful when you do that report because we will have you back here again and ask you about that. It will be a very thorough hearing once again.

And I have to tell you that in our own family--and I know there are lot of people in this room who have autistic children and grandchildren--a normal child, nine shots in 1 day containing thimerosal and the MMR vaccine, and 10 days later he is gone. I just have to tell you that is really bad and we have an epidemic. We have to find the reason why.

Mr. Waxman. Mr. Chairman, my observation is this: autism is an awful disease and we have to do everything we can to fight this disease. But when we are trying to figure out how to fight a battle, you only have a certain amount of resources. If we take those resources and continue to go over and over and over a line that seems to me not very promising, we have an endless task of trying to reevaluate this theory, to try to prove whether it is a negative or a positive. It seems to me that we ought to make some decisions about whether we ought to be asking the scientists where we should put the money to fight autism.

Are we going to continue to reevaluate and have another committee reevaluate Dr. Wakefield's theory? I do not want to say that we should ignore it. I do not know the answer. I am not a scientist. I cannot give an answer. But I do not know that is the best place for money to fight autism.

And I would be interested in our committee trying to find out from scientists--I do not think scientists who disagree with Dr. Wakefield should be treated as if they are our enemy. These are people from the Institute of Medicine. They have devoted their lives to fighting disease. They are trying to fight autism.

We ought to consult with them, not challenge them. We are doing more than challenging them, we are trying to impugn their integrity because they have not come to the same conclusion as Dr. Wakefield.

We can keep putting money into Dr. Wakefield's theory over

and over and over again to where we could say, maybe it is true and maybe it is not, instead of saying, maybe it is not but maybe it is.

It seems to me at some point we ought to ask what the best use of money is. Should we be looking for a vaccine for autism? Should we be looking for medicines that can cure it? Should we be doing something to help the parents? Should we be using the money for research in trying to find out the causes? Or do we know the causes?

It seems like we approach this issue as if we know the cause and there is somebody trying to keep us from keeping it open. I do not think we know the cause and I would like us not to limit ourselves in our thinking and our approach to this problem as if we know this cause and what we have is a grand conspiracy to keep this cause from being public.

I think you have done a real service, Mr. Chairman, by giving a focus on this disease and suggesting that we need to understand that this a problem that is serious and seems to be on the increase and we ought to fight it. But let us not get diverted in our fight to an endless discussion of a theory that I think is not a very promising one, from everything I have heard in the hearings, we have had--and we have had many hearings on this one theory.

So I hope we can work together to figure out some other constructive ways to fight this disease because you and others have expressed so strongly, emotionally, and well that it is our obligation to do that.

Mr. Burton. Let me just end by saying that you have a great deal of constraints on your time, Mr. Waxman, and we have had a number of hearings. Generally, you come in and make a statement and then you leave and do not hear all the testimony and you do not have a chance to question all the witnesses.

I understand that you have these constraints on your time. I just hope that in the future when we have these hearings that you will be able to devote the time necessary to hear all the witnesses instead of just coming in and making a statement and leaving.

I do not want to cause acrimony between the two of us, but that is one of the problems. And I know you have demands on your time.

I want to say one other thing and then----

Mr. Waxman. I hope you will yield to me on that point.

Mr. Burton. I will yield to you.

Mr. Waxman. I do have a conflict in the time because I do not get to set the agenda and we have other committees and other demands. But I do have staff. And I do have an opportunity to read the testimony. And I do have a chance to evaluate what is said. I think in doing that I have a better picture of what the different people are saying than if I sat here and heard every single person but refused to believe those

that disagreed with my theory.

You can sit here for hour after hour and believe that those who say that I am right are telling the truth and those that say I am wrong are lying. That would be maybe a good use of time, but not a good use of process by which hearings ought to give us some conclusions.

Mr. Burton. As I understand it, the way that you come to conclusions is you look at a whole body of people, and you see if there is a causal link. As I understand it, you look for the commonality of things like autism. It seems that the vast majority of the people who are becoming autistic now--the one common link is that they all suffered in relatively close proximity to these vaccines, a huge percentage of them.

So there is a commonality there. So it is logical for many people--myself included--to conclude that a lot of these autistic kids are becoming autistic because of a combination of thimerosal, the MMR vaccine--I do not know what--but that is the commonality. That is the thing we see.

And we have heard that week after week, month after month, with a whole host of people testifying from around the world. Because of that, I think we need to take a very hard look and a very thorough look at these vaccines and the contents of vaccines and whether or not maybe separate vaccines should be given.

Instead of the MMR vaccine, maybe it should be a measles shot without preservatives in it. Maybe it should be a single mumps shot. Maybe a single rubella shot. I know it would be a lot more time-consuming and more costly.

We ought to find out if we need to have mercury or thimerosal in vaccines. As I understand it, if you have single shots, you do not really need that kind of preservative in there and you can give a child a shot that does not have a possible contaminant in it.

So I hope that in your review of these vaccines containing things like thimerosal you will look very closely at that and give us a report that will be very, very thorough.

Dr. McCormick, did you have a closing comment you would like to make?

Dr. McCormick. I do not think anyone sitting around our table is not concerned at our committee meetings about the safety of vaccines. That is why we are there. But also millions of children get these vaccines without developing the autistic symptoms. What we are looking at in the epidemiologic literature is the comparison of those with the vaccine and without to see to what extent we can draw the association with autism.

So that information does not support the linkage. But I do not think there is anybody sitting around our committee table that is not concerned about the safety of vaccines and is not coming to it from a neutral point of view that if they saw a

risk they would not call it.

Mr. Burton. I understand and I appreciate your comment.

But I will tell you this: it used to be 1 in 10,000 and in Indiana it is 1 in 400, and in Oregon it is 1 in 190 kids that are autistic. There has to be a cause and it appears as though one of the contributing factors are some of these vaccines.

With that, thank you very much for being here. We stand adjourned.

[Whereupon, at 3:15 p.m., the committee was adjourned to reconvene at the call of the Chair.]

[Additional information submitted for the hearing record follows:]

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AUTISM--WHY THE INCREASED RATES? A ONE-YEAR UPDATE

THURSDAY, APRIL 26, 2001

House of Representatives,
Committee on Government Reform,
Washington, DC.

The committee met, pursuant to notice, at 10:10 a.m., in room 2154, Rayburn House Office Building, Hon. Dan Burton (chairman of the committee) presiding.

Present: Representatives Burton, Gilman, Morella, McHugh, Weldon, Waxman, and Cummings.

Staff present: David A. Kass, deputy counsel and parliamentarian; Mark Corallo, director of communications; S. Elizabeth Clay, professional staff member; Robert A. Briggs, chief clerk; Michael Canty, legislative assistant; John Sare, deputy chief clerk; Corinne Zaccagnini, systems administrator; Kate Anderson, Jon Bouker, and Sarah Despres, minority counsels; Ellen Rayner, minority chief clerk; and Teresa Coufal, minority staff assistant.

Mr. Burton. Good morning. A quorum being present, the Committee on Government Reform will come to order.

The minority ranking member will be here shortly, as will some of the other panelists. I ask unanimous consent that all

Members' and witnesses' opening and written statements be included in the record. Without objection, so ordered.

I ask unanimous consent that all articles, exhibits and extraneous or tabular material be included in the record. And without objection, so ordered.

We're going to be hearing today from the National Institutes of Health, the Centers for Disease Control and Prevention and the Food and Drug Administration. Autism is a neurobiological disorder. It locks a person inside himself or herself. This disorder, which leaves children like my grandson, Christian, unable to express themselves or interact with others, is now at epidemic levels in this country, and I mean epidemic.

One in 400 children in Indiana, 1 in 190 children in Oregon, 1 in 150 children in Brink Township, NJ. How has the Department of Health and Human Services responded to this epidemic? Have our health agencies recognized this dramatic rise and acted accordingly? If we generously estimate that NIH has focused $60 million on autism, and that's generous, autism research out of a $20 billion budget, that would mean that their investment is 0.003, three thousandths of 1 percent.

Does that adequately address an epidemic that affects between 1 in 190 children in Oregon and 1 in 500 children nationwide? I'm including in the record a document taken from the NIH Web site this morning that shows research initiatives at the NIH and their funding for a 3-year period. We'll give you all copies of this, we'd like for you to take that back with you.

According to this document, NIH estimates they will spend $45 million this year on autism. This is compared to $136 million on sleep disorders and $434 million on vaccine development, which could be part of the problem, especially if it's got mercury in it. Two of the issues that were discussed at length yesterday were the concerns that the dramatic rise in autism may be related to the MMR vaccine and mercury exposure through childhood vaccines. We do not yet have enough research evidence to make a conclusion one way or the other. Our health agencies need to fund clinical and laboratory research that will get the answers.

As we learned yesterday, epidemiological studies cannot answer these questions. Epidemiology is important for looking at incidence and prevalence, but not in answering questions about causality. I have a short video showing the effects of mercury on the brain. I think that's simply saying that we're moving to get new vaccines on the market that have little or no mercury. It's a step in the right direction, but I continue to be concerned on behalf of the 8,000 children a day who may be exposed to mercury through their childhood vaccines until the current supply is used up.

And why that isn't being recalled by the health agencies of

this country, the FDA, I cannot fathom. As we speak, kids are having mercury shot into their arms, and we know it's a toxic substance. We had toxicology experts here yesterday talking about it and what it does to the brain. We're going to show a video on what it does to the brain.

And yet the people in the health agencies continue to allow that to be done. And I cannot figure out why.

Yesterday we also heard about research that the NIH is funding at the University of Rochester regarding mercury in autistic children. We'll hear today how research is to evaluate the level of mercury in the serum, the hair and the urine of children receiving the currently recommended childhood immunization schedule.

I hope that the reports will include the hair and urine data as Dr. Haley, a leading mercury expert, suggested. Simply reporting the blood data will be misleading. To only report the blood data and not analyze and report the hair and urine samples would be an injustice. We need to look at it all.

And I want to tell you something. We have 113 Members of Congress that have signed up for the Autism Caucus. We're going to end up with about 270, 280. And we're probably going to have over half the U.S. Senate in the caucus. And if you think this is going to go away, you guys are blowing smoke. Because I'm telling you, I'm going to make sure that everybody in the Congress knows the problems and knows what's facing us. If the health agencies don't deal with this and deal with it quickly, you're going to have a big problem over there.

I've also talked to Tommy Thompson, new head of the Health Department. He's going to continue to talk to you, on a regular basis, if we don't do something about this. It's unconscionable that we have thousands and thousands of children being inoculated and vaccinated with vaccines that have toxic substances in them, and we see a horrible increase in the number of people that are autistic and we continue down the same path.

I just don't understand it. Last year the Centers for Disease Control and Prevention reported that they did not know why so many children in Brick Township, NJ, had autism. They conducted a thorough evaluation of environmental toxins and numerous other potential factors, but chose not to include vaccine history as a part of their evaluation and report. Why is this?

I believe vaccines are so important, but why they put three and four and five and six and seven and eight and nine together at one time, with mercury and other toxic chemicals in them into our kids, I just don't understand. We have an epidemic on our hands, and we cannot ignore any potential path that may lead to ending the epidemic.

With that, we have this brief video that we'd like for you to see that shows the effects of mercury on the brain and I

hope you'll pay particular attention to this.

[Video shown.]

Mr. Burton. That test was done in June 1999, almost 2 years ago. I don't know if our health agencies are aware of it, but in your comments today, I hope you'll address whether or not you're familiar with that study, and whether or not our health agencies have done like studies or taken an interest in that and can respond to it.

[The prepared statement of Hon. Dan Burton follows:]

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Mr. Burton. Do you have an opening statement, Mr. Gilman?

Mr. Gilman. I want to commend the chairman and our committee for looking into this problem, one that's long overdue, and I thank you for the opportunity to be here.

Mr. Burton. Thank you, Mr. Gilman. I don't know if you're familiar, but Congressman Chris Smith and Congressman Doyle have formed what's known as the Autism Caucus. I don't know if you're a member yet, but I hope you will join so we can make sure every member is aware of the problems with it.

Let's start with Dr. Rennert. Do you have an opening statement?

STATEMENTS OF OWEN M. RENNERT, M.D., SCIENTIFIC DIRECTOR, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT, NATIONAL INSTITUTES OF HEALTH; KAREN MIDTHUN, M.D., DIRECTOR, OFFICE OF VACCINE RESEARCH AND REVIEW, FOOD AND DRUG ADMINISTRATION, ACCOMPANIED BY SUSAN ELLENBERG, M.D., DIRECTOR, OFFICE OF VITAL STATISTICS AND EPIDEMIOLOGY; NORMAN BAYLOR, M.D., ASSOCIATE DIRECTOR, REGULATORY POLICY, OFFICE OF VACCINES; AND DR. COLLEEN BOYLE, ACTING ASSOCIATE DIRECTOR, SCIENCE AND PUBLIC HEALTH, CENTER ON BIRTH DEFECTS AND DEVELOPMENTAL DISABILITIES, CENTERS FOR DISEASE CONTROL AND PREVENTION

Dr. Rennert. Mr. Chairman and members of the committee, I'm Dr. Owen Rennert, Scientific Director of the National Institutes of Child Health and Human Development at the NIH. I appreciate the opportunity to provide information on behalf of the NIH Autism Coordinating Committee about ongoing and planned research activities at the NIH that are relevant to autism and pervasive developmental disorders.

Autism, as you know better than I, is a cruel disorder, not only as a result of the disability it causes, but also because

it is an illness that challenges the emotional bond between child and parent. In its most severe forms, it effectively isolates that child socially, cognitively, emotionally and linguistically, denying other family members even the opportunity to console and comfort.

In light of these immense human costs and the significant public health burden that autism brings with it, the NIH is working to focus the research community with ever-greater intensity on this terrible disease. We appreciate the continued involvement that parents have given us in that effort.

The Children's Health Act of 2000 called for expansion, intensification and coordination of autism related scientific programs at NIH. I'm pleased to report that significant progress is being made, including toward the establishment of a new network of centers of excellence in autism. The act directed the Secretary of Health and Human Services to establish an interagency autism coordinating committee, which will include NIH, the Centers for Disease Control and Prevention and other HHS agencies.

Yesterday, Secretary Thompson delegated to NIH authority for establishing this coordinating committee. And we can assure you, it will have at least three members from the parent community of children with autism.

There has been considerable expansion and enhanced coordination of autism research efforts at NIH. The amount of NIH support autism related research grew from $22 million in fiscal year 1997 to $52 million in fiscal year 2000. This demonstrates the commitment of Institute members to the broad intensification of autism research efforts.

As you requested, Mr. Chairman, we have supplied for the record the 10-year funding history of NIH sponsored autism related research, the list of projects funded in fiscal year 2000. We will also be supplying the abstracts of those funded grants shortly.

Effective this week also, NIH has released an RFA, request for applications, containing setaside funds for research support for the development of autism centers applications. This is part of an overall plan to support a variety of investigative teams and wherever possible, to recruit the participation of outstanding investigators who previously have not worked in autism research. These grants would be funded in September 2001 if meritorious applications are submitted.

A second RFA will be issued in fiscal year 2002 to solicit applications for the centers of excellence with funding of the first of these centers targeted for early in fiscal year 2003. NIH anticipates a pool of approximately $8 million per year, which will be available for the first 5 years of the funding of those programs.

The Children's Health Act of 2000 calls upon NIMH, the Institute of Mental Health, to take the lead in providing a

program under which samples of tissues and genetic materials are donated, collected, preserved and made available for autism research. NIH presently supports ongoing efforts by Harvard's brain tissue resource center, UCLA and the University of Miami's tissue banks, and recently special supplements were awarded to target acquisition of necessarily biological materials from individual with autism for focused study.

The network. In 1997 through an RFA, the National Institutes of Child Health and Human Development with co-funding from the National Institute of Deafness and Communicative Disorders, established the networks on the neural biology and genetics of autism, referred to as the collaborative programs of excellence in autism.

Currently, we have enrolled nearly 2,300 patients with well diagnosed autism in the network and are gathering data from their families. A major ongoing CPEA initiative, a part of this network that is co-funded by NICHD, NIDCD and the CDC is the autism regression vaccine study. A principal goal of this study is to assess temporal association between measles, mumps, rubella vaccine and the onset of autism and attempts to differentiate early and late onset forms of the disorder.

Another aim of this study is to try to replicate studies of persistent measles infection in children with autism versus those children who are not affected. Stage one of the project, which got underway in September 2000, includes 1,600 well diagnosed cases of autism and 1,250 healthy controls. Individual vaccination records as well as records of the onset of autism, specifically looking at the age of onset, the age of recognition and the age of the diagnosis, will be examined in this study.

Stage two of this project will attempt to replicate previously reported findings regarding abnormal measles antibody titers and persistent measles infection. In this phase, investigators will examine 250 children with early onset autism, 250 children with the regressive form of autism, 250 healthy controls matched to early onset cases, as well as 250 controls matched to regressive autism cases.

Neuroscience research, as you know, requires that we understand the pathogenesis and cause of autism, and is the most promising approach to ultimately developing targeted effective treatments. Until the brain mechanisms responsible for the manifestations of autism are understood, it will not be possible to develop truly targeted interventions.

Treatment research also is currently focused on studying the efficacy and safety of promising treatment interventions which are commonly used in the community without adequate testing or are aimed at specific impairing symptoms. These include both psychosocial and pharmacologic interventions.

Last October, neuroscientists, including autism researchers, parents, advocates and NIH program staff,

participated in a 1-day brainstorming session on the role of the environment in autism which was organized by the National Institutes of Environmental Health Sciences. This group identified key priorities, large scale epidemiologic studies to determine autism incidence and prevalence trends, studies to describe the natural history of autism and to identify meaningful subgroups that may be at increased risk from environmental exposures in studies specifically to examine the proposed association between regressive autism and thimerosal in vaccines.

Mr. Burton. I don't know how much longer your opening statement is, but we'd like to get to the questions as quickly as possible.

Dr. Rennert. I'll abbreviate it.

I simply would indicate to you that there are ongoing studies of several institutes amongst the ones you mentioned, the one at the University of Rochester, which attempt to look at hair, urine, serum levels of children having received a thimerosal and mercury derivatives, of children having received immunizations, those who have had thimerosal containing vaccines and those who haven't.

Preliminary data, as you were told yesterday, shows no difference in blood levels. I do not have at this point in time the complete analysis, because it hasn't been completed.

There are also studies at several centers that are looking at the pharmacokinetics, the metabolism, the disposition and the disposition in tissues such as brain of mercury when administered as thimerosal, mercurial mercury in monkeys. There are another set of studies that have been funded in November 2000 that are carrying out somewhat similar experiments in rats. These again look at the cellular distribution patterns of mercury in tissue, including the brain, and also are attempting to evaluate the role of immune activation in altering brain levels of mercury after exposure to thimerosal.

The last comment that I'll make in a general way is that as you know, the Children's Health Act authorized a longitudinal study to investigate basic mechanisms of environmental disorders and environmental factors, both risk and protective, that influence health and developmental processes.

In the context of environment, one is talking about chemical, physical, social behavioral influences on children who have critical windows of vulnerability during development, during which time environmental exposures could have a greater influence and diseases of increasing prevalence, such as autism and asthma, are two targeted elements of this. Planning for this study, which will follow about 100,000 children across the United States from birth into adulthood, is currently underway, with pilot studies scheduled to occur in fiscal year 2002.

The other comments I was going to make related exclusively to the efforts of the NIH to increase its dialog with the

parents and the public community with regard to what our priorities should be, how we conduct our research as it relates specifically to autism. The only thing to highlight there is as a consequence of those efforts, there is a list server presently available that provides up to date information about autism related research activities at the NIH, there is an NIH Web page which also allows you to identify all the research that presently is funded by NIH and gives you information about advocacy groups, the scientific literature, etc.

In closing, we at NIH understand the passion of parents and families of those who have been affected by autism and related disorders and share your concerns for quickly unraveling the mystery of autism. Thank you, Mr. Chairman.

[The prepared statement of Dr. Rennert follows:]

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Mr. Burton. Dr. Midthun.

Dr. Midthun. Mr. Chairman and members of the committee, I'm Dr. Karen Midthun. I'm the Director, Office of Vaccine Research and Review of the Center for Biologics Evaluation and Research,

FDA. With me today are Dr. Susan Ellenberg and Dr. Norman Baylor. Dr. Susan Ellenberg is Director of the Office of Vital Statistics and Epidemiology, and Dr. Norman Baylor is the Associate Director for Regulatory Policy in the Office of Vaccines.

Mr. Chairman, as a physician and a parent, I want to express to you, the members of this committee and to parents that I'm aware of the devastating effects of autism on children and their families. I'm here to assure you that we are working diligently to ensure that the vaccines we license for use in the United States are shown to be safe, pure and potent. I appreciate the opportunity to participate in this hearing on autism and to respond to the committee's concerns regarding a potential link between vaccines and autism.

The Office of Vaccines regulates the investigation and licensure of vaccines. FDA's regulatory process for licensing vaccines has for decades served as a model for other countries. To date, the existing data do not demonstrate a causal relationship between vaccines and autism. However, I want to assure this committee, the public and especially parents that FDA takes these concerns seriously.

One concern that has been raised relates to the use of thimerosal, a mercury compound as a preservative in some vaccines. FDA recognizes and supports the goal of reducing exposure to mercury from all sources. Consistent with this goal, for several years, FDA has encouraged manufacturers to develop new vaccines without thimerosal as a preservative, and to remove or reduce the thimerosal content of existing licensed vaccines.

Initial results of this effort were realized at least a year prior to the enactment of the FDA Modernization Act of 1997, with the licensure of new thimerosal-free vaccines. As required by Section 413 of FDAMA, FDA conducted a review of the use of thimerosal in childhood vaccines. A review revealed no evidence of harm caused by thimerosal used as a preservative in vaccines except for local hypersensitivity reactions.

Under the U.S. recommended childhood immunization schedule, the maximum cumulative exposure to mercury from thimerosal at the time of this review in 1999 was within acceptable limits for the methyl mercury exposure set by FDA, the Agency for Toxic Substances and Disease Registry and the World Health Organization. Of note, all these guidelines contain a safety margin and are meant as a starting point for evaluation of mercury exposure, not absolute levels above which toxicity can be expected to occur.

However, during the first 6 months of life, cumulative exposure to mercury in some cases could have exceeded the more conservative limits of the EPA depending on the specific vaccine formulations used and weight of the infant. The clinical significance of exceeding EPA's limits is not

currently known. Nevertheless, reducing exposure to mercury from vaccines is warranted and achievable, in part because in the United States, it is possible to replace multi-dose vials with single dose vials, which do not require a preservative.

I am pleased to be able to report substantial progress in the efforts to reduce thimerosal exposure from vaccines. At this time, all routinely recommended licensed pediatric vaccines being manufactured for the U.S. market contain no thimerosal or contain only trace amounts in the final formulation. Prior to the recent initiatives to reduce or eliminate thimerosal from childhood vaccines, the maximum cumulative exposure to mercury by routine childhood immunizations during the first 6 months of life was 187 and a half micrograms. With the newly formulated vaccines, the maximum cumulative exposure during the first 6 months of life will now be less than 3 micrograms of mercury, more than a 98 percent reduction.

In an effort to better characterize any toxicity that could have accompanied an exposure to thimerosal from vaccines, FDA is in the process of nominating thimerosal to the National Toxicology Program for further study.

Reports of developmental delay following vaccination have been submitted to the Vaccine Adverse Event Reporting System [VAERS]. Although VAERS reports by themselves usually cannot establish a causal relationship between a vaccine and an adverse outcome occurring after vaccination, further study of these reports can sometimes provide important clues and suggest directions for further research.

FDA takes these reports seriously and has begun a followup study of VAERS reports of autism. In addition, FDA is pursuing research involving the characterization and development of an animal model for autism. While looking at ways to improve the safety of vaccines, we must keep in mind that childhood vaccines have contributed to a great reduction in vaccine preventable diseases, including polio, measles and whooping cough.

Today, it is rare for American children to experience the devastating effects of vaccine preventable illness. However, vaccines, like all medical products, are not risk free, and FDA is committed to continuing its efforts to reduce these risks whenever possible.

In conclusion, FDA continues to work diligently with manufacturers to eliminate or reduce exposure to mercury from thimerosal in vaccines. As stated previously, at this time, all routinely recommended licensed pediatric vaccines being manufactured for the U.S. market contain no thimerosal or contain only trace amounts in the final formulation.

Although no causal relationship between vaccines and autism has been established, FDA, along with other Health and Human Service agencies, continues to pursue research activities to

increase our understanding of any potential relationship between vaccines and neurodevelopmental disorders. Although the prevention of disease through the use of vaccines is a tremendous public health accomplishment, there is more work to be done. I assure you that the Office of Vaccines at FDA will continue to make regulatory decisions or recommendations regarding vaccines based on the best scientific evidence to protect the public health.

Mr. Chairman, I appreciate the committee's interest in this area, and look forward to continuing to work with you on this in the future.

[The prepared statement of Dr. Midthun follows:]

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Mr. Burton. Thank you.

Dr. Boyle.

Dr. Boyle. Good morning, Mr. Chairman and members of the committee. I'm Dr. Colleen Boyle, Acting Associate Director for Science and Public Health in the newly established Center on Birth Defects and Developmental Disabilities at the Centers for Disease Control and Prevention.

I have with me today Dr. Roger Bernier, an epidemiologist

and Associate Director of Science for the National Immunization Program at the CDC.

Thank you for the opportunity to update you on CDC's activities related to autism. One major change since last year is that CDC has established, at the direction of Congress, a new center, the National Center for Birth Defects and Developmental Disabilities. This center will increase CDC's efforts to discover causes and develop preventive strategies for birth defects and developmental disabilities, including autism.

First, Mr. Chairman, I want to stress that CDC is committed to understanding the prevalence of autism, identifying its preventable causes and establishing and evaluating prevention programs. We've made considerable progress over the last year toward fulfilling this commitment. Last year, we mentioned that CDC and the Agency for Toxic Substances and Disease Registry were about to report on an investigation on the prevalence of autism in Brick Township, NJ. The investigation found a rate in Brick that is high compared to many previous studies.

However, there are few very recent studies, none in the United States, that have reported rates in this range, which suggest that the rate of autism may be considerably higher than previously thought. To increase our ability to monitor autism prevalence in the United States, in September 2000, CDC competitively funded health departments in Arizona, South Carolina, Maryland and New Jersey to establish monitoring programs for autism in their States.

CDC is also completing the analysis of the first year of autism monitoring data gathered from its own metropolitan Atlanta developmental disability surveillance program. Our report should be complete later this year.

This September, as directed by Congress, CDC will competitively fund up to four centers of excellence in autism epidemiology to conduct collaborative epidemiologic studies. The research objectives of these studies will be determined by an independent oversight committee, and representatives from parent and consumer groups will be invited to provide input to the oversight committee in planning the epidemiologic study.

CDC has also developed a wide range of activities that are responsive to the needs of parents of children with autism and health care professionals working with these children. For example, CDC funds a program at Marshall University in West Virginia of an intensive community support program for families with young children with autism. As part of the centers for excellence in autism and epidemiology, we expect to fund projects of model intervention programs for children with autism, of the economic and social costs of autism, and of studies to look at the natural history of autism.

Some parents have expressed concern about the potential link between autism and vaccines. Although the weight of the

scientific evidence does not support such a link, CDC is committed strongly to assuring vaccine safety. The concerns raised regarding autism and vaccines have focused primarily on thimerosal, a preservative in some vaccines, and on the measles, mumps and rubella vaccine. Today, all manufacturers are producing for immunization only vaccines that are free of thimerosal or have only trace elements of thimerosal.

As shown in figure one of my testimony, the thimerosal content of pediatric vaccines purchased by States through CDC's contract has dramatically decreased since 1998. CDC is actively investigating whether there have been any adverse effects related to thimerosal in vaccines. Preliminary analyses of the vaccine safety data link have not supported a link between thimerosal containing vaccines and autism.

It has been suggested that vaccination, particularly with the MMR vaccine, may be related to the development of autism. Substantial scientific review does not support this suggestion. First, the American Academy of Pediatrics executive committee stated in March 2001 that there is a considerable body of evidence that does not support a causal relationship between MMR vaccine and autism or inflammatory bowel disease. Second, the IOM stated just this week that existing evidence does not favor a causal relationship between the MMR vaccine and autism.

In addition, Dales et al. recently reviewed changes over time in the MMR coverage and autism diagnoses in California. There was a 373 percent relative increase, in the prevalence rate of autism between 1980 and 1994 while the MMR immunization coverage was relatively flat over that same period.

To date, the weight of the scientific evidence does not support a causal relationship between vaccines and autism. Nevertheless, because of the continuing concern of parents, we are committed to conducting research to evaluate this matter. At present, we are conducting a study in Atlanta, another in Denmark, and we are collaborating with NIH, with their centers and programs of excellence in autism to further examine the relationship between vaccines and autism.

While we must remain vigilant to assure the safety of vaccines, we must also remember that vaccines benefit the individual child and the public by protecting persons from the consequences of infectious diseases. While we've made great progress to reduce the number of cases of vaccine preventable diseases, threats posed by vaccine preventable diseases are known and are real.

We want to assure you that CDC knows how important it is to find the causes of autism and prevent this disorders. We are committed to conducting research that will lead to these answers. With the support of Congress, we have made a good beginning by funding autism monitoring programs with several States and the Centers of Excellence in Autism Epidemiology to look at causes of autism. CDC's efforts will continue until we

have found the answers that will enable us to prevent this serious condition that affects so many American children.

Thank you, Mr. Chairman and members of the committee, for the opportunity to testify before you today. Dr. Bernier and I would be happy to answer any questions that you may have.

[The prepared statement of Dr. Boyle follows:]

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Mr. Burton. I neglected to have you sworn. Would you all please stand?

[Witnesses sworn.]

Mr. Burton. Dr. Boyle, why is it that there's a reduction in thimerosal in vaccines that are being produced today? Did not our health agencies request that thimerosal be removed from

vaccines as the newly produced vaccines?

Dr. Boyle. I think we've made considerable progress in reducing the thimerosal content.

Mr. Burton. So you've asked that thimerosal be reduced in vaccines, have you not?

Mr. Bernier. I think the answer is that this was done as a precautionary measure.

Mr. Burton. Why?

Mr. Bernier. Because it was feasible to do, and there are sources of exposure to mercury that we cannot control, such as that from food. So----

Mr. Burton. I'm talking about the vaccine. Why is it that you have started at our health agencies to reduce the amount of thimerosal in vaccines, as a precautionary measure?

Mr. Bernier. As a precautionary measure.

Mr. Burton. OK, as a precautionary measure. That would lead one to believe that you're not really sure whether or not thimerosal causes some problems. Otherwise, why wouldn't you just leave it in there and say, hey, we've run all these tests, there's no causal link whatsoever? So why even move to take it out of there?

Mr. Bernier. There is a theoretical risk.

Mr. Burton. OK, so there's a theoretical risk. Then why have we not recalled the vaccines that have thimerosal in them right now, while you're testing this? If there's any question whatsoever about what we're putting into our kids' arms, and their bodies, and if you're reducing thimerosal because you think there may be a causal link, as a precautionary measure, why don't you recall the thimerosal that's in doctors' offices that are being injected into kids as we speak until you're sure? Because obviously you're not sure or you wouldn't be taking it out anyway. Why don't you recall it?

Mr. Bernier. I can give you my comments. The FDA may wish to weigh in on this issue of recall. But as succinctly as I can put it, Mr. Chairman, being safe means being safe from disease as well as being safe from the side effects of vaccine.

Mr. Burton. Let me ask you this question, then. Can you create a measles vaccine and do we have a measles vaccine that does not have thimerosal in it?

Mr. Bernier. Yes, that's correct.

Mr. Burton. Can we create a mumps vaccine that does not have thimerosal in it?

Mr. Bernier. That's correct.

Mr. Burton. Then why are you putting thimerosal in it?

Mr. Bernier. At the present time, as Dr. Midthun and Dr. Boyle mentioned, we have made very good progress, and I can say to you we are not putting in thimerosal any longer in the vaccines that are being produced.

Mr. Burton. So if you're not, if you're not, as a precautionary measure, then why are you leaving vaccines on

doctors' shelves and in drugstores around this country that are being used in facilities where they supply them, are being used, if you're not putting them in new vaccines, as a precautionary measure? Why don't you recall the supply that you have out there until you are absolutely sure, beyond any doubt, that thimerosal has no causal link to autism? Why don't you recall it?

Dr. Midthun.

Dr. Midthun. Under the Public Health Service Act, in order to make a mandatory recall of vaccine, there has to be an imminent or substantial hazard to the public health. As the weight of the evidence does not support a causal link between thimerosal----

Mr. Burton. Then why are you taking it out of the new ones?

Dr. Midthun. As Dr. Bernier said, it's a precautionary measure. It's recognized that mercury in large doses is toxic and any way that we have of reducing the exposure to mercury over which we have control is something that is desirable to do.

Mr. Burton. Let me tell you, my grandson was very healthy and very normal and spoke and ran around like every other child. He got nine vaccines in 1 day. He got 41 times what's the allowable amount of mercury through thimerosal in 1 day. And 10 days later, we lost him. Now, we're trying to get him back.

Now, there's a lot of parents out there that are getting all these shots when their children's immune systems are depressed, they've got colds, and they're getting these shots, several of them at a time, with thimerosal in them. As a precautionary measure, if you think there may be a causal link, don't you have any latitude whatsoever to recall those and say, we're not going to destroy this, but we're going to hold these supplies in abeyance until we know for sure, until all the tests have been done?

Dr. Midthun. Not under the Public Health Service Act. That's not what would allow us to make a mandatory recall.

Mr. Burton. But you are taking thimerosal out of vaccines, as a precautionary measure?

Dr. Midthun. That's correct.

Mr. Burton. How long are these studies going to take, Dr. Rennert?

Dr. Rennert. We hope to have answers of various phases within the next 2 to 3 years.

Mr. Burton. Oh. Do you know how many kids are going to be vaccinated today? Do you know that in California, it used to be one child every 6 hours was becoming autistic. It's now one every 3 hours. In the United States, 1 out of 400 to 500 kids are autistic. And in some parts of the country, it's under 200. And boys have a four times more prevalence of getting autism than girls.

So if you go to Oregon, 1 out of 190 kids are autistic, that means 1 out of 50 boys being born are going to be autistic. And you're telling me these studies are going to take 2 to 3 years, and at the same time the studies are going to take 2 to 3 years, you're going to keep mercury in vaccines that you just saw from that Calgary, Canada study what mercury does to brain cells?

I mean, come on. If there's any doubt whatsoever, and you say it's a precautionary measure you're taking, then why in the heck don't you get that stuff off the market until you've tested it thoroughly? And if it's going to take 3 years, put it some place for 3 years, in a storage box, and if the tests don't prove out, you've still got it, and the pharmaceutical companies can still get their money.

Now, on these tests that you're doing, you said you're testing the blood for mercury. Are you testing hair and urine samples?

Dr. Rennert. Yes. In the studies that were done by Navy and the University of Rochester, there are samples that have been obtained for study of hair and urine concentrations as well.

Mr. Burton. Have you had any results from that yet?

Dr. Rennert. No, sir. The study as far as I know has just been completed and the analysis is occurring. I don't have the data.

Mr. Burton. How long will it take to get that analysis?

Dr. Rennert. I would imagine--to be honest, sir, I don't know. I don't think it will be long, but I will attempt to find out and give you an answer.

Mr. Burton. We would like to have copies of the analysis as quickly as you get them. We'd like to have any records that you have whatsoever about the analyzing of blood, hair, urine, whatever it is, regarding mercury and thimerosal in these kids.

You know, you were talking about how vaccines have reduced measles, mumps, rubella, diphtheria, all these other things. And that is great. And we really appreciate what vaccines and pharmaceutical companies have done for this country. Because they've saved a lot of lives. And what you've done has been very laudable.

But when you have a child who is autistic, from the time he becomes autistic until he dies, they estimate that the cost to our society is $5 million, for each child. Now, if we have 1 in 400, and the cases are rising at a very rapid rate, do you have any idea what that's going to do to our economy? Not now, but 5, 10, 15, 20 years from now. And so every precaution that should be taken must be taken and must be taken now. Because this is not only a health issue, it's an economic issue that's not going to go away.

I mean, we're talking about trillions and trillions of dollars if we don't find an answer. If you've got substances, aluminum, formaldehyde, mercury, in these vaccines, and you

have this huge rise and you're not absolutely sure that mercury's not causing it, you ought to get it out of there. You ought to recall this stuff. Because the doctor just said, Dr. Bernier just said that they are producing and can produce vaccines without mercury in them, without thimerosal.

Now, granted, you might not be able to put three or four different vaccines in one vial. Because as I understand it, you put the mercury in there to keep everything pure so they can be used, and won't be tainted. But if you go to single vials with single vaccines, sure, the parents would have to have more shots. But if it's going to be safer, then why not do it? And why wait 3 years for studies if you think that there may, even the most remote possibility, be a causal link.

If you look at some of these studies, like we've seen, and I am not a scientist, I'm not a doctor, I'm just a grandfather who has an autistic kid, and I didn't even know what autism was until a couple of years ago. But when you see the huge number of people that are contacting us through e-mail and through conferences, there's one going on right here, you've got to take the proper precautions. You can't say, let's wait 3 years and let this go on.

So as I said earlier, and I'm going to yield to my colleagues here, as I said earlier, we have 113 members in the Autism Caucus. They will be supplied with every bit of information we get, not only from you folks, but from Calgary, Canada, and from around the world and from the experts we have here. And I will be taking special orders on the floor of the House. I'll be going down there on a regular basis, reading into the record and talking to the American people, about the problems that we have.

So the pressure that you're feeling, if any, now, I don't know if you are or not, but the pressure you're feeling right now is going to be magnified as many times as I can make it, until our health agencies either come to some conclusion that's scientifically provable, or they get that stuff out of there, in particular thimerosal. And I don't know why, if you're coming up with vaccines that don't have these toxic substances in them, as I believe they are, I don't understand why you don't recall that stuff. Get it off the market.

FDA, can you do a voluntary recall for manufacturers the same as the rotavirus recall?

Dr. Midthun. That was not a voluntary recall. The manufacturer on their own initiative withdrew their product from the market.

Mr. Burton. Can you contact the people that manufacture thimerosal, and I know who it is, can you ask them to recall it temporarily?

Dr. Midthun. That would be something that would be voluntary on their basis.

Mr. Burton. You can't write them a letter and say that

because of the concern of thousands and thousands of parents and because we're in the process of doing research on this, we think it would be prudent to recall thimerosal products until we run all of our tests, which may take as much as 3 years?

Dr. Midthun. I'm sure that the companies are well aware also of these concerns over autism----

Mr. Burton. But you can't even write them a letter?

Dr. Midthun. It's their choice to make a voluntary recall, and they know that they have that choice, sir.

Mr. Burton. So you're not going to do anything?

Dr. Midthun. Under the PHS Act, we can make a mandatory recall for the reasons that I indicated. And the company, of course, on its own volition, can do anything it would like in terms of making product available or deciding not to distribute it any longer.

Mr. Burton. I found out yesterday that there's a lawsuits pending, I believe in, I think it's Mississippi, regarding mercury toxicity and how it's affected children. And if that lawsuit is successful by the people who are bringing the suit, it will probably involve a great deal of money to the pharmaceutical company that produces this product, and other pharmaceutical companies that use it in their vaccines.

I wonder, I just wonder if perhaps one of the reasons why FDA is not pounding these pharmaceutical companies to get this off of the market, especially when you look at this Calgary study about mercury and the toxicity of it, maybe there's not pressure being exerted by pharmaceutical companies on our health agencies because they're afraid of what might happen in that lawsuit if they do withdraw it from the market. Is there any validity to that kind of thinking?

Dr. Midthun. I really couldn't say. I do not know, sir.

Mr. Burton. OK, Mr. Gilman.

Mr. Gilman. Thank you, Mr. Chairman. I want to thank you for raising these issues.

Permit me to request that my opening statement be made part of the record.

Mr. Burton. Without objection.

[The prepared statement of Hon. Benjamin A. Gilman follows:]

[GRAPHIC] [TIFF OMITTED] T6856.267

[GRAPHIC] [TIFF OMITTED] T6856.268

[GRAPHIC] [TIFF OMITTED] T6856.269

Mr. Gilman. And I do have several questions. I think what Chairman Burton is raising I think is quite pertinent. I'm surprised to hear that, Dr. Midthun, you're reluctant to issue any letter to the manufacturers if there is some concern. You say there is some mandate in the legislation that permits you

to make some of these corrections?

Dr. Midthun. Under the PHS Act, the FDA can make a mandatory recall if there is an imminent or substantial hazard to the public health. And as I noted before, the preponderance of the evidence does not suggest that there was a causal relationship between thimerosal containing vaccines and autism. Thus, there is no substantial or imminent hazard that would authorize us to make a mandatory recall, sir.

Mr. Gilman. And yet, you are making a request that the thimerosal not be included in the future production of vaccines because of some concern? Is that correct?

Dr. Midthun. As Dr. Bernier noted, wherever it is possible to reduce exposure to mercury, that is a goal that we would like to achieve. Because there are many aspects of exposure that we don't have control over. For example, environmental food intake and thus, it's considered a precautionary measure that we can take. It's achievable, we can move from multi-dose vials that require a preservative to single dose vials. That's what we have been doing, and actually have made a substantial achievement toward reaching, as I noted before, currently all vaccines being manufactured for pediatric use under the routine childhood immunization schedule, either contain no thimerosal or only trace amounts.

Mr. Gilman. And that's based on your recommendations?

Dr. Midthun. That's based on working collaboratively together with the other public health service agencies and also the manufacturers, that it was agreed that this would be an achievable goal, and it would be good to reduce the exposure to mercury whenever possible.

Mr. Gilman. So there is a consensus in the thinking of the medical world that it would be preferable to eliminate that possibility in providing vaccines for children, is that correct?

Dr. Midthun. It's recognized that mercury in larger amounts is a toxin. And thus, it is good to be able to reduce exposure. You can never eliminate exposure. But it is good, where you can, to be able to reduce it.

Mr. Gilman. I will yield.

Mr. Burton. Let me just ask, is mercury a cumulative thing in the body?

Dr. Midthun. I'm not a toxicologist.

Mr. Burton. We had one yesterday. And the toxicologist, Mr. Gilman, said that if you get a shot with mercury in it and then you get another one and another one, there's a cumulative effect. And our children are getting 26 shots by the time they go to school.

I might add, did you get a flu shot?

Mr. Gilman. Yes, I did.

Mr. Burton. You got thimerosal. You got mercury in your body from that shot, and Dr. Eisel, our admiral, I called him

about it, and he didn't even know it was in there.

Mr. Gilman. That raises another good question. You have taken some precautionary measures. What have you done with the public so that they're aware of these problems? What is your educational process, what have you done in the educational process to the consuming public with regard to these concerns that you have in the medical community?

Dr. Midthun. Our labeling for products indicates what is in the product. In the case where there is a preservative, it is so stated. And----

Mr. Gilman. I'm not asking just labeling. I'm asking you, have you undertaken educational initiatives for the consuming public so they'd be aware of these problems?

Dr. Midthun. We believe that the vaccines are safe and effective, including those vaccines that were licensed with thimerosal as a preservative, sir.

Mr. Bernier. Mr. Gilman, if I might add something, because we've discussed this at CDC in anticipation that we might have this question. I think one of the things that CDC has done, at least, is we generally try to work with the provider community to try to provide information about these matters. So in the last 22 months, during the time when this episode has been ongoing, there have been repeated publications, for example, in the morbidity and mortality weekly report at CDC, there have been joint statements between the Government agencies and the American Academy of Pediatrics and the American Academy of Family Physicians.

So we have worked to put information in the hands of the providers, so that they could address the concerns of the parents. Also, we have had on our Web site information about these matters. We have a hot line where parents can obtain information. So I wouldn't want to leave the impression that we haven't been proactive, if you will, about putting information out there. Because I think we have been.

Mr. Gilman. Well, you're saying you're putting it in the hands of the providers. What about the consuming public? What are you doing? You're a government agency. What are you doing about educating the public about these dangers? What has been done by your agency or any of the panelists who are here representing our government agencies? What's been done to make the consuming public aware of these mercury problems?

Mr. Bernier. Well, like I said, at least speaking for CDC, traditionally we make, we work through the providers to address the concerns of the parents to make sure----

Mr. Gilman. You don't go beyond the provider? If the provider fails to make the information available, you're satisfied?

Mr. Bernier. Well, we have also the vaccine information statements that parents are given prior to vaccination, and that's one direct connection that we have with the parents at

the time of vaccination.

Mr. Gilman. Are these statements that your agency makes to the parent?

Mr. Bernier. Are they what, sir?

Mr. Gilman. Are these statements that you make available to the parent?

Mr. Bernier. Yes.

Mr. Gilman. How is that distributed?

Mr. Bernier. These are widely available, they're required by law to be made available to all the parents when children are immunized, before every immunization----

Mr. Burton. If the gentleman would yield.

Mr. Gilman. I'd be pleased to yield.

Mr. Burton. And then we'll get to Dr. Weldon.

Mr. Gilman, do you ever use a nasal spray?

Mr. Gilman. No.

Mr. Burton. Does your wife, or any of their friends?

Mr. Gilman. My wife does.

Mr. Burton. Do you know that most nasal sprays have thimerosal in them?

Mr. Gilman. I didn't know that.

Mr. Burton. Yes. There's mercury in a great many products that we use as adults. And there's a tremendous rise in the number of cases of Alzheimer's. And mercury has a debilitating impact on the brain, as you saw, you probably didn't see it, in that Calgary study. So it's not only the children that are being affected by this, in my opinion. And I'm not a scientist. It's all of us.

Because we're getting mercury through the environment, but we're getting it in nasal sprays, and the health agencies, not too long ago, took mercury out of all topical dressings, because they said it would leach into the skin and cause problems. And yet, it's in nasal sprays, it's in a lot of products we use as adults, and it's in our vaccinations, like the flu shot that you received.

Mr. Gilman. Mr. Chairman, if I might reclaim my time. It would seem to me there's a responsibility by our agencies, whether it be NIH, whether it be CDC, whatever agency is involved in regulating our vaccines, that we make more information available to the public of the dangers of mercury, and make it available not only just to potential users of the vaccine, but to the entire public.

So I'm urging those panelists who are here today to address that problem, since it is a problem that can affect millions and millions of our population.

Just one other question, Mr. Chairman. Parents are becoming concerned about the vaccines that are already on the market that have not been recalled, but many are unaware what's being done to make some recall or are unaware of your preventive actions or your concerns, because you have directed the

manufacturers to take some steps to remove this product.

But what have you done with the product that's still on the shelves around the country?

Dr. Midthun. It remains on the shelves, sir.

Mr. Gilman. And could be used?

Dr. Midthun. And could be used, that's correct.

Mr. Gilman. Shouldn't you have some responsibility to remove that, if you are concerned about its use?

Dr. Midthun. Again, as I mentioned, there are certain conditions that allow us to make a mandatory recall. And that is not one of them. You have to have an imminent or substantial hazard to the public health in order to make a recall.

Mr. Gilman. Are you concerned that if some of these products are used, they could cause some problems in the health of young people?

Dr. Midthun. The evidence does not show that there is a causal relationship between thimerosal as used in vaccines and autism.

Mr. Gilman. And yet you recommended that it not be used in future manufacturing, is that correct?

Dr. Midthun. That's correct, because if we can decrease exposure to mercury in ways that are available to----

Mr. Gilman. If you're concerned about the increase in exposure, then why not take these products off the shelves and prevent their distribution? If you really are sincerely concerned about the use of these products, it would seem to me there's an absence of responsibility here by your agency.

Dr. Midthun. We have to follow the regulations as they are written, sir.

Mr. Bernier. Mr. Gilman, could I add, I want to, I think, try to correct an impression that I think is being generated here. That is that the vaccine is not being recalled then nothing's happening. I think nothing could be further from the truth. Please allow me to just take a minute to explain what has changed between, in the last 22 months and today. And a lot has changed.

I think the impression is, well, if we don't accomplish a recall that somehow this problem is not being addressed. And I think there are two or three things I'd like to point out.

Mr. Gilman. Doctor, if I might interrupt, when we have faulty tires on vehicles, we demand that they be recalled. If we have a medication that's on the shelf that could create some problem, it would seem to me there's enough evidence, even though it's not fully explored, that there's enough evidence available that these products should not be allowed to go out to the consuming public.

Mr. Bernier. Mr. Gilman, we have no faulty vaccines on the shelves.

Mr. Gilman. You've already testified before us, at least Dr. Midthun has testified that as a preventive measure, they're

recommending to the producer not to use this product. It would seem to me that's enough evidence to take the rest of the product off the shelf.

Dr. Midthun. We've not recommended that a product not be used. We have worked with manufacturers to reduce the use of thimerosal as a preservative in vaccines.

Mr. Gilman. And you've done that because you have a concern about the future health of young people, isn't that correct?

Dr. Midthun. We have concerns about overall exposure to mercury from all sources in the environment. And this happens to be a source that we can control by switching to single dose vials in large part.

Mr. Gilman. And these other products that are still on the shelf could contribute to their poor state of health, is that right?

Dr. Midthun. We do not believe that the products out there, we believe that they are safe products, sir.

Mr. Gilman. No further questions.

Mr. Burton. Dr. Weldon.

Dr. Weldon. Thank you, Mr. Chairman. I want to thank all the witnesses for testifying. I certainly thank your efforts in trying to answer and address the issues and concerns we have.

Dr. Rennert, you testified, I believe, that the total spending at NIH will be $52 million on autism related research? Correct me if I'm wrong, that is including a lot of autism related research, but the actual figure on autism specific research is smaller than that, is that correct?

Dr. Rennert. I can't tell you that for sure. I will tell you that the list we submitted is correct. We will go back and review it and provide you with the information.

Dr. Weldon. Yes, I would like you to personally provide that to me, because I have had people come to me and say the net was cast pretty wide to come up with a figure that high, and that the figure for autism specific research is actually about a third or less of that.

And the reason I bring that up is, I had my staff pull a Congressional Research Study on AIDS. The figures that were provided to me from CRS is that there's 300,000 Americans currently suffering with AIDS, and 115,000 living with HIV. Now, I realize some people estimate that those figures are quite a bit higher, and that there's a substantial cohort in the population who have exposure to HIV, they're carrying HIV and they don't know it.

But if we use those figures and those figures have appeared in the media, that's about 415,000 people. The Federal expenditures on research and treatment and the various care for those patients with AIDS is $10.9 billion. Now, if we just look at the research number, I have a figure of $3.1 billion in the year 2000. I could not get the 2001 figure.

Now, I'm told we have about a similar number of kids with

autism. That's also very debatable, if you look at autism spectrum disorder, you get a much larger number. When I do the math, it comes out to, for research, about $7,000 per person with AIDS and about $140 for each child with autism. Another way to look at that figure is for every $7 we spend on AIDS related research, we're spending 14 cents on autism related research.

Do you, and I would ask any of the panelists to comment on this, do you feel that, and I feel the ultimate responsibility for this rests with the Congress, not with you, OK? So I'm not trying to make you feel bad. I think we have a responsibility to make sure that our money is spent, or the public's money, the taxpayer money, is spent appropriately. Do you think this is an appropriate level of funding, a relatively appropriate level of funding?

Dr. Rennert. You've evoked my bias as a pediatrician. I believe our future is with our children. What I can tell you is that we will spend more money on autism research. The numbers that I've presented, regardless for the moment of the magnitude, represent an increase in funding at least in recent times, for this area. And I certainly subscribe to the notion that this is an area that should be an area of focus and emphasis for us.

Dr. Weldon. Well, does anybody else want to comment?

Dr. Boyle. Sure, I'd be happy to.

Dr. Weldon. Are there adequate levels of funding for the types of research studies that need to be done on this?

Dr. Boyle. We direct money at CDC as directed by Congress. But I can tell you that in the last year, we have gotten a substantial increase in our funding for autism. And that's really allowed us to develop the State surveillance, State monitoring programs that I referred to in my testimony. It's allowing us to develop the infrastructure to actually be doing a very large study of the epidemiology of autism.

So I feel that we have made substantial progress. But we have a lot further to go.

Mr. Gilman. Would the gentleman yield?

Dr. Weldon. I'd be happy to yield.

Mr. Gilman. Have any of you made a request for additional moneys that have not been allocated for your autism research? Have any of your agencies made a request for additional sums in the budget that were not allocated to you? Or were you all satisfied with the way the funds were being allocated?

Dr. Weldon. If I could ask it a different way, were all of your requests granted to you by your superiors within the agencies you work in?

Dr. Midthun. May I just say that FDA, and the Office of vaccines, we don't have the ability to ask for funding for studying autism per se. Our mission is to regulate vaccines.

Dr. Weldon. What about CDC and NIH?

Dr. Rennert. The answer for NIH is no.

Dr. Weldon. We'll make sure your future is secure in the year ahead.

Dr. Boyle, I've got to ask you a question related to what you're doing. We had a physician testify yesterday about this increasing incidence issue. And I think you came into my office once and we talked about this, and the change in the diagnostic manual. He made a very good point. Where are all the adults? If the prevalence isn't increasing, if the incidence isn't increasing, then where are all the adults? In all of these studies, you're looking at prevalence and incidence. Are you looking at prevalence in adults to try to make a determination to answer that question, is the rate increasing?

Dr. Boyle. Our studies have been directed at children. We primarily look at school age children, children age 3 to 10. That is a very good question. And as may have come up yesterday, the prevalence, we call it prevalence only because we think most of it has to do with sort of prenatal etiology, so that someone is either born with the condition or with the specific genetic predisposition for the condition. So we thought we'd refer to prevalence.

Dr. Weldon. Well, I would recommend you look at that issue, looking at the disease prevalence throughout all age groups in the population. Because I think that's a very, very critical question, if we are going to try to get----

Dr. Boyle. I think Dr. Amaral testified yesterday about efforts in California to address the issues of sort of changes in diagnosis, as many researchers have suggested, as well as the greater awareness of the condition and the impact that has had on the increase in the number of cases seen in California. Actually, I think that's going to be a very interesting study. It's really going to be able to shed some light on what's happening.

Mr. Burton. Can we come back to you, Dr. Weldon? Mr. Waxman is here and he wants to ask a few questions, then we'll come right back to you.

Mr. Waxman. Thank you, Mr. Chairman.

Dr. Bernier, the CDC has explained that it is opposed to recalling thimerosal-containing vaccines because it's concerned about shortages. In fact, I understand there is a concern about a shortage of DTaP vaccines. At the hearing yesterday, one of the witnesses suggested that stocks of non-thimerosal vaccines are adequate and that there was no need to keep thimerosal-containing vaccines on the shelves.

Can you explain your concerns about shortages? For instance, if the DTaP vaccine containing thimerosal were recalled, what possible effect would that have on our children?

Mr. Bernier. Yes, Mr. Waxman, it is correct that at the present time, for DTaP, there is a very tight supply situation. We have two additional manufacturers that have left the market

in the recent past, and we are now left with only two manufacturers. And there are back orders at the present time that cannot be filled because the amount of available vaccine is not adequate to fill those back orders.

So if in fact there was to be issued a strong preference for thimerosal free DTaP, or if there were to be a sudden recall of the existing DTaP vaccine with thimerosal, this would produce spot shortages which would create, we think, delays in children being immunized, which could lead to disease very quickly.

In 1999 alone, there were 15 deaths from pertussis in the United States. This year already we've had five deaths from pertussis. So the need to continue the coverage with DTaP is very real. These are not hypothetical or theoretical risks. We know that creating shortages will produce coverage problems, will increase the risk of children to these diseases.

Mr. Waxman. Last year, CDC testified that they were actively monitoring possible adverse effects of thimerosal, the mercury-containing preservative that's being phased out of vaccines. CDC found no link between thimerosal and developmental delays. Have you continued to monitor for any of these effects, and what has your surveillance shown?

Mr. Bernier. Well, we have continued at least in the look at the autism question. In the original results from the vaccine safety data link, there was no evidence of a link between thimerosal exposure and autism. In the last year, an additional number of cases has accumulated. I believe somewhere in the vicinity of an additional 40 cases. When we add those cases to the ones that we looked at before, we reached the same conclusion. It has not altered the original conclusion, which was that there was no link between exposure to thimerosal and autism.

Mr. Waxman. Thank you. Dr. Midthun, at the hearing yesterday Dr. Haley testified about the toxicity of thimerosal-containing vaccines. He suggested that the thimerosal in vaccines was harmful to children.

In the pre-licensure phase, is the vaccine tested for toxicity?

Dr. Midthun. Yes, it is. The vaccines are usually evaluated in a very large number of infants, if that's the target population for whom they're intended. They are tested with regard to the entire formulation. And thus, if there were to be any acute toxicity, that would be noted in the clinical trials that are done in support of the license application.

Mr. Waxman. Does this mean that the entire vaccine, including all of its component parts, is tested for toxicity?

Dr. Midthun. That's correct. The vaccine in entirety is tested.

Mr. Waxman. So if a vaccine were toxic, this should be revealed in the prelicensure phase, is that correct?

Dr. Midthun. Yes, that's correct.

Mr. Waxman. What did the toxicity testing of vaccines with thimerosal reveal? Did this testing indicate that the thimerosal is likely to pose health dangers for children?

Dr. Midthun. The clinical studies did not suggest that, sir.

Mr. Waxman. So why did the FDA move quickly to remove thimerosal from vaccines?

Dr. Midthun. Because we felt it was an achievable goal. It was a way where we could reduce the overall exposure to mercury among children, and it was something that was achievable, because we could switch from multi-dose to single dose vials. In the United States that was something that was feasible.

Mr. Waxman. Dr. Boyle, Dr. Wakefield testified at yesterday's hearing that we need active surveillance of vaccine adverse events. Can you explain what CDC does to actively monitor potential problems associated with vaccines?

Mr. Bernier. CDC is actively looking at vaccine safety events through the VAERS system. We are monitoring events and when events occur that create cause for concern, we have the resource represented by the vaccine safety data link population, which is a way of, provides us an easier means of testing hypotheses that may arise from adverse events that are detected.

So we have this detection arm and then we have a testing arm where we can test hypotheses. For example, this was one of the ways in which it worked recently with rotavirus and intussusception, where both arms of the vaccine safety mechanisms were put into play in order to address that concern.

Mr. Waxman. Thank you very much. Thank you, Mr. Chairman.

Mr. Burton. Let me just followup on what Mr. Waxman said. I know he has to leave and he's probably not going to hear the response, but did you folks test the rotavirus vaccine before you put it out on the market?

Dr. Midthun. I've not been involved with the rotavirus vaccine trials.

Mr. Burton. It was tested by FDA, wasn't it?

Dr. Midthun. It was tested by FDA.

Mr. Burton. And in 9 months it was recalled, wasn't it?

Dr. Midthun. Maybe I could ask Dr. Baylor. I wasn't there at the time.

Mr. Burton. You don't have to ask him. It was recalled, because one child died, there were several serious problems, intestinal problems where there was surgery involved. And it was recalled.

Dr. Midthun. I just spoke with Dr. Baylor. It wasn't actually a recall, either a mandatory or a voluntary recall. The company decided to withdraw it from the market, sir.

Mr. Burton. Well, because one child died, and a whole host of them were injured. I mean, you know, you can cut it either

way you want to. The fact is, they took it off the market, and it had been tested. So you folks are not infallible.

Now, the DPAT shot, are they still manufacturing that with thimerosal in it?

Mr. Bernier. No, Mr. Chairman, they are not.

Mr. Burton. They're not. But you say that they're not producing enough of the single shot vaccines to take care of the needs of the country at the present time?

Mr. Bernier. At the present time, there is a shortage in the supply, correct. They are back ordered, and the new vaccine that they are producing is not adequate to meet the demand at the present time.

Mr. Burton. How long will it take for that to be adequate?

Mr. Bernier. I think the FDA could have a better idea of that. My impression is that it's, well, I mean, relatively short, and I'm thinking of a few months. But I don't have the information.

Mr. Burton. So in a few months, they could have the supply up. Now----

Mr. Bernier. Could we just get FDA, because I don't want that to be on the record, if that's true or not.

Mr. Burton. How long will it take for them to get the single shot vials, doses up to safe level?

Dr. Midthun. I can't give you the exact time line. But I do know that there are two more lots potentially containing thimerosal that the company intends to release. But after that, they will then be releasing only the thimerosal reduced versions.

Mr. Burton. How many shots are in a lot?

Dr. Midthun. That's proprietary information, sir.

Mr. Burton. Do you want me to subpoena it?

Dr. Midthun. I would be happy----

Mr. Burton. You get it for me, or I'll subpoena it. I want it.

Dr. Midthun. I would be happy to respond to the chairman's letter on that.

Mr. Burton. Because what we're talking about, there's thousands and thousands of shots of DPAT that you're going to put into the system and kids are going to get those shots because of the shortage.

Now, let me ask you, what's the likelihood, let's say it takes 6 months, let's say it takes 6 months to get the single shots up to snuff to where you've got a supply, let's say it takes 6 months. How many kids do you think are going to die in 6 months because they don't get that shot?

Mr. Bernier. I can't estimate, Mr. Chairman. I can tell you that as I mentioned earlier in my testimony, this is not hypothetical. In 1999, there were 15 deaths associated with pertussis. And already, there have been five deaths this year. So if we created a situation where we abruptly said, you must

use thimerosal free vaccine, that would create shortages which would lead to delays which would lead to what I'm calling days of lost protection.

Mr. Burton. I understand. You've made your point. Let me just say this. I want the names of the producers of the DPAT shot. And I'm going to subpoena records from them to find out how much is in a lot, how they have two more lots that they have to use, they have two more lots. I want to find out how long it would take for them to produce the diphtheria, tetanus and the pertussis vaccines individually. I'm going to find out how long it's going to take.

Because I suspect that those lots have a lot of shots in them and there's a lot of money involved, a lot of money involved. And as a result, they want to sell those before they go ahead and get their lots of individual shots up to snuff. And I think it's money, I really believe that.

I think that there is mercury in those vaccines, and during the time that you say two or three or four or five or six or seven children are going to possibly die, and we don't want any child to die, according to my figures, there are 16 children a day that's going to come down with autism. A day. That's 17,520 children are going to be at risk for autism in the next 3 years while studies are going on, if mercury has something to do with it, as many, many people believe.

Scientists, toxicologists, it's not just me. We had a whole litany of doctors from all over the world talking about this yesterday. And what you're saying is one thing. But what scientists and doctors and studies have already shown is that mercury does have a debilitating impact on the brain. So you're talking about children at risk. In 3 years that it's going to take to go through these studies, 17,520 children are likely to become autistic. If you folks are wrong, how are you going to live with yourselves?

The gentlelady is recognized.

Ms. Ros-Lehtinen. Thank you so much, Mr. Chairman. I regret that I have not been able to be here for the entire hearing due to an overbooked schedule. But I have the testimony and I look forward to reading it tonight. As I had said before, we have two good friends of our family, Charles and Patience Flick, who have two children who are afflicted with autism. I know what a terrible toll autism can take on a family. Everything that the Flick family does is related and surrounded by Bonnie and Willis and their care and what will happen to them. And any steps the Flick's take, Bonnie and Willis are at the foremost of their thoughts.

Bonnie is a little more high functioning and was able to go to Disney World with us. Willis is unfortunately so overstimulated by the environment that he can barely leave his house. Everything is too much sight and sound for him. So I look forward to seeing the fruits of the pressure that Chairman

Burton is bringing to bear on this issue. We need to improve research dollars, and have more research going into the causes of autism, to help lead us to a cure. Because I know how devastating that affliction is, not just on the children who have it, but on their families.

We look forward to getting more evidence about the relationship between vaccinations and the rise, dramatic rise in autism rates. I know that many are not in agreement with that, but I congratulate Chairman Burton for his steadfast devotion and his bravery, in spite of all of the attempts of the scientific and health community trying to make this seem like there's no tie-in whatsoever. I don't think that we should leave any stone unturned. If mercury is a factor, we should give serious consideration to revamping our vaccination program and looking at other possible factors involved in the dramatic rates in autism across the country.

So I thank you, Chairman Burton, on behalf of the many Flick families throughout the United States. Thank you, Dan.

Mr. Burton. I thank the gentlelady.

Mrs. Morella, do you have any comments or questions?

Mrs. Morella. Actually, I commend you for the ongoing series of hearings that you've had on autism. We all care about it. I'm really here to listen, to learn and then to do what I can to lead and I know you have medical experts before you, many of them who are involved in laboratories in my district, NIH and of course FDA, and I value CDC.

I'm also interested in the kind of funding that you do have. Really, we work very hard, just as an example, to double the funding for NIH for that 5 year plan we had, so that by 2003 we would realize it. We are well on our way, this is our 4th year. I'm curious, with regard to autism, and I must say, a lot of the leadership on looking into autism obviously has come from the chairman, although I do wear sometimes my little jigsaw puzzle ribbon which is autism, the puzzle pieces, right, which we are trying to put together.

I understand from your testimony, and I guess this would be Dr. Rennert, that $1 million is being set aside to fund innovative treatment proposals, and that you have 30 applications. How do you work with that? Are you kind of a magician?

Dr. Rennert. No, I think one works with it by trying to fund as many grants as one can, and that the limit is the number of dollars.

Mrs. Morella. So how many do you think you can?

Dr. Rennert. Well, I think again, the response I would make is that the amount of funding we could use is equivalent to the number of meritorious proposals that there are. And it depends on where you set the bar.

Mrs. Morella. Sounds like a political answer to me.

Dr. Rennert. No, I can't give you a precise number. But the

point is quite clearly, we could use more funding to fund more proposals and more research on autism.

Mrs. Morella. It just seems to me that of the 30 applications and obviously probably not all would meet the qualifications, the peer review, what it goes through, but certainly $1 million isn't going to fund more than a couple of them, probably.

Dr. Rennert. Three to four is what that would fund.

Mrs. Morella. So it does say something about the need for us to begin to look more into that in terms of the adequate funding.

Then I note also, looking at Dr. Boyle's testimony, and I wasn't here to hear you synopsize it for the committee, but you mentioned that CDC, NIH and 10 NIH funded centers and programs of excellence in autism are collaborating on a case control study of developmental regression. Each of these centers was awarded funds through the NIH competitive process.

Can you give us like a time line on it, how that is going?

Dr. Boyle. Actually, I may let my colleague at NIH address that.

Dr. Rennert. Again, the program was initiated in 1997. And at this point in time, as we mentioned in our testimony, there are approximately 2,300 patients with well defined autism that are a part of the network and the study. The second part is with regard specifically to the question of the temporal association between vaccination and the onset of autism, as well as a study of the potential effects of mercurials in vaccines as preservatives.

There are at the present time 1,600 cases that are being used for the study. And the phase one part of the study will look at 250 cases of patients with early onset autism, 250 patients with regressive autism, and a corresponding number of controls for each group. That work now is in the second phase where the analysis will begin and the study of the biological specimens that were obtained.

A third part, because you mentioned it in regard to funding, I forgot to point out though it was in my written testimony, that in fact we will release in the coming year an RFA or request for applications for the competitive renewal and the commitment to renew these centers for another 5 years. Clearly, our hope will be that over time, that we could add more centers to this. But specifically, the element of study that ought to be completed, as I was asked by Chairman Burton in the next 2 years or so, is that these studies linking or attempting to establish whether there's an association or what the association is between vaccination and thiomercurials will be completed.

Mrs. Morella. Within 2 years, then, that's what you're saying, 2 to 3 years. Fine. Thank you, Mr. Chairman.

Mr. Burton. Let me just say to the gentlelady, in 3 years

is what we thought was going to be the study, but if we waited 3 years to have a conclusion drawn, and we continue to use these kinds of vaccines, we're all for vaccinations, but not with some of these things like mercury in them, there would be 17,520 new children that would probably be autistic. That is if mercury did have something to do with it.

I think we're about to wrap this up. We have a number of questions we'd like to submit to you for the record. I don't want to keep you here all day. Do we have any parents that have autistic children in the room? Would you raise your hands?

How many of you believe that your children were adversely affected by something in the vaccines? Would you raise your hands? Is that everybody or almost everybody? About 80 percent; 8 out of 12, maybe 9 out of 12. That's what we're getting in e-mails by the hundreds and thousands.

Now, maybe you folks are right, maybe mercury doesn't have anything to do with it. Maybe the thimerosal doesn't. But they think it does. And there's a growing body of these people. And they're getting organized all across the country, and so is the Congress of the United States. So I really hope that you'll take a hard look at this. Because it isn't going to go away. And as I said before, it's going to cost this country trillions of dollars.

In any event, do you have any other questions?

Mrs. Morella. No, I don't, but of course I hope on the basis of all of this that if you can expedite so that we can come to some conclusions, because I can recognize the passion, but also the desire for patience that's so difficult for the chairman. And I would agree with him, if it's been going on since 1997, we should have some results. Thank you very much.

Mr. Burton. Thank you, Congresswoman Morella.

We will submit these for the record.

There are documents that we'll be requesting. If there's a problem with you giving those because of confidentiality of any kind, if you would let us know and we'll be happy to legally send a subpoena to get that information, because we want to make sure we have as much research material as possible.

We'd also like to know who are the manufacturers of the DPAT shot.

Dr. Midthun. I believe Ms. Clay has that.

Mr. Burton. OK. We'll be contacting them to get records on the supply that they have and how long it will take to go to single shot vials.

With that, thank you for being here. We stand adjourned.

[Whereupon, at 11:45 a.m., the committee was adjourned, to reconvene at the call of the Chair.]

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