CDC-sponsored MMR study supports Wakefield's findings

By
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The CDC tried again and …failed again
But this time, it validated
Andrew Wakefield's findings

Note from the author:
The following critique was to be published on the Web Site of the Vaccine Autoimmune Project on Monday September 15, 2008.
Unfortunately the VAP web site was the target of malicious hacking.
I am grateful to John and Jackie Fletcher for their invitation to feature it on JABS.
FEY

A study sponsored by the Centers for Disease Control and Prevention (CDC) and funded by the American Academy of Pediatrics (AAP) was published on *PLoS ONE* on September 4, 2008.

PLoS ONE, an international, peer-reviewed, open-access, online publication by the Public Library of Science features reports of original science and medicine research.

The recent CDC-sponsored publication was titled

"Lack of Association between Measles Virus Vaccine and Autism with Enteropathy: A Case-Control Study"

It described research conducted at Columbia and Harvard Universities and findings from three renowned laboratories.

The authors reported "strong evidence against association of autism with persistent MV RNA in the GI tract or MMR exposure". They also confirmed that the "Results were consistent across the three laboratory sites." (1)

This critique should cast a cloud on the authors' selection of cases, investigations, results, conclusions and statements to the media.

At the end, the only thing left standing will be the now-undeniable fact that biopsy

findings from Dr. John O'Leary's laboratory are just as reliable as those from two of the best laboratories in the United States.

Keeping that in mind, one must wonder how Dr. Ian Lipkin, apparently speaking for all the authors, could proclaim: "We are convinced there is no link between MMR vaccination and autism."

Is Dr. Lipkin truly "convinced" that just because this study of only ***five*** cases with post- MMR autistic and gastro-intestinal symptoms ***could*** not detect an association of autism with "persistent measles virus RNA in the GI tract or MMR exposure", a link between MMR vaccination and autism simply does not exist?

Does he really want us to believe ***that?***

On a personal note: It has not been easy for me to criticize a publication whose lead author I respect as a person and a pioneering researcher. As it will become evident, Dr. Hornig was not responsible for the part of the study I found most problematic.

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Dr. Marie McCormick of the Harvard School of Public Health, the chairman of the Institute of Medicine Immunization Safety Review Committee and the scientist who was supposed to "uncover the truth" about vaccines and autism described the new CDC-sponsored study results as "definitive and significant" adding: "This is the nail in the coffin, the final bit of research we were looking for to finally discredit this link between the measles vaccine and autism." (2)

By her statement, Dr. McCormick disqualified herself as a scientific referee, compromised the Institute of Medicine and confirmed two facts we all very much suspected:

1. That when she convened all the meetings, she was not ***really*** trying to find the scientific truth but only interested in discrediting any possible MMR-Autism connection
2. That ***she was not yet convinced*** that the MMR vaccine did not precipitate regression in a small percentage of children when she was preaching that message and telling the world that autism research needed to be focused elsewhere

Not to be outdone by a northerner, William Schaffner, MD, chairman of the department of preventive medicine at Vanderbilt University echoed:
"It's a "fabulous and terrific study… It is convincing because it takes the original concept of the profoundly flawed [earlier] study and does it the way it should have been done the first time… This really closes the scientific inquiry into whether

measles or MMR vaccination causes autism…" (3)

May be Drs. McCormick and Schaffner should read the whole paper a second time.

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Internet publication

I frequently publish on the Internet, not because my articles are not good enough to be published in peer-reviewed journals but because I just don't have the patience, at my age, to deal with the antics of certain editors. (4)

But this "definitive and significant study", this CDC-sponsored research from two of the best U.S. universities and three of the best laboratories in the world, ***why was it published online?***

Why was it not in the September issue of *PEDIATRICS,* the journal of the American Academy of Pediatrics (AAP), the organization that ***funded*** the project?

Why was it not in the New England Journal of Medicine (NEJM) where even Danish research is published and protected or …the Journal of the American Medical Association (JAMA) that is always so willing to help "friends in need"?

The answer to these questions is: I don't know.

I certainly tried but I was unable to find out why reputable medical journals, not only here but also in the United Kingdom, where MMR is a national obsession, refused to publish this CDC-sponsored publication by some of the best names in the business.

Why did all these fearless friendly editors suddenly get cold feet?

I was personally taken back when I read the statement describing the role of the sponsors in the new study. Were the editors of those major publications also concerned enough with the following to refuse to publish the manuscript?

> **"Members of the funding organization (AAP) and its sponsor (CDC) participated along with experts in virology and neurovirology, autism pathogenesis, and vaccine design and safety; representatives of the autism advocacy community; and study collaborators in an Oversight Committee that reviewed and agreed to all aspects of study design prior to data collection. The final decision to submit for publication was the responsibility of all study collaborators."**

In any case, the manuscript was submitted to the Public Library of Science *PLoS*

ONE, a prestigious Internet site on June 29, accepted on August 8 and as previously mentioned, published September 4, 2008.

In spite of the heated presidential campaign and a very busy hurricane season, its fallout is guaranteed: The CDC has had a lot of experience circulating and spinning such studies!

It would be interesting to know whether the *PLoS ONE* reviewer wondered like I did about those experts on "vaccine design and safety" who served on the study Oversight Committee, why they were needed and what did they do exactly?

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Transparency

When one is examining the findings of a CDC-sponsored study based on biopsies from specific sites in a very particular cohort, findings that could prove that the MMR vaccine does NOT cause autism in a small percentage of children, ***a priority at the CDC***, one must be fully assured that the sponsor's role is most transparent.

In this important study, ***the role of the CDC at every level and every stage should have been clearly stated beforehand and clearly adhered to***.

The statement about the role of the sponsors (above) is strange to say the least. The Food and Drug Administration (FDA) would have never accepted such a statement from the sponsor of a study investigating an arthritis medication, an antihistamine or a vaccine.

One of the best articulations of "Study Transparency" I have ever heard was by Professor Walter O. Spitzer M.D., M.P.H., F.R.C.P.C, Emeritus Professor of Epidemiology at McGill University in sworn testimony at the December 10, 2002 Hearing of the Government Reform Committee of the House of Representatives. The scientific world lost Dr. Spitzer before he could start working on one of his dreams: An international study of autism rates in developing countries. I can only imagine how interested he would have been in the exploding prevalence of autism among Somalis in Michigan… and its causes.

The study Dr. Spitzer was discussing in 2002 was the CDC-funded "Big MMR study from Denmark" by Madsen, that no one remembers, and that I discussed recently. (4)

Obviously, principles involving the careful harvesting of biopsies from specific pathological areas in a small child and the meticulous reporting of their related findings have to be much more stringent than those related to epidemiological studies.

This is what Professor Spitzer stated in part at the congressional hearing:

> **"*The concerns are about the process of funding, the interaction of sponsors with protocol formulation and approval, compliance with protocol, the role of investigators vis-a-vis sponsors in the actual conduct of research and the input of CDC epidemiologists in the preparation of the report with its conclusions*:**
> ***a) Was there a protocol?***
> ***b) Who approved it?***
> ***c) Were there changes as the study progressed?***
> ***d) Who approved the changes?***
> ***e) Who monitored work-in-progress?***
> ***f) Who approved the final report?***
> ***g) Was there a Scientific Advisory Board?***
> ***h) What exactly was the role of the CDC and its professionals?"***

For "Total Transparency" Dr. Spitzer advocated:

> ***1. That the main protocol should be published in advance of the fieldwork, notably including the analysis plan with attendant definitions declared in advance.***
> ***2. A Scientific Advisory Board be created to monitor all phases especially protocol changes in progress and proposed publications.***
> ***3. A Community Advisory Board to look at conflicts of interest in finances.***

It clearly seems that "None of the above" took place in this recent study!

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When finding nothing is wonderful

Researchers like to discover things and they are very happy when they do.

Scientists charged by the CDC or the U.K. Department of Health to investigate certain aspects of the MMR vaccination-autism puzzle seem on the other hand to be truly elated when they find N O T H I N G because they know that their "achievement" will be enthusiastically applauded.

Our health authorities have somehow convinced themselves and …people that if someone discovers something that does not suit their beliefs, that discovery becomes nil and void if someone else creates a similar study and somehow comes up with N O T H I N G.

Obviously the more difficult the research and intricate the accomplishment, the easier it is for the other camp to fail to duplicate it.

On May 28, 2006, an article appeared in a London paper describing the findings of a study from Wake Forest University School of Medicine in North Carolina titled

“Scientists fear MMR link to autism.” According to the report, 275 children with regressive autism and bowel disease were evaluated and 82 were carefully and completely tested. Of those, 70 had evidence of measles virus. The lead author of the study was quoted as saying: “Of the handful of results we have in so far, all are vaccine strain and none are wild measles. This research proves that in the gastrointestinal tract of a number of children, who have been diagnosed with regressive autism, there is evidence of measles virus.” (5)

As I fully expected, just 3 days later, Reuters Health Information NY reported on a different study from the U.K. titled “No Evidence of Measles Virus in MMR-Vaccinated Autistic Children.” That study, published in the May issue of the Journal of Medical Virology, found that “contrary to the findings of earlier studies, measles virus genetic material ***was not detected*** in the blood of MMR-vaccinated autistic children with development regression”.

That British study was authored by Dr. M.A. Afzal et al, of the National Institute for Biological Standards and Control in Hertfordshire, U.K. who used several assays to test for measles genome sequences in leukocyte preparations obtained from ***15 children*** with autism who had received the MMR vaccine as part of their routine immunization schedule.

Dr. Afzal attested that there was no evidence of measles genomic fragments in any of the children examined, in spite of the fact that the methods he used were "highly sensitive, specific, and robust" and capable of detecting "measles virus RNA down to single figure copy numbers per reaction." As expected, the Reuters' report added: “Given the rigorous methods employed, the researchers believe that measles virus material genuinely did not exist in the patient's blood samples”.

Intrigued, I reviewed the literature and discovered that quite often when Dr. Wakefield or a supporter published a paper, Dr. Afzal published one of his own, shortly thereafter. Wakefield and colleagues reported interesting findings and predictably Dr. Afzal always reported finding N O T H I N G, immensely pleasing the U. K. DOH and the vaccine manufacturers.

Wakefield’s publications always made a lot of sense and many are still easily available. (6)

Few remember the “nothing” studies and where they were published

My report “When finding nothing is wonderful” is still accessible. (7)

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The recent CDC–sponsored study
Problems

Many people only read the abstract of a publication and the very first sentence of the abstract of the recent study is wrong:

"The presence of measles virus (MV) RNA in bowel tissue from children with autism spectrum disorders (ASD) and gastrointestinal (GI) disturbances was reported in 1998"

Wakefield never mentioned measles virus (MV) RNA in his February 1998 landmark article. In addition, the statement does not even adequately summarize the first paragraph of the publication that states otherwise:

> ***Beginning in 1998, Wakefield and colleagues reported intestinal abnormalities, including reactive lymphoid hyperplasia in ileum, in children with autism and other developmental disturbances [1]–[8]. These findings, combined with parent-reported associations of timing of onset of behavioral abnormalities with MMR administration, led to the hypothesis that MMR contributed to autism pathogenesis [1]. Subsequent studies from this group reported MV RNA in bowel biopsies and peripheral blood mononuclear cells (PBMC) from children with ASD [9]–[12].***

A more accurate first sentence would have been:

"In 2002, Uhlmann, Martin, Shiels, Wakefield and O'Leary reported finding evidence of measles virus RNA in 75 of 91 intestinal biopsies from children who developed autism and had certain typical gastrointestinal (GI) findings following MMR vaccination" but that would have obviously created a problem …right off the bat!

For those readers who would have wondered: "How come the U.K. study had 75 positive cases and this CDC-sponsored study from Columbia & Harvard had only one?" the authors of the new study could have certainly not been able to blame O'Leary, his laboratory and his findings.

So …why were the findings so different?

75 out of 91 vs. 1 out of 25

The answer to that question is SELECTION / SELECTION: Selection of the cases and selection of the biopsy site

In the British study, the highly-focused team of Andrew Wakefield carefully studied ***the cases that fulfilled the study criteria*** and the matched controls.

In Boston (see Subjects Characteristics), "The clinical indications for endoscopic/colonoscopic procedures commonly noted in both AUT/GI and GI groups included recurrent abdominal pain (RAP), gastroesophageal reflux, vomiting, and food allergies."

At the Royal Free Hospital in London, an *experienced* pediatric gastro-enterologist performed the procedures and obtained the biopsies under fluoroscopy ***from the affected areas of ileocolonic lymphonodular hyperplasia in children known to have the new variant of inflammatory bowel disease.*** The result: His biopsies yielded impressive findings.

In the CDC-sponsored study,

"Biopsy material was obtained from terminal ileum and cecum under direct supervision of the team gastroenterologist. For analyses of MV RNA, four random samples were taken from superficial mucosae of ileum and cecum. Additional specimens were acquired at sites indicative of inflammatory GI lesions, if present. All samples intended for RNA analysis were frozen immediately in coded tubes…"

The first sentence suggests that the team gastroenterologist did not perform the procedure himself but ***supervised*** a fellow or a resident - who obtained the "biopsy material".

When an attending surgeon supervises a resident performing a surgical procedure such as an appendectomy, he or she effectively "assists" the doctor in training by standing on the other side of the table and helping at every step …sponging, retracting, tying etc

Supervising a colonoscopy with biopsy (s) on a small child is totally different of course. There is not enough room at the foot of the operating table for two adults and all the attending can do is scrub, gown and "supervise".

But why were ***cecum*** biopsies obtained in this study?

Didn't the study gastroenterologist know that the pathological entity that Wakefield described was called ***ileal*** lymphonodular hyperplasia?

Didn't the team read the British paper where it is clearly stated that the MV RNA "was predominantly detected in dendritic cells in reactive follicular hyperplastic centres in ***ileal*** biopsies from affected children"?

Didn't anyone remember that Wakefield's team did ***not*** find evidence of measles virus protein in biopsies from the colon including the cecum?

The real problems with the site selection were that:

A: All the unwarranted cecal biopsies were effectively useless

B: Because we do not know how many there were, we cannot even ***start*** to guess what impact they had on the study results.

Let us now examine the second sentence in the above paragraph and the statement ***"four random samples were taken."***

I take that statement as meaning that the biopsy samples were obtained in a random fashion and therefore not *necessarily* from the involved and inflamed areas. I am obviously not a surgeon but I strongly suspect that a surgeon investigating a lump in the breast of a woman would not be taking four "random" biopsies in that breast or … the other breast.

I would dare say that when one takes random biopsy samples, one is likely to get random results unless the pathology is diffuse and widely spread.

Lastly, let us look at the very next and even more amazing sentence "Additional specimens were acquired at sites indicative of inflammatory GI lesions, if present" for which the only printable comment is:

"You must be kidding!"

Did Lipkin and friends hope to find evidence of measles virus presence in tissues that were scarcely or not at all inflamed?

Did they seriously want to compare their biopsy results with those obtained by an experienced specialist from the reactive lymphoid expansion of very inflamed intestinal areas?

Which brings us to the puzzling second paragraph of the "Discussion"?

After the authors assuredly announced in the first paragraph that they "found no differences between AUT/GI and GI control groups in detection of MV sequences in RNA extracted from ileal or cecal biopsy specimens", they added the following in the ***very next*** *paragraph*:

> ***Our results differ with reports noting MV RNA in ileal biopsies of 75% of ASD vs. 6% of control children [10], [41]. Discrepancies are unlikely to represent differences in experimental technique because similar primer and probe sequences, cycling conditions and instruments were employed in this and earlier reports; furthermore, one of the three laboratories participating in this study performed the assays described in earlier reports. Other factors to consider include differences in patient age, sex, origin (Europe vs. North America), GI disease, recency of MMR vaccine administration at time of biopsy, and methods for confirming neuropsychiatric status in cases and controls.***

Are the authors really saying what I think they are saying?

Are they really telling us that if they had attempted to replicate the Uhlmann study they would and could have, in all likelihood, obtained identical results?

Is that what they are really telling us?

If so, ***how did they come up with their results instead?***

Did the poor sample just happen?

And are we to believe that in spite of all of the above, "LACK of EVIDENCE" after such a study is equivalent to "NO EVIDENCE" just because the authors say so?

Is that how science works nowadays?

As long as you are famous and belong to a prestigious institution, you can do any study and simply anoint it.

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Other concerns

What did the authors mean by "Failure to replicate the original study design may contribute to continued public concern with respect to the safety of the measles, mumps, and rubella (MMR) vaccine."? (Abstract-Background)

Do they really think they replicated the British study when the number of subjects was different, the patient selection was different, the biopsy sites were different…and so much that mattered was different?

How can the Columbia / Harvard researchers write that "This study provides strong evidence against association of autism with persistent MV RNA in the GI tract or MMR exposure" and …intimate that Wakefield's research does not count, when in spite of all the problems with their own study ***they found evidence of measles virus RNA in one boy with post-MMR autism and gastrointestinal symptoms?***

Why did they need to tell us that 47 children were recruited, when the "final study population consisted of 25 cases (AUT/GI group) and 13 controls (GI control group) presenting consecutively for ileocolonoscopy who received at least one dose of MMR and completed all study procedures"?

Concerning the statement: ***"The majority of study subjects were in the 3–5 year age stratum and below the age recommended for second MMR (4–6 years; expectedly, 80% of cases and 69% of controls received only one MMR prior to the study (P = 0.36)."***

> Why did the authors not just say that 20 of 25 cases & 9 out of 13 controls received only one MMR instead of using percentages and a ***P*** value?
>
> If children are required to receive two MMR vaccinations before starting school and their parents are vilified and threatened with police dogs or complaints to social services if they don't, wasn't a serious flaw built into the study when 80% of the sample only received one dose of MMR vaccine? Wouldn't a better selection, namely the inclusion of cases vaccinated twice, have increased positive yields?

Lastly, why did the Columbia-Harvard researchers not perform serological studies based on those developed by Dr. V. K. Singh? Were they concerned about their results?

In a small but very impressive U. S. study, Bradstreet, El Dahr et al reported the presence of Measles Virus (MV) Genomic RNA in the cerebrospinal fluid (CSF) of

three children with regressive autism following MMR vaccination encephalopathy. The three children also had evidence of MV genomic RNA in their ileal lymphoid nodular hyperplasia biopsies.

In that study, the serological testing performed on the serum and the CSF yielded valuable confirmatory information. (8)

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So why am I so pleased with the new study in spite of its problems?

Because this CDC–sponsored study proved that:

"Results were consistent across the three laboratory sites."

In other words: That Dr. John J. O'Leary's Histopathology Laboratory at Trinity College Dublin ***consistently*** returned findings that were identical to those of the highly specialized laboratories at Columbia University and the certainly highly motivated facility of the Measles, Mumps, Rubella, and Herpesvirus Laboratory Branch of the CDC in Atlanta, Georgia.

The recent study in fact supports Andrew Wakefield's findings.

The children described in the Uhlmann 2002 study, including my grandson, really and truly had evidence of measles virus genomic RNA in their ileal biopsies as confirmed by the now-vindicated O'Leary laboratory.

Obviously I never doubted that… not for a second.

Andrew Wakefield would have never published doubtful results and he certainly would have never reported findings to me that he was not absolutely certain of.

He is simply not that kind of a researcher.

He is certainly not that kind of a man.

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In the United States, the Vaccine Injury Compensation Program is administered jointly by the U. S. Court of Federal Claims, the U.S. Department of Health and Human Services (HHS) and the U.S. Department of Justice (DOJ).

The recent Columbia-Harvard study is likely to create difficulties for the DOJ legal team representing HHS in the on-going vaccine-autism litigation.

Not long ago, the team imported a British professor to testify that the O'Leary laboratory findings were not to be trusted. When asked what he was being paid to testify in the Washington DC, the expert said: "It's $250 an hour while I am here and $125 an hour while I'm traveling and nothing while I'm sleeping I think. And also my airfare and hotel are being paid for."

When asked about his prior work relative to the now defunct United Kingdom MMR litigation and whether he really "spent roughly 1,500 hours at 150 pounds sterling" he answered "Yes that is correct." He then added that his checks came from the solicitors but that the funds actually came from Merck, Aventis and GSK.

In another exchange with plaintiff's attorney, the expert revealed that his salary was 60,000 pounds sterling. If this is per annum, and if the doctor works 40-hour weeks, then he was making less than 29 pounds sterling an hour at his regular full time job, if my calculator is right.

At the time of this writing, one pound sterling equals $1.77.

A medical writer in the U.K. interviewed the expert upon his return and declared that his report on the O'Leary lab was "…key to the collapse of the anti-MMR litigation in the UK". He then added that when the lawyers at the Legal Services Commission discovered "this authoritative investigation concluding that O'Leary's findings were unreliable they realised that, putting this together with the wider evidence against the MMR-autism thesis, the litigation had no chance of succeeding." (9)

One must wonder what the Legal Services Commission is thinking now.

Does the Commission still think that the British expert was right?

Does it still think that justice was served?

As for us in the United States, we are certainly grateful that the recent CDC-sponsored MMR study from Columbia and Harvard Universities finally put a last nail in the coffin of the claim that Andrew Wakefield's work was not to be believed because his biopsy results from Dr. O'Leary's laboratory were not reliable.

LET US HOPE THAT GOOD RESEARCH CAN BE PUBLISHED NOW!

LET US PRAY THAT JUSTICE PREVAILS!

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