When Finding Nothing Is Wonderful By F. Edward Yazbak , MD , FAAP

Scientists are expected to discover things. They are applauded when they do and sometimes ostracized when they don't.

Mainstream researchers investigating the connection between autism and the measles-mumps-rubella (MMR) vaccine, however, seem pleased when they find nothing. They hurry to publish their “findings” to the jubilation of “authorities.”

Repeating the performance a few times further cements the belief that if “orthodox” first-class researchers cannot find a connection between the triple vaccine, the measles virus and regressive autism, then, indeed, none exists.

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There was a big commotion in the U.K. last month, when new research from the United States seemed to confirm the presence of intestinal findings in children with regressive autism, which were similar to those reported by Andrew Wakefield, MD, in 1998.

On May 28, Sally Beck of The Mail on Sunday wrote a long article on the study at Wake Forest University School of Medicine in North Carolina titled “Scientists fear MMR link to autism.”

In the American study, 275 children with regressive autism and bowel disease were evaluated. Of the 82 children completely tested, 70 proved positive for the measles virus. Beck quoted Stephen Walker, MD, the team leader 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.”

Several other Sunday papers reported the story in the U.K. , while not much about the Wake Forest research was mentioned in the American media.

On May 31, as if on cue, Reuters Health Information in New York published an account of a different study headlined “No Evidence of Measles Virus in MMR-Vaccinated Autistic Children.” It said “contrary to the findings of some earlier studies, measles virus genetic material was not detected in the blood of MMR-vaccinated autistic children with development regression, according to a report in the Journal of Medical Virology for May.”

The Reuters report went on, “In the present study, Dr. M.A. Afzal, from the National Institute for Biological Standards and Control in Hertfordshire, U.K., and colleagues 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 the routine immunization schedule in the U.K.”

According to the British researchers, there was no evidence of measles genomic fragments in any of the children examined, in spite of the fact that the methods used were "highly sensitive, specific, and robust" and capable of detecting "measles virus RNA down to single figure copy numbers per reaction."

The Reuters' report ended reassuringly: “Given the rigorous methods employed, the researchers believe that measles virus material genuinely did not exist in the patient's blood samples.”

Two friends, one in Wisconsin and the other in California, both very informed about vaccine and autism matters, wrote to me almost simultaneously asking the same question: “Can this really be a coincidence?” that we have a study published supporting the MMR-autism connection and almost immediately another contradicting it?

I answered them that I did not know for sure but that in the past, “Dr. M.A. Afzal, from the National Institute for Biological Standards and Control in Hertfordshire , U.K. ” had published several articles that seemed strategically very well-timed.

The differences between the two recent studies deserve repeating:

In the U.S. study, measles virus genomic RNA was actually found in the gut of 70 affected children and the viral results of another 200 children with typical gut pathology are still pending.

In the U.K. study, the researchers “could not detect” measles virus genetic material in the blood of 15 MMR-vaccinated children with autism.

It is essential to also point out that the above-mentioned M.A. Afzal is not N.A. Afzal, a pediatric gastroenterologist attached to the Centre for Pediatric Gastroenterology at The Royal Free Hospital, London , U.K.

It was at the Royal Free Hospital that Andrew Wakefield practiced gastroenterology for years and where he was the shining star before he dared to “rock the boat” and was forced to resign. It is also at the Royal Free and University College Medical School in London that Brent Taylor, one of Wakefield 's most vocal critics, is professor of community pediatrics.

N .A. Afzal published his first study with the Royal Free team in December 2002. He published two more studies in 2004 and one in 2005. The abstracts of all four studies did not contain any reference to autism and vaccines.

M.A. Afzal, on the other hand, is a member of the virology department at the National Institute for Biological Standards and Control (NIBSC). The Institute is a respected multi-disciplinary scientific establishment with national and international roles in the standardization and control of biological substances including viral and bacterial vaccines. Since 1976, the institute has been directly funded by the United Kingdom Health Departments.

Members of the U.K. Health Departments have led the charge against Wakefield and his theory and have spent enormous amounts of money on an MMR awareness campaign. Elizabeth Miller, Director of the U.K. Health Protection Agency's immunization department, co-authored, with Taylor , several anti-Wakefield studies.

But back to M.A. Afzal of the NIBSC, who according to Reuters was certain in 2006 that the measles virus material genuinely did not exist in the patients' blood samples because he and his team did not find it. He must have been aware that a Japanese team from Tokyo University led by H. Kawashima had found the same “genetic material” in the blood of children with autism in 2000 : “In order to characterize the strains that may be present, we have carried out the detection of measles genomic RNA in peripheral mononuclear cells (PBMC) in eight patients with Crohn's disease, three patients with ulcerative colitis, and nine children with autistic enterocolitis...”

Kawashima discovered and reported that " the sequences obtained from the children with autism were consistent with being vaccine strains" and that the results were concordant with the exposure history of those children.

So how come Team Tokyo found vaccine-strain measles virus genomic RNA in peripheral mononuclear cells of vaccinated autistic children in 2000 and Team U.K. found nothing in 2006?

The answer to that perplexing and rather sensitive question may be in a very interesting study that was published in the Journal of Medical Virology in May 2003, titled appropriately "Comparative evaluation of measles virus-specific RT-PCR methods through an international collaborative study" and authored by both Afzal and Kawashima , in addition to renowned experts A.D.

That international panel found, "Comparison of RT-PCR assays established in house at various places revealed that laboratories could differ in sensitivity by as much as 1,000-fold in terms of the ability to detect measles virus sequences in clinical samples. The study indicates that PCR findings, positive or negative, are questionable if they are not supported by the associated data demonstrating the overall sensitivity of the assay applied. Measles virus-specific RT-PCR-based assays need to be validated using standard virus preparation or nucleic acid-based target templates. A correlation between real-time quantitative PCR and the conventional PCR for measles virus is highly desirable."

The above is simply noted with interest.

Coincidence after coincidence

Andrew Wakefield published his now famous article, "Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children," in The Lancet on Feb. 28, 1998.

Before that date, M.A. Afzal published a total of 16 studies and was the lead author in nine of them. Twelve works were about mumps and four dealt with assorted virology topics. Afzal did not write a single article or publish any research dealing with measles, MMR, autism, inflammatory bowel disease or related subjects before Wakefield 's landmark article.

Since Feb. 28, 1998, M.A. Afzal has published 20 articles: 13 were about measles, MMR and related topics; six dealt with mumps; and one was on other viral topics. He was lead author in 13 of the 20.

The first Afzal paper on the topic of measles titled "Absence of measles-virus genome in inflammatory bowel disease" was also published in the February 28, 1998 issue of the Lancet, five pages after Wakefield 's article.

An abstract of the Afzal research was not available for quoting, but it appears from the title that the virologist and his colleagues at the NIBSC did not find measles-virus genome in patients with inflammatory bowel disease.

Measles infection and inflammatory bowel disease

In the summer of 1998, Balzola, Khan, Pera, Bonino, Pounder and Wakefield reported measles IgM immunoreactivity in patients with inflammatory bowel disease (IBD). Their research revealed specific and fluctuating immune response to measles virus in patients with Crohn's disease and ulcerative colitis.

Afzal and colleagues published “Absence of detectable measles virus genome sequence in inflammatory bowel disease tissues and peripheral blood lymphocytes” in the Journal of Medical Virology . According to the authors, in spite of using a “highly sensitive measles-specific RT-PCR-nested PCR system,” they failed to detect the presence of measles virus in 93 colon biopsies and 31 peripheral blood lymphocyte preparations, examined and obtained from patients with IBD and non-inflammatory controls.

It seems from the above that M.A. Afzal was looking for evidence of viral presence in the colon (large intestine) and did not find any. Wakefield had better luck, a little later, when he looked for such evidence in the ileum. Afzal was certainly aware that the children tested by the Royal Free Team had ileal lymphonodular hyperplasia.

In virology, as in life, it's always better to look in the right spot.

The fact that Afzal could not find evidence of measles genomic RNA in the peripheral blood in 1998 is not surprising. Eight years later, as noted earlier, he still can't.

Measles virus and Crohn's disease

In April 1999, Wakefield , Montgomery and Pounder published “Crohn's disease: the case for measles virus.” They reported, “We and others have suggested that measles virus may be causally related to Crohn's disease, and that the associated risk is an atypical pattern of exposure.… The data for Crohn's disease suggest that persistent infection may follow early low dose exposure and low zone immunological tolerance. The changing pattern of measles virus exposure this century would be consistent with a shift toward lower dose of infection. Such an exposure would also be consistent with persistence of the virus at very low copy number within discrete foci of granulomatous inflammation….”

Afzal, Minor, Armitage and Gosh published “Measles virus and Crohn's disease” in June of the same year. An abstract of the publication is not available for review but the similarity of the two titles is simply astonishing.

2000: MMR safety review

In their careful and detailed scholarly article on MMR safety, “Measles, mumps, rubella vaccine: through a glass, darkly,” Wakefield and Montgomery reviewed the safety testing of MMR vaccine or lack thereof.

In “Clinical safety issues of measles, mumps and rubella vaccines,” Afzal, Minor and Schild did not directly respond but essentially reviewed all the studies that had been done by the anti-Wakefield camp and had failed to identify the presence of measles virus genomic RNA in patients with IBD. In the available abstract, M.A. Afzal stated, “Based on the published data reviewed here, it can be concluded that there is no direct association between measles virus or measles vaccines and the development of Crohn's disease, a conclusion which is supported by most epidemiological findings.”

The above statement obviously can be correct. On the other hand, presuming that because the studies reviewed did not reveal a relationship between measles vaccine and IBD that none exists appears somewhat presumptuous.

As to the safety of the MMR vaccine, one need only mention one of the conclusions of the recent comprehensive Cochrane MMR Review: “The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate.”

April 2002

In “Potential viral pathogenic mechanism for new variant inflammatory bowel disease,” Uhlmann and associates, including Wakefield , published results of their meticulous research. It revealed that “75 of 91 patients with a histologically confirmed diagnosis of ileal lymphonodular hyperplasia and enterocolitis were positive for measles virus in their intestinal tissue compared with five of 70 control patients. Measles virus was identified within the follicular dendritic cells and some lymphocytes in foci of reactive follicular hyperplasia. The copy number of measles virus ranged from one to 300,00 copies/ng total RNA.” The authors concluded, “The data confirm an association between the presence of measles virus and gut pathology in children with developmental disorder.”

M.A. Afzal and associates did not immediately respond. Instead, they published two well-written but highly technical papers on the newest-available, very delicate PCR testing procedures. The 2003 publication was discussed earlier. The second, published in the Journal of Medical Virology in May 2004, is listed for completion.

The Afzal group response to the 2002 Uhlmann paper seems to be the most recently published study (May 2006) in the Journal of Medical Virology . It was reported by Reuters and discussed earlier.

“Leukocyte preparations from children with documented evidence of MMR vaccination and confirmed diagnosis of autism were examined by several assays designed to target multiple regions of the measles virus genome sequence. No sample was found positive by any method. The assays applied were highly sensitive, specific and robust in nature, and were based on the amplification of measles virus RNA transcripts by real-time quantitative RT-PCR (QRT-PCR) as well as by conventional RT-PCR-nested PCR. The assays applied were potentially able to detect measles virus RNA down to single figure copy numbers per reaction. The amount of total nucleic acid extract of leukocytes subjected to various measles virus-specific investigations was several-fold higher than minimally required of a sample where measles virus persistence is well documented. This study failed to substantiate reports of the persistence of measles virus in autistic children with development regression.”

Again one should mention that M.A. Afzal and associates investigated only 15 children with autism “who had received the MMR vaccine as part of the U.K. routine immunization schedule.” If these children had early-onset autism and happened, as clearly stated, simply to have “received the MMR vaccine as part of the U.K. routine immunization schedule,” they may not necessarily have the typical findings of autistic enterocolitis.

The children in the Wakefield studies have regressive autism, a totally different entity; in most, the very clear regression seemed to have been chronologically related to their MMR vaccination.

Conclusions

This review cannot ascertain whether the recent publication by M.A. Afzal and associates was a response to the 2002 study by Uhlmann et al or was intended to pre-empt the recent important report from Wake Forest University.

It does demonstrate, on the other hand, a sudden and intense interest on the part of Afzal in measles virus genomic RNA, the MMR vaccine, autism and inflammatory bowel disease starting in 1998.

As more future studies supporting and confirming the Wakefield findings are published in the U.S. and elsewhere, it would not be surprising if M.A. Afzal and his associates continued their sophisticated research and still found nothing, as they have all along.

Future publications by the group will be celebrated by the vaccine authorities and medical groups, as long as they continue to report negative findings.

The medical authorities will undoubtedly declare that because Afzal and friends found nothing , there was, indeed, nothing and, therefore, that the measles virus and the MMR vaccine are not in any way responsible for the sudden regression of a small percentage of children, who are genetically predisposed to autism.

And that would be truly tragic.

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