

I have no conflict of interest to declare.

### Hiroaki Matsubara

Department of Cardiovascular Medicine, Kyoto Prefectural University School of Medicine, and Director of Cardiac Stem Cell Project, Translational Research Center, Kyoto University Hospital, Kyoto, Japan (e-mail: matsubah@koto.kpu-m.ac.jp)

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## The lessons of MMR

See pages 750 and 820

This week, *The Lancet* prints a partial retraction—a retraction of an interpretation<sup>1</sup>—from the majority of authors of a paper published in February, 1998, by Andrew Wakefield and colleagues.<sup>2</sup> Wakefield and one other co-author, Peter Harvey, have not signed this retraction statement. We hope to publish their response very shortly. The original report<sup>3</sup> made clear that the authors “did not prove an association” between measles, mumps, and rubella (MMR) vaccine and a newly described syndrome of bowel disease and autism. But the authors did raise the possibility of a link, on the basis of parental and medical histories, and they suggested that “further investigations are needed to examine this syndrome and its possible relation to this vaccine”. This interpretation of their data, together with a suggestion made by Wakefield during a separate press conference held at the Royal Free Hospital that there was a case for splitting the MMR vaccine into its component parts,

triggered a collapse in confidence in the UK’s MMR vaccination programme. It is the interpretation expressed about a connection between the vaccine and the new syndrome that is now being retracted. Today’s retraction comes after debate following the release of new information 2 weeks ago about the circumstances surrounding the publication of this work.<sup>3</sup> An enormous amount of effort has gone into reviewing and analysing the events before and after publication of the 1998 article. It is now time to look forward.

### Autism research

In 1943, Leo Kanner described 11 children with a condition that differed “markedly and uniquely from anything reported so far”.<sup>4</sup> He believed that the characteristics of these children, the fundamental feature of whom was their “inability to relate themselves in the ordinary way to people and situations from the beginning of life”, constituted a syndrome, one that he described as “an extreme autistic aloneness”. The recognition of such a distinct clinical entity was important, even urgent at that time. Kanner described how several of the children who had been introduced to him were inappropriately labelled as “idiots or imbeciles”. One lived in a “state school for the feeble-minded, and two had been previously considered as schizophrenic”.

Since Kanner’s report, autism and autism-like conditions have become common diagnoses<sup>5</sup> and exercise much media attention.<sup>6</sup> There is a strong underlying genetic basis to autism. But the idea of a “late-onset” variant<sup>7</sup> raised a possibility that there might be psychological and organic factors contributing to autism’s cause and course. One unexpected consequence of the debate surrounding MMR has been a redirection of public attention to a condition that has often been neglected by medicine. In a review of the epidemiology and causes of autism, for example, the UK’s Medical Research Council (MRC) summarised existing knowledge and identified strategic themes deserving further investigation (panel).<sup>8</sup> There are large and surprising gaps in our knowledge of a condition that affects as many as 6 per 1000 young children.

The UK Government announced a further £2.75 million of new and ring-fenced money for autism research in 2002. The first funding decisions by the MRC are expected in May this year. The MRC is strongly committed to autism research, presently funding seven research projects at a cost of over £4 million. To make the best of what are still limited

### Future strategic themes in autism research<sup>8</sup>

- Case definition
  - Improving phenotypic identification
- Epidemiological frameworks
  - Pinpointing environmental and genetic influences
- Integrated research strategies
  - Developing a comprehensive neurosciences approach
- Hypotheses about abnormal physiology
  - Requiring experimental rigour and independent replication
- Research capacity and the service interface
  - Promoting collaboration, career development, and child-care and support service expansion
- Lay participation
  - Strengthening research networks through partnership

resources, it is important that the Council's steering group set up to implement the findings of its 2001 report, together with other major national and international grant-giving bodies, establish a funders' forum for autism research to fine-tune strategy and avoid unnecessary duplication of research effort. The UK Government should extend its initial and welcome commitment to autism by pump-priming research with a further ring-fenced lump sum to the MRC of at least £12.5 million—£2.5 million annually over 5 years. Such sustained investment is vital if properly designed longitudinal studies to examine genetic and environmental factors in autism are to be constructed. Compare these modest sums of funding, for example, with the US National Institute of Health's budget for autism research of \$70 million by 2003. NIH is also committed to creating STAART (Studies to Advance Autism Research and Treatment) centres—eight of which have been launched in the past 2 years, at a cost of \$65 million, spread over 5 years. This approach might well have merit in the UK.

### Research integrity

The latest debate surrounding Wakefield and colleagues' paper has been enormously confusing. Public inquiries have been sought into the way ethics committees operate, how the legal services commission makes its decisions, and even, once again, into the safety of vaccines. A preliminary investigation by the UK's General Medical Council is underway. A furious debate about the actions of almost all protagonists has taken place. The press has become the courtroom for this very public dispute. But the media cannot be the only place to charge, investigate, prosecute, defend, judge, and pass verdicts on those who have been accused of research misconduct.

In 2000, a group representing the UK's Committee on Publication Ethics (COPE) drew attention to a collective institutional failure to take allegations of research misconduct seriously.<sup>9</sup> The absence of formal mechanisms within many universities and at a national level to investigate claims with visible due process means that publicly aired allegations leave everybody involved scrambling to respond in the best way they can. COPE has produced helpful guidance on how to deal with allegations of misconduct. But with no national body to which one can refer these allegations, the danger is that in any ensuing media furore good people are hurt by smear and innuendo. The appearance of institutions investigating themselves, while accepted as the norm in science and medicine, does little to strengthen public trust in a system that has such critical societal influence, and thus which requires transparent lines of accountability.

Present scientific and medical institutions have failed to act after years of encouragement and embarrassment. It is now up to Government to step in to create Britain's first Council for Research Integrity. Please, ministers, do so and do it now.

### Vaccine safety

In a review of the unintended effects associated with MMR, Jefferson and colleagues<sup>10</sup> found that the reporting of safety outcomes in MMR vaccine studies was inadequate. Here is a constantly repeated scenario in health-technology assessment (another example: the row over the safety of calcium-channel blockers). A product undergoes limited testing for efficacy and safety. It is licensed. A signal of concern is thrown up.

There is no valid set of safety data to which one can turn to answer these queries. Public concern grows and confidence in the technology may be jeopardised. Appropriate studies are hastily completed to confirm or refute the original signal of potential risk. An answer eventually comes, but too late to have prevented a great deal of anxiety.

Jefferson has suggested a solution to this problem.<sup>11</sup> He recognises that vaccines pose particular challenges to investigators given their frequently universal coverage, which precludes the possibility of any controlled long-term experimental assessment. Instead, he proposes creating a library of evidence, drawing together widely dispersed data from published papers, manufacturers' technical reports, and researchers' personal files. In this way, loss of crucial information would be minimised and gaps in existing evidence could be identified and filled early on. This idea is sensible and deserves further consideration.

### Public engagement

Many doctors and public-health officials have been frustrated by the debate over MMR. I have shared this frustration. One newspaper fancifully called our recent statement (see page 820) about the 1998 *Lancet* paper part of an "orchestrated campaign" to bolster MMR programmes.<sup>12</sup> In fact, the events leading to today's partial retraction were sudden, sparked by an investigation by a newspaper, *The Sunday Times*. Our response was to determine answers to very specific allegations. We have had no contact with anybody at the Department of Health or elsewhere in Government, vaccine manufacturers, or lawyers involved in ongoing litigation. There was no orchestrated campaign.

But there are fair questions to be asked about the style of government and expert response to claims about the safety of MMR. Three reactions have been discernable. First, there has been an appeal to evidence. The Department of Health's [www.mmrfacts.nhs.uk](http://www.mmrfacts.nhs.uk) website contains a superb collection of materials designed to help parents make the "decision in your own time and on your own terms". The difficulty is that in a post-BSE era, where government advice is no longer immediately taken on trust, the weight of accumulated evidence carries less force if it comes from government than it once did.

Second, public-health officials have disparaged as "poor science" evidence that appears to contradict their official message. This approach has a cost. The reason that today's retraction is partial and not total is that the discovery of a possible link between bowel disease and autism is a serious scientific idea, as recognised by the MRC,<sup>8</sup> and one that deserves further investigation. Although dismissing the entire 1998 *Lancet* paper as poor science gives a clear and correct message to the public about the status of any claim regarding the safety of MMR, in scientific and clinical terms it is both wrong and damaging. The autism-bowel disease link was considered part of a series of physiological observations judged by the MRC to be "interesting and in principle worth investigating". Subsequent research has yielded conflicting findings.<sup>13,14</sup> This work should be supported.

Third, there has been an effort to starve critics of legitimacy by refusing to engage them face-to-face. For example, when the drama *Hear the Silence* was broadcast on British television in December last year, there was a boycott of a subsequent discussion by many of those who could have best articulated the case for MMR. The reason advanced was that rational debate would not

change the minds of an extreme few who believed MMR to be unsafe no matter what the evidence presented to them. Also, the composition of the panel discussion did not reflect the large measure of consensus that MMR is safe. Instead, it portrayed the issue as a finely balanced scientific exchange, when in truth there is very little scientific uncertainty.

How should we debate and discuss matters of public health concern? Certainly, with all the evidence before us. But perhaps this evidence is best provided by neutral and trusted third parties—not the Government. In the UK, one might turn to the Consumers' Association, which publishes the respected *Drug and Therapeutics Bulletin*. Certainly, with strong public-health messages. But care must be taken not to dismiss important work that deserves continued support. And certainly robustly. But also directly, recognising that wider public trust is best fostered neither by referring to abstract evidence alone nor by official pronouncements of reassurance, but by explaining face-to-face<sup>15</sup> in transparent, human, even anecdotal terms with personal stories, why a particular course of action is being advocated.

Persuading the public to support vaccination is not only a matter of winning an argument. It is also about understanding the reasons why parents are and are not inclined to take their children for immunisation.<sup>16</sup> The complexity of this decision demands a more nuanced response from the public-health community than it has so far received.

#### Publishing controversial new ideas

It seems obvious now that had we appreciated the full context in which the work reported in the 1998 *Lancet* paper by Wakefield and colleagues was done, publication would not have taken place in the way that it did. These are difficult judgments to make in hindsight. For example, our sensitivity to potential conflicts of interest is very much higher today than it was in 1998.<sup>17–19</sup> What we will not do is to become profoundly conservative in our decision making about original ideas. A forum to raise new and sometimes unpopular thinking, even on the basis of what at first might appear flimsy evidence, is important<sup>20</sup>—and often vitally so for clinical medicine and public health.<sup>21</sup> How we discuss this new thinking then becomes the central question to answer,<sup>22</sup> not whether we should publish it or not.

Information that once could be confined to a small community of professionals is now open to wider distribution and comment—accurately or otherwise. No matter how many qualifying phrases or parallel reassuring editorials an editor might run, a new finding or a controversial claim is impossible to control. This places great responsibility on editors, scientists, and press and public-relations professionals to avoid encouraging anybody to go beyond the data or interpretations described in a paper. It is the job of journalists to tempt scientists to do otherwise. But we can all do better to adjust the volume of our message according to the validity of the information before us. Editors have a responsibility to be involved in all aspects of a paper's dissemination, whether in the pages of a medical journal or on the platform of a press conference.

Finally, what of the calls for a public inquiry into this entire affair? An inquiry would certainly provide an opportunity to investigate, once again, all the issues

that have made this matter such a troubling one for so many. To that extent it would be welcome. But public inquiries are easy to demand, and less easily able to deliver on expectations. They can sometimes entrench division rather than relieve it. Would it not be better to create a more positive process that emphasises reconciliation, progress, and partnership? A collaborative consultation, perhaps, between equals: members of the autism lay community (including parents and possibly in conjunction with the Consumers' Association, which has a strong interest in public information and, through the *DTB*, MMR<sup>23</sup>), clinicians responsible for the care of children with autism and related disorders, the MRC, and the Health Protection Agency. Call it, say, "MMR and autism: learning the lessons". For there are, indeed, lessons to be learned.

Richard Horton

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