MMR: risk, choice, chance

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The unfolding of the measles, mumps and rubella (MMR) controversy reveals some of the key features of the cultural climate affecting matters of health and illness in contemporary society. A high level of anxiety around issues of health is reflected in a heightened sense of individual vulnerability to environmental dangers (such as atmospheric pollution, electromagnetic fields, bioterrorism) and in a general aversion to risk, particularly in relation to children. This mood has proved responsive to views sceptical, if not hostile, towards science and medicine and associated professionals, particularly in the sphere of immunization. The result is that uptake of MMR vaccination in the UK has fallen, from a peak of 92% in the mid-1990s to a national level of 82% in 2003 (at the age of two); in London uptake is now less than 75%—much less in some areas—causing a significant risk of outbreaks of measles. In the USA too, the proportion of parents opting out of regulations requiring immunization as a condition of school entry has increased significantly in some areas, though these controversies appear to have had little impact so far in continental Europe.

Issues of risk, choice and chance are central to the controversy over the MMR vaccine that erupted in the UK in 1998 and has continued into the new millennium. Parents with young children have had to balance the risk that the vaccine might cause autism against the risk that, if they miss it, they might get measles (and its complications) or mumps and rubella (though these are of lesser concern). Some have demanded the choice of having the immunization in the form of three separate vaccines—a choice adamantly denied them by the Department of Health.

An important contribution to the MMR vaccination controversy has come from parents of autistic children, some of whom reject the notion that this disorder is a random genetic misfortune and insist that it is—at least in part—the result of some environmental insult (identified, more or less categorically, as MMR). In the USA, parents also blame vaccines for causing autism but they focus on vaccines containing the mercury-based preservative thimerosal (which is included in the diphtheria, tetanus, pertussis (DTP) vaccine, but not in MMR, because it contains live ‘attenuated’ viruses). In both countries, parents are pursuing litigation against vaccine manufacturers in campaigns that have contributed to wider anxieties over immunization.
This chapter addresses this recent controversy in the context of the prevalent cultural climates, both lay and medical. The concepts of risk, choice and chance are used as a framework for understanding recent events, reactions and actions.

**Balancing risks**

The notion that, over MMR, parents are confronted with comparable risks (of autism or measles) is itself part of the problem. There is in fact no genuine equivalence of risks, and the presentation of the issue in a formally ‘balanced’ way in the media has contributed to unwarranted parental anxieties.

If there is a risk of autism from MMR, it is so small that it cannot be quantified. In the 1998 Lancet paper that launched the controversy, Dr Andrew Wakefield and colleagues at the Royal Free Hospital in London claimed to have identified, on the basis of colonoscopy studies in 12 children with autism or related disorders, a hitherto unrecognized form of inflammatory bowel disease—‘autistic enterocolitis’\(^2\). The authors further noted that, in eight of the 12 cases they described, the parents attributed the onset of symptoms of autism to the MMR jab (which they had received, on average, 6 days before the behavioural changes). Dr Wakefield postulates a causal sequence in which MMR causes persistent measles infection in the gut; this results in a distinctive ‘enterocolitis’, which in turn produces a ‘leaky bowel’ which allows toxic ‘opioid’ peptides (derived from the breakdown of gluten and casein, contained in wheat and dairy products) to enter the blood stream; passing to the brain, these peptides cause autism.

The authors of the Lancet paper conceded that they “did not prove a link between MMR vaccine and this syndrome [autistic enterocolitis]” (p. 641)\(^2\). Indeed they did not produce any evidence for a link, beyond recording the conviction of some of the parents that there was one. The proposed chain of causality is supported only by analogy and speculation. They did however indicate two areas in which further research might test their hypothesis. First, they suggested that, if there were a causal link, a rising incidence of autism might be anticipated after the introduction of MMR in the UK in 1988. Second, they indicated that ‘virological studies’ were ‘under way’ to establish whether specimens of bowel affected by ‘autistic enterocolitis’ revealed evidence of measles infection.

A subsequent epidemiological study\(^3\) analysed the records of around 500 children with autism, born in North London between 1979 and 1998. The authors found that, though the number of cases had increased steadily, there was no sudden ‘step-up’ or change in the trend line after the introduction of MMR in 1988. There was no difference in age at diagnosis between the cases vaccinated before, or after 18 months of
age, and those never vaccinated. There was no clustering of developmental regression in the months after vaccination. They concluded that “our analyses do not support a causal association between MMR vaccine and autism” (p. 2026)³. Further studies by the same group, carried out in response to changes in the hypothesis being advanced by Dr Wakefield (notably his retreat from the requirement of a close temporal relationship between MMR and onset of symptoms), came to the same conclusion⁴,⁵.

A number of other epidemiological studies in different countries also failed to show any link between MMR and autism⁶,⁷. Because of their fairly small and stable populations and their comprehensive medical records, Scandinavian countries have provided some of the most reliable studies⁸,⁹. Perhaps the most robust is a retrospective cohort study that included all children born in Denmark between 1991 and 1998¹⁰. More than 80% had received MMR, and a total of 738 had been diagnosed with autism or an autism spectrum disorder—at similar rates in immunized and non-immunized groups. The authors found that there was no association between the age at the time of vaccination, the time since vaccination or the date of vaccination and the development of autistic disorder. They concluded that this provided strong evidence against the hypothesis that MMR vaccination causes autism.

In a response to the failure of epidemiological evidence to support his hypothesis, Dr Wakefield has modified it. He now believes that MMR causes only a minority of cases of autism, in individuals in whom there is some genetic vulnerability, compounded by other environmental factors. These include food allergy, antibiotic use, ear infection, multiple concurrent vaccine exposure, a strong family history of atopic and autoimmune disease, and exposure to mercury. Commenting on the study by Madsen, he argued that this subset may be “no more than 10% of diagnoses”¹¹. He argued that the effect of the number and complexity of cofactors was “to reduce statistical power to the extent that such studies fail to offer any convincing evidence either way”. Or as he put it in a newspaper interview, “retrospective studies like this are meaningless”¹². But it was retrospective studies like this that Dr Wakefield specifically invited in his Lancet paper.

The end result of this process of shifting the goalposts is that MMR, once blamed for producing an autism epidemic, is now claimed to be a factor in causing autism in a number of cases too small to discern by epidemiological methods. But we know that such methods are capable of detecting rare adverse effects of immunization, such as a rash caused by a deficiency of platelets in the blood (idiopathic thrombocytopenic purpura) at a rate of one in 32,000 vaccinations (around 20 cases a year)¹³. Detecting a subset the size of 10% of all cases of autism should be fairly straightforward. The fact that exhaustive research has failed to detect it is strong evidence that it does not exist.
In the course of 2002, the results of two virological studies carried out in the Dublin laboratory of Dr Wakefield’s collaborator Professor John O’Leary were published. In the first, researchers claimed to have identified fragments of the measles virus in intestinal tissues of children with inflammatory bowel disease and developmental disorder. However, this study did not indicate whether the children had had measles or the MMR vaccine. Apart from technical concerns about the reliability of the methods used, even if these findings were confirmed and replicated, the presence of measles virus fragments in the gut would not prove that they caused either inflammatory bowel disease or autism. In response to the controversy generated by his paper, Professor O’Leary issued a statement insisting that he had “not set out to investigate the role of MMR in the development of either bowel disease or developmental disorder, and no conclusions about such a role could, or should be, drawn from our findings”.

In a presentation in June 2002 to a US congressional committee on autism in Washington, Dr Wakefield claimed that a new study, due to be published by Professor O’Leary, had confirmed that the measles virus present “in the diseased intestinal tissues of children with regressive autism” was indeed derived from the MMR vaccine. For Dr Wakefield, this constituted “a key piece of evidence in the examination of the relationship between MMR vaccine and regressive autism”. Professor O’Leary, however, promptly rejected Dr Wakefield’s interpretation of his work, insisting that it “in no way establishes any link between the MMR vaccine and autism”. Indeed, he strongly recommended that parents should give their children MMR. This study was immediately challenged on the grounds that the method used could not reliably discriminate between wild and vaccine strains of the measles virus. When he was presented with this information at the Washington hearings, Dr Wakefield accepted that the conclusion drawn by the paper “was not justified”.

In contrast with the risk of autism, the risk of measles, though small, is real and quantifiable. The Peckham Report on immunization policy, published shortly after the introduction of MMR, surveyed the recent experience of measles in Western countries and estimated that for every 1000 cases notified, there would be 0.2 deaths, 10 hospital admissions, 10 neurological complications and 40 respiratory complications (p. 2). These estimates have been borne out in recent minor epidemics, in the Netherlands (1999: three deaths), in Ireland (2000: three deaths) and in Italy (2002: three deaths). It is worth noting that half these deaths were in previously healthy children. Though mumps is rarely fatal, it is an unpleasant disease with unpleasant complications (meningitis, pancreatitis, sterility). The congenital rubella syndrome, in which multiple profound disabilities, including deafness, blindness and mental handicap, result from damage to the fetus during early pregnancy, has become increasingly rare since the introduction of MMR.
According to a survey carried out at the height of the MMR controversy in early 2002, 53% of those interviewed believed that, because both sides of the debate received equal media coverage, there must be equal evidence for each. Though almost all scientific experts reject the claim of a link between MMR and autism, only 23% of those interviewed were aware that the bulk of evidence favours supporters of the vaccine. The authors note the generally uncritical treatment of Dr Wakefield’s position, commenting that “the connection between the MMR vaccine and autism is a speculative claim made by Wakefield with questionable scientific data to support it” (p. 23). Despite this, they continue, “Wakefield’s claims were not comprehensively or systematically challenged in media coverage”, with the result that “the weakness of empirical evidence in support of Wakefield’s claim was never fully aired” (p. 23). Furthermore, “attempts to balance claims about the risks of MMR jab tended merely to indicate that there were two competing bodies of evidence” (p. 23).

The right to choose separate vaccines

Dr Wakefield first suggested that parents should give the MMR in its three separate components, at intervals of 12 months, at the press conference launching his February 1998 Lancet paper. This proposal was not included in the paper and is in no way supported by it: it was not backed by any of Dr Wakefield’s 12 co-authors. Demand grew slowly before December 2001, when—in response to a question from the Conservative MP Julie Kirkbride, a campaigner for separate vaccinations—Prime Minister Tony Blair refused to disclose whether his son Leo had received the combined MMR. Claiming that this was a private matter, he indicated his support for the official policy on MMR. To the public, Mr Blair’s stand seemed disingenuous: few doubted that if Leo had been immunized his parents would have been happy to publicize the fact. If the prime minister’s family doubted the safety of MMR, why should the public trust it? Over the following months, the whole issue increasingly assumed a party-political form. The Sun launched its ‘Give us a choice campaign’ and the Daily Mail also took up the cause.

The key problem was that New Labour’s stand against separate vaccines ran counter to one of its central policy themes—the empowerment of the individual consumer, particularly in public services. This point was well made by the National Autistic Society in its March 2002 ‘position statement’:

“The Government promotes choice in many areas of public policy. In rejecting it here it may fail to recognize assertions of patients’ autonomy.
and a perception of paternalism may well have caused some of the reluctance to vaccinate"\textsuperscript{22}.

The problem that emerged with MMR is that individual choice cannot be reconciled with a mass childhood immunization programme.

Mass immunization is a policy for preventing diseases at a population level. It requires that individual children be immunized, but decisions about what diseases to immunize against, when and how, can only be taken from the perspective of society as a whole, taking into account the nature of the diseases, the efficacy and availability of vaccines, and other factors. It cannot be operated on a vaccine ‘pick and mix’ basis. For every individual, the question of whether or not to get immunized depends on a judgement of the balance of benefits and risks. In the past, this was fairly straightforward: the risk of infectious disease was significant and the consequences of infection serious; the small risk of vaccine complications was widely regarded as one worth taking. The problem with MMR is that as the diseases have become uncommon, the risk of adverse effects, however rare, looms ever larger. However, once a significant proportion of the population opts out of the immunization, then the risk of the old diseases returning inevitably increases. The further, peculiar, problem of the recent MMR crisis is the emergence of a section of society prepared to opt out of the immunization (and accept the risk of disease for their children) in response to a risk which is entirely speculative.

The government’s consistent promotion of an individualistic outlook means that any appeal to a collective commitment to sustain ‘herd immunity’ is doomed. To criticize parents for making decisions that were selfish or self-seeking in the climate of consumer sovereignty promoted by New Labour seemed simply perverse. In the early 1990s, a qualitative study of parental attitudes to immunization had noted that “herd immunity carried little weight with parents committed to homeopathy” (p. 47)\textsuperscript{23}. Ten years later, it carried little weight with anybody.

Opting to give MMR as its three separate components makes little sense. Some campaigners blame the measles component of MMR for causing inflammatory bowel disease and autism. If they believe this, then why shouldn’t the separate measles vaccine carry the same risks? Others believe that it is giving the combination of three vaccines in one go that causes damage to the infant immune system. But there is no evidence that this is the case, and much evidence to the contrary\textsuperscript{24}. Nor is there any scientific basis for any particular interval between the three separate vaccines. Dr Wakefield suggests 12 months; some clinics give them 6 months or 6 weeks apart. No research has been carried out to explore the consequences of giving MMR in its separate components.

Whereas the benefits of separate vaccines are nebulous, the dangers are clear. For however long the full programme of immunizations is
delayed, the child is vulnerable to infection with the diseases protected against by the later immunizations. If children get one injection every 12 months from their first birthdays, they will be three before they are fully protected. If their parents also choose to give their ‘pre-school booster’ in three separate vaccines, they could be well advanced in junior school before the programme is finished. If parents choose to give their children MMR in the form of separate vaccines, this will certainly leave all these children unprotected for longer and—as some clinic appointments are inevitably missed—may leave some unprotected forever. The resulting pool of unimmunized children creates the opportunity for outbreaks of measles (and mumps and rubella).

If the government were to offer separate vaccines as an alternative to MMR, it could be legitimately accused of putting political expediency before its responsibility to public health. Demanding the right to choose separate vaccines amounts to asking the public health authorities to collude with parents’ decisions to expose their own children—and other people’s children, irrespective of their parents’ choices—to an increased risk of infectious diseases.

Autism parents: ‘something happened to him’

“There was a time when he was fine. Something happened to him. That’s what I know in my heart.” Christine Shields (played by Juliet Stephenson) ‘anguished mother of a child diagnosed as autistic’ in Hear the Silence, Channel 5’s drama on the MMR-autism link, broadcast on 15 December 2003.

When a child, who had appeared to be developing normally up to the age of 18 months or later, starts to manifest the distinctive features of autism, it is understandable that parents should attribute this to some external event. Given that the MMR jab is customarily given after a child’s first birthday, it is not surprising that, in some cases, it appears that autistic features first appeared shortly afterwards.

The intuition that MMR might cause autism is further supported by two perceptions. The first is that a pattern of regression after a period of apparently normal development is a novel—or at least a much more common—form of presentation of autism. The second is that we are experiencing an ‘autism epidemic’, that a once rare disorder has suddenly become widespread, and that this has taken place in the period since MMR was introduced in Britain in 1988. In fact, further investigation confirms that neither of these perceptions can be sustained. The pattern of regression has been found to occur in around a third of cases of autism in numerous studies over the past half century, long before MMR. There is no evidence that this proportion has increased in
recent years. Though controversy continues to surround the explanation for the increased prevalence of autism, most authorities believe that it can be largely attributed to increased awareness of the condition among both professionals and the public, and the widening of diagnostic categories (bringing in some at either end of the spectrum of cognitive abilities who would not previously have been included)\textsuperscript{26–28}.

The parental focus on vaccines as a possible cause of autism has been encouraged by the recent growth in popularity of ‘unorthodox biomedical’ theories and therapies in autism, particularly in the USA\textsuperscript{29}. With the support of a number of prominent activists and numerous local groups, and with the help of the internet, this trend attracted growing international support among parents in the late 1990s\textsuperscript{30,31}. Advocates of this approach do not deny a genetic contribution to autism but, given that research in this field has so far had little practical consequence, they focus on environmental factors, biochemical and immunological mechanisms and treatments with vitamins and minerals, hormones (secretin), immune therapies and exclusion diets (especially gluten-free, casein-free)—and vaccines\textsuperscript{32}. It is fair to say that neither the theories nor the therapies of the unorthodox biomedical movement have been scientifically validated.

Convergence

Just as mainstream medicine has pursued a conciliatory line towards alternative health trends such as homeopathy, leading researchers and clinicians in the world of autism have not sought to challenge the outlook of the unorthodox biomedical movement—particularly as this has attracted growing support among articulate, well-organized and well-informed parents. But this indulgence towards irrational and unscientific trends has seriously compromised the health authorities as they have had to face up to the consequences of the growing influence of these trends and their impact on the uptake of vaccines. In the late 1990s, the anti-vaccination outlook, which emerged a decade earlier from under the wing of homeopathy, converged in the campaign against MMR with autism parents supporting the unorthodox biomedical approach\textsuperscript{33,34}. Leading figures in the campaign were Dr Wakefield, who became more closely aligned with the anti-immunization and autism parents groups after his departure from the Royal Free Hospital in December 2001, and the solicitor Richard Barr, who coordinated more than 1000 parents in a class action against the vaccine manufacturers. More than £10m of legal aid funding and the support of sympathetic journalists ensured that the campaign against MMR had a major public impact.

Given the prevailing cultural climate of anxiety about health and aversion to risk, the campaign against MMR has, despite its lack of scientific basis, put the programme of mass childhood immunization in jeopardy. This
programme depends on a consensus on a number of principles. It requires that parents accept a small risk (of adverse reactions), to avoid a greater risk (of disease). It requires that parents accept a small risk to their own child, to reduce the risk to other children who are unable to have particular vaccines (by fostering ‘herd immunity’). It also requires that they comply with the programme by bringing their children to clinics for a series of immunizations (in Britain a total of five visits for 16 vaccinations, up to the age of five; the US schedule involves eight visits and at least 23 vaccinations).

One strategy that has been rendered ineffectual by the decline in uptake of MMR is that of the ‘free-rider’. In the past, a cynical parent might calculate that, by not getting their child immunized, they could avoid the risk (however small) of adverse reactions, yet take advantage of the herd immunity resulting from the fact that more than 90% of parents decided to take the risk of immunizing their children. Of course, this strategy only works so long as only a tiny minority of parents adopt it. Now that 20% or more of parents are not giving their children MMR, then adding to this number only increases the risk (of measles, etc.) to your child and to other children.

The immunization policy version of the familiar ‘tragedy of the commons’, when self-interested actions undermine collective benefits, has led to pressures to introduce the sort of coercion of the free-rider that takes place in the USA. When a series of measles outbreaks spread through schools in the 1970s causing significant morbidity and mortality, parental pressure supported the enforcement of regulations demanding proof of immunization as a condition of school entry\(^3\). One disadvantage of this system is that it results in parents delaying immunization until shortly before school entry; the voluntary British system was—until recently—more effective at ensuring that children were protected from a much earlier age. Despite their differences, in practice both systems rely on a high level of consensus in favour of immunization, which is increasingly difficult to achieve in our fragmented, postmodern, societies.

Perhaps above all, a national immunization policy requires a degree of trust in doctors, scientists and politicians to devise a programme that provides the optimum protection for society against infectious diseases. In relation to MMR, the erosion of trust and the growth of risk aversion have gravely weakened the consensus underpinning the immunization programme. If, as now seems likely, measles—and the rest—return, society may pay a high price for this retreat into irrationality.

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