ACTA SCIENTIFIC MEDICAL SCIENCES

Volume 2 Issue 7 October 2018

Commentary

Commentary: M-M-R 30 Years On

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Received: August 23, 2018; **Published:** September 14, 2018

Critique

From 1972 to 1992 I was a family doctor within the English National Health Service (NHS), chiefly in Lincolnshire. I was (and remain) an advocate of mass infant immunisation against infectious disease. The killed strains of several bacterial diseases, plus live attenuated polio, measles and rubella vaccines, were all available and officially recommended, throughout my career. Mumps vaccine had become available in 1967 but was not then adopted by the NHS. Medical opinion at the time was that mumps was best contracted naturally before puberty when it was harmless, and resulted in life-long immunity. The vaccine's manufacturer did not claim such long-lasting protection, and global uptake must have been disappointing. As for Rubella, this was administered to all girls in secondary schools at age 12, then considered to be safely before any risk of pregnancy.

I still consider that single measles vaccine demonstrates all that is good about vaccination. The wild disease is very infectious by droplet inhalation: it is hard to avoid once an outbreak has begun. Most of the dangerous adverse effects occur in victims who happen not to be well at the time of infection. Prior vaccination - when the child is well - with a single dose of single vaccine, is a very effective protection for the remainder of their life. This is partly because measles seems seldom to occur in adults, whether or not vaccinated: the vaccine offers about 15 - 20 years' protection.

A formulation combining live vaccines against measles, mumps and rubella (MMR) was developed by Merck and licensed in the USA in 1971. The new formula was marketed enthusiastically across the world, and eventually adopted by the NHS in England in 1988. I had instinctive misgivings about this from the start, but it took me a shamefully long time – many months - to realise why.

The fundamental justification for immunisation is that it makes acquisition of immunity safer for the victim, than wild infection would have been. It is most effective when mimicking natural infection as closely as possible - live oral attenuated polio vaccine being the best example. However, a key characteristic of systemic viral infections is that - unlike bacteria - they do not normally cohabit the same body. Simultaneous infection with two or more of measles, mumps rubella and chicken pox, is rare [1]. Viruses infect individual cells and enforce replication of themselves: the first particle in a particular cell excludes others, even of the same type.

Thus, combination of several live viruses in the same vaccine preparation, departs considerably from imitating nature. The policy is potentially hazardous. Victims find coping with just one of measles and mumps quite challenging: coping simultaneously with live representatives of three such infections could overwhelm some children.

Coincidence in the body also raises the possibility of interference between the component vaccines. Simultaneous administration makes it possible for all three components to invade cells, although not of course the same ones. Incubation of each vaccine can therefore proceed simultaneously as intended, in separate cells. Incubation ends, however, with rupture of the primarily infected cells and release of a much larger inoculum of replicated virus particles into the general circulation. It is unlikely that all three vaccine cultures will emerge simultaneously: their incubation periods are different, and quite variable. Measles is likely to emerge first in a given individual, followed probably by rubella a few days later, more or less coincident with mumps: but individual cases will vary widely. It is therefore likely that one vaccine will succeed in developing, but then deter any others that erupt a few days later. There is some hope that the rather long incubation of rubella will

mean that, in some individuals, it emerges from incubation after the quicker measles infection is already spent, and so can challenge the candidate properly: but this cannot be relied upon to provide herd immunity.

There are therefore good grounds for questioning the wisdom of the MMR combination and for that matter any other combinations of live systemic virus vaccines. In practice, the introduction of a second dose of MMR in 1996 betrays reduced official confidence in its reliability: failure of one dose to protect in around 5% of recipients, was the reason given. The continuing incidence of measles outbreaks 22 years later [2] is unlikely to result from reduced vaccine uptake. In the UK in 2016-17 this exceeded 91% by age two years, having peaked at around 94% from 2014 to 2016 [3]. 95% uptake is the target.

Personal Experience

Family doctors were strongly steered by guidance papers and remuneration schemes towards using MMR, which quickly replaced single vaccines in the supply chain. Disinclination to vaccinate with MMR against parents' wishes, was part of the reason for my early retirement from the NHS. I continued to practice privately, and was approached by a considerable number of parents to provide single vaccines. By then, very strong pressure to accept MMR was being exerted on parents by public advertising and clinic briefings circulated by the Department of Health Vaccines Group, under the leadership of Professor David Salisbury. Routine supply of the single component vaccines was restricted by change in the regulations. However, rubella vaccine was still available singly, to cater for new mothers who had been found during pregnancy still to be susceptible to rubella: vaccination was offered at the postnatal clinic. And when MMR was introduced, children who were already part-way through a single vaccine programme, were permitted to complete it. This only came about after intense and intelligent lobbying by one remarkable parent, whose child was in that position.

There was therefore a legal way to help parents who asked for single vaccines. Once a dose of unrestricted rubella vaccine had been administered, single measles and mumps vaccine doses could be obtained for the part-vaccinated child. In practice, mumps was seldom given in early childhood: I advised parents to let the child catch mumps if it broke out near them, and only vaccinate if that had failed before the child left primary school. I would have preferred also to defer rubella until that age, but its role in legalising the process prevented this. And by the time the mumps dose became due, I could see no reason to administer it singly. A child confidently immune to rubella and measles could accept MMR for its mumps content, would get a useful boost to rubella, and a gratuitous boost to measles immunity which would do no harm.

A while into this phase of my practice I was asked by Desumo Information and Healthcare Ltd to operate the same policy at their clinic in Worcester, and I did so until February 2002 [4]. Some months into this period I received a letter from the General Medical Council (GMC) accusing me of malpractice, on the strength of a complaint by Professor McCluskey, then Director for Public Health in Worcestershire. He had not visited the clinic, which was held only a short walk from his office, but his allegations had not been verified by taking references, because of his good standing and perhaps the severity of the charges. I was to appear before them in public under their urgency procedure, because I was "putting the lives of children at risk." I would have been next after Harold Shipman to be dealt with in this way [5].

The process was long and very public, with much heated discussion in both popular press and medical journals. Public health doctors sided with my accuser, most others with me. I was anonymously tipped off by a civil servant that the accusation had originated in London, and simply been channelled through Worcester. The Director for Public Health in Lincolnshire wrote to every other doctor in the county asking for evidence of my malpractice: no-one replied, but one showed me the letter.

I was rather looking forward to my day in court, which would have had a strong press corps in attendance. But in the end the GMC backed down: their accusations presumed that I was acting on the recommendation of (then) Dr Andrew Wakefield, already being hounded (with others) for suggesting an association of MMR with bowel disease and autism [6]. Once it was clear that I was not, lawyers advised that they had no case. They disposed of the matter during a routine GMC session held in private. I was fully exonerated, but asked to meet my original accuser, in Worcester. Without preamble, he demanded to know why I had not provided him with reports on the vaccines I had administered. I had done, and said so. A pile of these reports was then found, a few minutes later, on the desk of an unhappy clerk in his department, who had firstly not known what to do with them, and later been too terrified to mention their existence.

The reason was simple, and came to light during that Worcester meeting. During the nationwide computerisation of the vaccination call and recall system, which coincided with the introduction of MMR, NHS officials forgot to tell the IT consultant that single vaccines were still an option. Consequently the system did not allow for the reporting of single vaccines. The oversight was not noticed until roll-out, when officials declined for some reason to correct it - cost probably - but instead make MMR all-but obligatory: hence the clerk's dilemma, and my year of infamy.

Conclusions

MMR was misconceived. Whether or not it causes "ileal lymphoid nodular hyperplasia, non-specific colitis (or) pervasive development disorder in children" [7] it is not as effective as was originally expected: the single vaccines are more effective and at least as safe. The pressure on British parents to accept MMR, results from an uncorrected error during computerisation of the NHS nationwide infant vaccination call-recall scheme, which coincided - too closely for comfort - with the roll-out of MMR and the controversy surrounding Andrew Wakefield.

Bibliography

1. Hofman I., *et al.* "Simultaneous chickenpox and measles infection among migrant children who stayed in Italy during the second half of June 2011". *Clinical Practice* 1.4 (2011): 113.

2. "Measles EPIDEMIC WARNING: Number of UK cases QUADRUPLES in first six months of 2018" (2018).

3. Childhood Vaccination Coverage Statistics, England, 2016-17.

4. Desumo Information and Healthcare Ltd ceased trading around 2009 and was dissolved on 11th April 2013.

5. Harold Frederick Shipman was an English general practitioner and serial killer. On 31st January 2000 he was convicted of fifteen murders of patients under his care. There were probably many more.

6. Wakefield and colleagues had noticed coincidence of a new bowel disorder, autism and previous MMR vaccination in 12 child patients at his clinic in the Royal Free Hospital. Their 1998 report in The Lancet brought down on them a hurricane of criticism which went on for a decade – and in Wakefield's case, still does. See reference 7.

7. Taken from the title of a research paper by Wakefield, Murch, Walker-Smith et al, published in The Lancet in February 1998 but retracted from the published record by the journal's editor in February 2010. Wakefield was struck off the English Medical Register but now prospers in the USA.

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