Household contacts of cases should be treated with a single dose of a standard treatment or alternative treatment if allergic to penicillin. If a case attends a childcare centre or school the childcare or class mates should be treated. For cases and contacts, and their families, emphasis should be given to thorough hand and face washing, the use of individual clean towels and to ensuring that these are available in affected households or schools.

It is reassuring to know that the penicillin MICs for the Central Australian isolates continue to fall in the fully sensitive to less sensitive range, 0.0125 to 0.5mg/L, and that PPNG has not emerged as a problem in Central Australia and in the NT[5]. Standard treatment, therefore, is still adequate to treat conjunctivitis caused by the current strains of *N. gonorrhoeae*. While recognising the diagnostic role for air-dried smears in remote settings, and for PCR testing as used in the Kimberly, it is prudent to culture and susceptibility test at least sentinel samples during an outbreak in order to monitor the antibiotic MICs.

The place, if any, of pharyngeal carriage as a reservoir for transmission does need to be further considered. However, the ability to control outbreaks with penicillins, and without ceftriaxone or spectinomycin, suggests that pharyngeal carriage was not an important contributor to this outbreak. Pharyngeal swabs are not routinely recommended in outbreaks unless patients are symptomatic. A preparedness to investigate this issue in the event of another outbreak should be considered.

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Current issues in immunisation

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The NCIRS was established by the National Centre for Disease Control, Commonwealth Department of Health and Family Services. The Centre analyses, interprets, and evaluates national surveillance data on immunisation coverage and vaccine preventable diseases. NCIRS also identifies research priorities, and initiates and coordinates research on immunisation issues and the epidemiology of vaccine preventable diseases in Australia.

This occassional report series in Communicable Diseases Intelligence provides commentary on topical immunisation issues.

Measles vaccine, inflammatory bowel disease and pervasive developmental disorder: is there cause for concern?

Janaki Amin, Peter B. McIntyre, Timothy C. Heath

On 28 February 1998, the *Lancet* published a report of a case series from the Royal Free Hospital, London suggesting a temporal association between measles-mumps-rubella (MMR) vaccine and an apparently new syndrome, consisting of an unusual type of inflammatory bowel disease (IBD) with pervasive developmental disorder (PDD).[1] This report was published with an editorial by Dr Robert Chen,[2] head of the Vaccine Safety and Development Activity National Immunization Program, US Centers for Disease Control and Prevention, which refuted its conclusion. Despite this, the subsequent intense media attention and public concern has challenged the integrity of the MMR immunisation program in the United Kingdom.

The hypothesis generated by the Royal Free Hospital group is that MMR is associated with IBD, and that IBD is associated with PDD. To examine this further, both microbiological and epidemiological evidence need to be considered.

The microbiological evidence

An association between wild and vaccine strains of the measles virus and IBD has been postulated since 1993.[3] Previous studies by the Royal Free group have reported detection of measles vaccine viruses in biopsies from patients with IBD, but other investigators have not been able to reproduce their findings.[4,5] Using nested polymerase chain reaction (PCR), a much more specific test than those used by the Royal Free Hospital group, Azafal et al.,[6] could not detect measles virus in the gut mucosal biopsies of patients with Crohn's disease or ulcerative colitis. The recent Royal Free Hospital study provided no evidence of vaccine virus in the bowel, brain or any other tissue of the reported subjects.

The epidemiological evidence

As highlighted in the *Lancet* editorial,[2] the Royal Free Hospital report is essentially one of hypothesis generation. The study design is a case series and does not enable conclusions to be drawn about causation. In addition, both selection and recall biases are likely to have affected the findings.

In the Royal Free Hospital case series, any association between MMR and IBD is likely to be inflated by selection bias arising from the referral of subjects to a group known to

be specially interested in an association between measles and IBD.

In 1997, a Canadian review of studies supporting and disputing the association between IBD and measles concluded that 'current scientific data do not permit a causal link to be drawn between the measles virus and chronic inflammatory bowel disease'.[7] A subsequent World Health Organization (WHO) report[8] updated the Canadian review and included a British case control study.[9] The WHO report found no additional support for an association between measles (disease or immunisation) and Crohn's disease.

The Royal Free Hospital group acknowledge that the reported intestinal and behavioural pathologies may have occurred together by chance, reflecting a selection bias in a self-referred group. Alternatively, they suggest that intestinal disease may play a part in the behavioural changes and cite three papers to support this hypothesis.[1] However, a recent French population-based study of conditions associated with autism found no link to IBD.[10] British data indicate a rise in the incidence of autism, but show that this started over a decade before the introduction of MMR in 1988, with no change since that time.[11] A recent review of British autistic spectrum disorders and medical disorders databases found that the incidence of IBD was nil among autistic children born since the introduction of MMR.[12] It is of note that, in the current Royal Free Hospital study, most subjects exhibited behavioural changes prior to bowel symptoms, arguing against the researchers' proposal that IBD is the antecedent for PDD.[1]

The association between vaccination and PDD was primarily based on parental recall. Estimating the time of onset of autistic behaviour is difficult. In addition, parents are likely to have linked this behaviour to other memorable events which occur at a similar age, such as immunisation. Onset of autism and MMR vaccination may appear associated in time because the mean age of children at which parents first report concern about child development is 18 to 19 months,[13] and over 90% of children receive MMR vaccine before their second birthday.[14]

Public health impact

Parental response to previous media coverage of the measles-IBD link is thought to have resulted in a 1% fall in MMR vaccine coverage during August to December 1996 in the United Kingdom.[15] While this was a small reduction, there are fears that further adverse press publicity about the current Royal Free Hospital study could result in a sustained fall in MMR immunisation, as occurred with pertussis in the 1970s following anecdotal reports that linked infant pertussis vaccination with brain damage.

The press release issued by the authors of the Royal Free Hospital paper stated 'The majority of opinion among the researchers involved in this study support the continuation of MMR vaccination'.[16] However Dr Wakefield, one of the study authors, is reported as saying 'that until this issue is resolved by further research there is a case for separating the three vaccines into separate measles, mumps and rubella components and giving them individually spaced by at least 1 year'.[16] This comment by Dr Wakefield was publicised by the media in the United Kingdom and led to greatly increased requests for separate doses of measles, mumps and rubella vaccines.

Implications for Australia

In view of Australia's proposed national Measles Control Program, information regarding the safety and side effects of MMR vaccination needs to be clearly communicated. On 23 March 1998, Sir Kenneth Calman, British Chief Medical Officer, convened a meeting of the Medical Research Council (MRC) and a group of national and international experts, including the World Health Organization, to review the work of the Royal Free Hospital Inflammatory Bowel Disease Study Group. Sir Kenneth concluded that based on current evidence 'there is no link between measles, measles vaccine, and either Crohn's Disease or autism'; 'there is no evidence that giving the component vaccines separately has any benefit'; and that 'giving the vaccines separately may even be harmful because it would expose children and their contacts to these serious diseases over a much longer period'.[17] We endorse this interpretation and consider that it needs to be confidently conveyed to both health professionals and the public.

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