NOT FOR PUBLICATION ARVI 87/1st MEETING

COMMERCIAL IN CONFIDENCE
COMMITTEE ON SAFETY OF MEDICINES
JOINT COMMITTEE ON VACCINATION AND IMMUNISATION
JOINT SUB-COMMITTEE ON ADVERSE REACTIONS TO VACCINES AND IMMUNISATION

Minutes of the meeting held on 6 February 1987 in Room 1611/12 Market Towers

Present: Professor R W Gilliatt (Chairman)
Sir John Badenoch
Professor Banatvala
Dr P E M Fine
Professor D Hull
Dr B M McGuinness
Dr C L Miller
Professor D L Miller
Dr D Reid

DHSS

Dr J Barnes
Dr D M Salisbury
Mr K L Fowler (Secretary)
Miss A Simkins

1. Confidentiality and Announcements

The Chairman reminded members that the proceedings, papers and information were confidential and should not be disclosed. He welcomed Dr Salisbury who will be taking over duties as Medical Assessor. The Chairman announced that Mr Digings, administrative assistant to the Committee, had moved to work in Mr Hale's office; he recorded the thanks of ARVI for the assistance given by Mr Digings.

2. Apologies for Absence

Apologies for absence had been received from Professor Lloyd, Dr Smith, Dr Bussey and Professor Glyn. The Chairman announced that Professor Lloyd had written to him resigning from the Committee because of pressure of other work. He recorded the thanks of the Committee for the work that she had done for ARVI.

3. Minutes of the Last Meeting

Several corrections were made to the draft minutes of the October meeting. It was decided that these should be retyped to incorporate the comments and that the agreed version should then be circulated to members.

4. Matters Arising from the Minutes

Item 4.1 - Adverse reactions to Trivax and Trivax D - six lines from the bottom

said that only seven cases and six controls had been given plain vaccine within twenty-eight days of onset of their neurological illness and only two cases and no controls within seven days. It was agreed that these figures were not large enough to justify any firm conclusions.

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Item 4.1 - the last sentence should read:

reminded the meeting that in his paper had found both local and systemic reactions less with adsorbed vaccines."

Item 5.1 - agreed to provide further details in relation to 5.1(3)c and 5.1(4).

Item 6 - Review of the safety and efficiency of desensitising vaccines.

enquired about future procedure for up-dating ARVI on adverse reaction reports to desensitising agents. reported that Yellow Cards concerning adverse reactions to these products were being coded now by another section of Medicines Division; it has been agreed to supply ARVI with future information on these reports on an annual basis.

Also in Item 6 - Treatment of anaphylaxis:

had received papers from and but unfortunately it had not been possible to arrange a meeting to finalise a paper to enable advice to be prepared for the Memorandum 'Immunisation Against Infectious Disease'. Members discussed the difficulty of distinguishing, fainting attacks from true anaphylactic reactions.

demonstrated a portable oxygen machine which could be used in conjunction with a portable resuscitator.

It was agreed to prepare a paper for the next meeting.

Item 8 - Any Other Business - Report on Tonsillectomy and oral surgery as contra-indication to the administration of oral poliovaccine.

The Chairman said that unfortunately was unable to attend this meeting and it was agreed to ask to report on this matter to the Spring meeting of the JCVI. Members agreed that there appeared to be a hypothetical risk of recipient poliomyelitis associated with these surgical procedures.

Item 7c - Yellow Card Reports
Product Defect Reports by Pharmacists.

reported that there was now greater selection with regard to Yellow Card Reports rendered by pharmacists. Where a pharmacist suspected that there was an adverse reaction he was encouraged to get the doctor who did the vaccination to make a report.

5. <u>Proposed Introduction of Combined Measles, Mumps and Rubella (MMR) Vaccine. A Paper by the Department</u>

ARVI/87/2

introducing the paper, said that at its November meeting the JCVI had proposed to change from the policy of administering measles vaccine preferably during the second year of life to one of administering measles, mumps and rubella (MMR) vaccine to both sexes. No decision had yet been reached on 'catch-up' vaccination of children of more than two years of age and the schoolgirl rubella vaccination programme would remain unchanged.

MMR vaccine was now used in nine European countries, also in the USA and Canada. Using this vaccine there was a benefit of increasing the uptake of measles vaccine. It was proposed to carry out trials of MMR vaccine in Hertfordshire, Somerset and Fife this year and these studies would be coordinated by the Communicable Disease Surveillance Centre (CDSC). It was also proposed to carry out serological surveillance of mumps and rubella and consideration would be given to making these diseases notifiable. Surveillance would also be undertaken of adverse reactions to MMR in these studies. ended by saying it was hoped that adverse reactions to rubella vaccine might be reduced by giving this vaccine to a younger age group.

asked if the Department was aware of other studies of MMR taking place, notably in Nottingham and in Oxford. confirmed that the Department knew of these studies.

asked the Committee to consider the published papers which had accompanied the Departmental paper on MMR vaccine.

5.1 Rubella Vaccine - 'how reactogenic is it'?
G V Griffin and K A Bryett
J Ind Med Res (1986) 14, p 316 ARVI/87/3

noted that this study had no control group and that the two rubella vaccines which were compared were derived from the same strain of vaccine virus. He remarked that joint pains were much less common among children than in adults after rubella vaccine.

5.2 Diffuse Retinopathy following measles, mumps and rubella vaccination - Gary S Marshall et al: Paediatrics Vol 76 p 989 (1986) ARVI/87/4

This paper described a diffuse retinopathy following vaccination with MMR. suggested that yellow card reports be searched for similar reactions and he agreed to take neuro-ophthalmological advice about the specificity of this syndrome.

5.3 Rubella-associated arthritis I comparative Study of joint manifestation associated with natural rubella infection and RA 27/3 rubella immunisation - Tingle, Allen et al, Annals of the Rheumatic Diseases (1986), vol 45, pages 110-114 ARVI/87/8

observed that this paper demonstrated that joint manifestation following rubella vaccination were much more likely to be transitory compared with those which follow natural rubella infection.

5.4 Postpartum Rubella Immunisation: Association with development of prolonged arthritis, neurological sequelae and chronic rubella viraemia - Tingle, Chartler et al. The Journal of Infectious Diseases (1985) Vol 152, pages 606-612 ARVI/87/9

This paper described six women who developed joint problems and neurological manifestations (paraesthesiae) following rubella vaccination. Rubella virus was also demonstrated in the breast milk of one of these patients nine months post-vaccination.
pointed out that this paper described no denominator and he mentioned that

there had been a response from the Centres for Disease Control (Atlanta) to this particular paper.* It was agreed to circulate this response to members.

6. Vaccine Related Poliomyelitis in Non-Immunised Relatives and Household Contacts - D E Bateman, G Elrington, P Kennedy, M Saunders
BMJ (1987) Vol 294, pages 170-171

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introducing this paper which described two contact vaccine-associated cases of poliomyelitis, said that it was unfortunate that the paper strongly recommended the vaccination of unprotected parents and other household contacts of infants receiving oral poliovaccine for the first time; he said that the JCVI would wish to change this advice because the risk of contact vaccine-associated poliomyelitis was replaced by an almost equal risk of recipient vaccine-associated poliomyelitis. What was now recommended was the washing of hands after changing babies napkins. Members suggested that a response should be made to the British Medical Journal concerning this article. It was agreed that the changes in the Memorandum 'Immunisation Against Infectious Disease', agreed by the JCVI at their October meeting, should come to the next meeting of ARVI.

7. Whooping Cough and Whooping Cough Vaccine

7.1 Whooping cough vaccine - CSM advice

said that the CSM had been asked to obtain the advice of ARVI concerning the statement made in paragraph 1.14 in the blue book (Whooping Cough, HMSO 1981, page 4).

The statement read:

> "No scientifically unassailable link has been established between DTP immunisation and serious neurological illness but we have come to the conclusion, on the basis of all present evidence, that there is a prima facie case that such a link may exist. We would also agree that the evidence suggests that the vaccine causes convulsions in some children."

The Committee were asked whether or not they remained content with this statement.

In the ensuing discussion it was noted that this extract was taken from the CSM statement contained in the 1981 Blue Book and was made at a time when vaccine hazards were receiving more scrutiny than natural pertussis. ARVI suggested that the statement be updated to read:

> "Although there is no scientifically unassailable proof that DTP vaccination causes serious neurological illness we are still of the view that a link may exist. However, such an association is an exceedingly rare event. We would also agree that the evidence suggests that the vaccine can precipitate convulsions in some children."

* J Inf Dis (1986) Vol 154 under correspondence Preblud S R et al, pages 367 and 368. Reply by Tringle A J pages 368 and 369.

7.2 MRC Sub-Committee on Whooping Cough Vaccine

reported that development of the acellular whooping cough vaccine in this country had received several setbacks. Initially it was hoped to carry out the trials with a Clinical Trial Exemption Certificate however the organisers had now been told that a full Clinical Trial Certificate would be needed. A controlled trial in Sweden had discovered three deaths among children taking part in the trial, although the number of these events did not reach statistical significance the findings had caused the organisers some concern. Finally the diphtheria component in one of the vaccines to be used in the British trial had failed its NIBSC test and therefore a replacement vaccine had to be sought.

7.3 A personal and family hisotry of seizures among persons reporting neurologic adverse events following immunisation with DTP or meales-containing vaccines. Presentation to the Immunization Practices Advisory Committee
John R Livengood - October 6 1986
(This draft paper was provided by Professor J M Dixon (Secretary of the Canadian National Advisory Committee on Immunisation.)

Members asked to provide the published version of this paper.

7.4 History of convulsions and use of pertussis vaccine - editorial Journal of Paediatrics 1985 Vol 107 pages 244 and 245

This paper was provided for information.

8. Effect of Influenza Vaccine in Patients Receiving Long-Term Warfarin Therapy -
Weibert, Lorentz, Norcross, Klauber and Jagger (1986)
Clinical Pharmacy, Vol 5 June 1986 ARVI/87/7

said that the Sub-Committee had for some time been interested in the possible effect of influenza vaccine on the metabolism of warfarin. The paper demonstrated that in patients on warfarin therapy influenza vaccine did tend to influence the prothrombin-time but that no untoward events were observed.

9. Suspected Adverse Reactions to Vaccines: The Reports on Yellow Cards Registered During the Period 12 September 1986 to 26 January 1987
ARVI/87/1

Introduced this paper.

(a) suspected adverse reactions to DTP vaccine given alone or with OPV.

During the current period sixty-nine suspected adverse reactions were reported. These include:

i. eight patients with reported convulsions including one, 170519, whose seizures were associated with pneumococcal meningitis.

ii. 169110, a nine-month old female who developed angio-oedema two minutes after being injected with DTP.

iii. 175296, a seven-month old female who developed thrombocytopenia the day after immunisation.

(b) Suspected adverse reactions to oral polio vaccine.

A patient (not reported on a yellow card) aged three-months who two weeks after receiving OPV developed lower motor neurone lesions of of the arms together with upper neurone lesion signs in the legs. Some sensory loss was noted. The patient developed difficulty in breathing and swallowing and died six weeks later. The final diagnosis was respiratory failure and poliomyelitis. Members expressed some doubt as to the diagnosis in this patient because of the presence of sensory symptoms and upper motor neurone signs.

(c) Suspected adverse reactions to diphtheria/tetanus vaccine.

During the period fifty-four reactions were reported, fifty of these included a mention of injection site disorder.

(d) Suspected adverse reactions to tetanus vaccine.

During the period twenty-three reports were registered; they consisted mainly of injection site disorders.

(e) Suspected adverse reactions to measles vaccine.

Eighteen reports were received during the period and included a report of sudden infant death syndrome. 170520, a fifteen-month old patient who died two to three days after measles vaccination. Autopsy revealed infection of the respiratory tract. The cause of death was described as:

(1) SIDS

(2) Possible upper respiratory tract infection.

ii. Convulsions

Four patients with convulsions were reported and one case (175708) of convulsions associated with otitis media.

iii. There were two reports of anaphylactic reactions and these should be associated with seven similar reports observed since February 1986 of reactions occurring within minutes of vaccination and all associated with vaccine from one manufacturer. It was suggested that the advice of be sought over these reactions.

(f) Suspected adverse reactions to rubella vaccine.

During the period there were three reports, one of syncope, one report of arthropathy and one girl who had a major convulsion within eight minutes of receiving the vaccine.

(g) Suspected adverse reactions to BCG.

There were three reports of injection site disorder.

(h) Suspected adverse reactions to influenza.

There were nineteeen reports of adverse reactions during the period all were of a relatively mild nature except in one case of non-fatal but severe anaphylaxis.

(i) Suspected adverse reactions to hepatitis vaccine.

There were thirteen reports during the period and these included one death.

170927, an Asian baby born to a mother who was a carrier of hepatitis B who was given BCG and hepatitis B vaccine at brith. One week later the child developed unexplained drowsiness, fits and then died. Autopsy revealed no abnormality apart from cerebral oedema. It was suggested that details of the histological examination of this patient might be obtained.

(j) Suspected adverse reactions to typhoid vaccine.

There were twelve reports, including two patients who had convulsions after vaccination.

(k) Suspected adverse reactions to cholera vaccine.

Two reports were received during the period.

10. Any Other Business

informed members that Professor Gilliat was retiring from his Chairmanship of the ARVI Sub-Committee to take up the post of visiting scientist at NIH Bethesda. Members of the Sub-Committee expressed their gratitude to Professor Gilliat for his invaluable work as Chairman since the formation of ARVI in 1980, and wished him well in his new post.

11. Date of the Next Meeting

The next meeting is to be held on Friday 5 June 1987.