Minutes of the Meeting held on Friday 25 June 1982 at Market Towers

Present: Professor R W Gilliatt (Chairman) Dr R Alderslade
         Professor J A Dudgeon Dr A Young (SKHD)
         Professor D Hull Dr T J Geffen
         Professor D Miller Dr Holgate
         Dr D Reid Miss Z Spencer
         Dr M H J Richards Mrs G Harrison
         Dr J W G Smith
         Dr J Barnes (Medical Assessor)
         Mr H M Morgan (Secretary)

1. CONFIDENTIALITY AND ANNOUNCEMENTS

1.1. The Chairman reminded members that the proceedings and information before them were confidential and should not be disclosed.

1.2. The Chairman announced that the date of the next meeting had been changed to the 29 October 1982. The Chairman asked that dates for ARVI meetings in 1983 be drawn up and circulated to members in the near future.

1.3. The Chairman said that he had received a letter from Dr Meade saying that owing to pressure of commitments he had to offer his resignation from the Committee. The Chairman suggested that members' appreciation of Dr Meade's work for the Committee be recorded in the minutes. This was agreed.
2. APOLOGIES FOR ABSENCE

Apologies for absence were received from Professor Lloyd, Dr Bussey, Professor Glynn, Dr Meade, Dr Pollock and Dr Wilson. Apologies were also received from DHSS officials, Miss Horridge and Mrs Patey.

3. MINUTES OF THE MEETING HELD ON 5 MARCH 1981

3.1. These were agreed and signed by the Chairman as a correct record, subject to the following amendments:
   i. Para 4.1 line 11, second word to be changed to 'supplied' from 'used'.
   ii. Para 4.1 line 12, last word should read 'IPV' not 'OPV'.
   iii. Para 4.1.3, second line insert after 'Sabin's' 'Type 3'.
   iv. Para 4.1.3, line four, after the word 'nitrogen' delete the rest of the sentence and insert 'might have led to a relative loss of less virulent particles'.

4. Adverse Reactions to Poliomyelitis Vaccine


(Paper ARVI/82/10A)

4.1.1. Dr Barnes said that he had omitted to include this paper with those which had been presented with paper ARVI/82/7 to the last meeting. The paper by Smith and Wherry described poliomyelitis surveillance in England and Wales during the period 1969-75. The authors had noted a fall in incidence of recipient

CORRECTION NOTE

Dr Smith said that the penultimate line of the summary on the first page of the published paper should read "Eleven additional paralytic cases were seen in patients in whom the infection was likely to have been acquired abroad".
vaccine associated cases from 1.1 per million doses of vaccine distributed
during the period 1962-64 to 0.4 per million doses during the period 1969-75.
The rate for contact vaccine-associated cases had changed from 0.6 per million
doses of vaccine distributed for the period 1962-64 to 0.2 per million doses in
the period 1969-75. Dr Barnes added that since 1975 the incidence of recipient
cases had risen in the two year period 1967/77 but had subsequently fallen;
the incidence of contact cases had remained at a level of 0.1 per million doses
distributed. Dr Chamberlain at the last meeting of the Committee, had given
slightly different estimated risk rates for both recipient and contact vaccine-
associated poliomyelitis in susceptible populations.

4.1.2. Members discussed reasons for the apparent decrease in incidence in
recent years of vaccine associated poliomyelitis and considered whether or
not there had been any variation in the virulence of the virus uses in OPV.
It was pointed out that differentiation of wild polio-viruses from vaccine
viruses in vaccine associated cases depended upon the use of market tests,
these had improved since the early 1960s. It was also noted that oral
polio vaccine was now less likely to be neuro-virulent because of improved
techniques of neuro-virulence testing. In addition there had been improvement
in the recognition and diagnosis of paralytic disorders and the vaccine
strains now circulating within the environment were more likely to be
vaccine related rather than wild strains.

4.1.3. The Chairman asked the Committee to consider other possible
neurological reactions to OPV. He reminded members of minute 5.3 of
the previous meeting in which Dr Chamberlain had described cases of
meningitis, encephalitis, convulsions and cot deaths, in which polio
virus had been identified by the PHLS suggesting previous immunisation
or contact with a vaccinated person. The virus identified was not
thought by Dr Chamberlain to be associated with the illness, except possibly
with five of the cases of meningitis, but even these were doubtful. Dr Smith quoted the definition of non-paralytic poliomyelitis, in the paper by Smith and Wherry, as being "that category of patients whose illness had been clinically diagnosed as non-paralytic poliomyelitis together with cases of encephalitis or aseptic meningitis in patients with cultural or serological evidence of infection with a poliovirus. Such patients may well include those in whom the association between illness and the virology findings is coincidental; they are included to provide an estimate of the highest possible number of non-paralytic cases". The Chairman drew the attention of members to Table 7 in the paper by Miller and Galbraith (1965) which quoted cases of neurological disease other than paralytic poliomyelitis in patients who received oral polio vaccine and to the similar Table in the paper by Miller, Reid and Diamond (1970). Although conditions such as encephalomyelitis and polynuritis (known to occur after other acute viral infections and vaccinations) were included, they were few in number and may have been due to a random time association rather than a causal association.

4.2. Adverse Reactions to OPV and IPV - Addition to a Paper Presented at the last meeting of ARVI (ARVI/82/7) ARVI/82/10B

4.2.1. Dr Barnes referring to the reports to the GSM of adverse reactions to oral polio vaccine said that in almost all of these OPV had been given in conjunction with triple vaccine or diptheria/tetanus vaccine. During the period 1964-75 there had been 36 reports of significant neurological reactions, in only four of these was oral polio vaccine recorded as being the only vaccine given. Members observed that in three of these four cases the interval between vaccination and the onset of symptoms would have been too short for oral polio vaccine to have been the cause of this reaction.
4.5. The Chairman drew the attention of members to the paper by the Ehrenguts (Ehrengut W & J, 1979 Develop biol-Standard 45 165-171) which described 59 cases of seizures following administration of OPV. Dr Barnes said that the majority of the patients were between 7 and 36 months of age. The authors claimed that OPV was the only vaccine given and implied that OPV was the cause of the convulsions because the peak incidence of seizures occurred between the first and eighth day after vaccination, a time period which coincided with the occurrence of viraemia following the administration of oral polio vaccine. Members pointed out that the estimated overall incidence of convulsions of 1 in 8,600 vaccinees (within 30 days of immunisation) was lower than the expected background rate of seizures; the clustering of convulsions in the first week after vaccination may have been due to bias on the part of reporting doctors who would be more likely to report a seizure at this time. It was not felt that any conclusion could be drawn from this study.

4.2.2. Professor Miller then referred to unpublished NCES data giving relative risk rates during different weeks of the first 28 days after vaccination with either DTP or DT. Since nearly all the children received OPV at the same time, encephalopathy due to the OPV might be expected to contribute late cases is with an onset after the first week. In fact the figures did not suggest an excess of late cases, whereas this was clearly seen after measles vaccination.

4.2.3. The Committee concluded that there was no good evidence to suggest that oral polio vaccine was a significant cause of serious neurological disease other than vaccine-associated poliomyelitis.

4.2.4. The Chairman asked members to consider inactivated poliomyelitis vaccine and asked Dr Barnes to introduce this subject. Dr Barnes said that most of the reported neurological reactions to IPV occurred when the vaccine
was given in conjunction with triple vaccine; therefore it was difficult to assess which antigen had in fact caused the reaction. He said, however, that there had been reports of reactions to quadruple vaccine (IPV and triple vaccine) both from this country (Dane D S et al (1967) Lancet vol 1, page 939: Haire M, Dane D S, & Dick G (1967) Medical Officer, vol 117, page 55) and from the Netherlands (Hannick C A, Cohen H: Pertussis vaccine experience in the Netherlands in Manclark C B, Hill J C (eds): International Symposium on pertussis D Hew (NIH) 79-1830, US Government Printing Office, 1979, page 279.) Hannick reported an incidence of shock and collapse of 1 in 3,500 children vaccinated, and convulsions in 1 in 2,500 children. The Committee noted that since the uptake of IPV in this country was now between 1 and 2,000 doses a year there was insufficient usage of the vaccine to indicate whether or not it was associated with adverse reactions. It was noted that the last anaphylactic reaction to IPV was recorded by the CSM in 1977.

4.2.5. Under the heading for Contra Indications to IPV on page 6 of the paper it was suggested that the last sentence on hypersensitivity should be more specific.

4.2.6. The Chairman invited Dr Smith and Professor Miller to assist in the preparation of a report for the parent committees on polio vaccines, to be seen in draft at the next meeting.

5. Advice from the CSM on papers presented by the Sub-Committee

5.1. Adverse reactions to influenza vaccine

The Sub-Committee noted the CSM's recommendation for further research into the suggested interaction between influenza vaccine and warfarin.
5.2. **Adverse reactions to rubella vaccine**

The Sub-Committee noted the CSM's comments on this paper. It was also noted that there was a mistake on line 3 of paragraph 2.2.1 - where 'poliomyelitis' should read 'polyneuritis'.

5.3. **Infantile spasms**

The Sub-Committee noted the CSM's comments on this paper.

6. **Adverse reactions to pertussis vaccine** ARVI/82/12 Nos A-B

6.1. **Letter from Professor D L Miller (Paper ARVI/82/12A)**

6.1.1 Professor Miller speaking to this letter said that the study of infantile spasms amongst the NCES cases revealed that although there was an excess of spasms occurring within a week of vaccination there was a deficit of spasms in the ensuing three weeks; the presumption being that vaccination unmasked a process which was already in progress. He referred to a letter by Dr A H Griffiths in the BMJ of the 24 April 1982 concerning the NCES Table V-12 of the EMSO Whooping Cough Report (1981), which claimed that there was little difference, over a 4 week period, in the percentage of pertussis immunisation in children admitted to hospital with serious neurological illness and in matched case controls from community lists. As a result Professor Miller had analysed convulsions and encephalitis taken together in the same way as infantile spasms. For the period 7-28 days after vaccination no consistent pattern emerged and it was clear that no deficit comparable to that observed in the case of infantile spasms was present. The slight overall deficit which appears in the composite NCES Table V12 of the report is in the main due to the cases of infantile spasms. Members suggested that it might be of interest to calculate the significance of the relative risk rate for convulsions and encephalitis (without infantile spasms) during the overall 28 day period.
6.2. Correspondence extracts from the British Medical Journal of the
24 April 1982 (vol: 284 Page 122-3) ARVI/82/12B

The Chairman drew attention to the letter from Professor G T Stewart
and said that the reply to the letter by Professor Miller and Dr Ross
had been Tabled. This reply had now been published in a recent British
the reply.

6.3. Papers concerning vaccination ARVI/82/12C

6.3.1. The NICHD Co-operative Epidemiological Study of Sudden Infant Death
Syndrome risk factors - (Department of Health and Human Services,
Public Health Service - National Institutes of Health Bethesda,
Maryland 20205)

Members noted the preliminary report of this study with interest and
expressed the hope that when the study was published in full that the
significance level of vaccination amongst the patients compared with the
control infants would be tested.

6.3.2. Convulsions following immunisation: Presentation and long-term
follow up. Paper by Hirtz, Nelson and Ellenberg. (April 1982
Neurology NY32(2) A 121 Item pp 58)

Members noted this brief report with interest.

6.3.3. Experimental model of post-pertussis immunisation encephalopathy:
linkage to the major histocompatibility complex. Paper by Steinman,
Zarvil, Waldor, and Lim (April 1982 Neurology NY32(2) A86 Item 9)

The Chairman suggested that the NCES in its follow-up might be able to
carry out HLA typing on patients who had had suspected reactions to
pertussis vaccine.
6.3.4. **DTP immunisation; a potential cause of the Sudden Infant Death Syndrome (SIDS)** William C Torch, Reno, NV - (April 82 Neurology NY 32(2) A169 Item 3)

Professor Miller pointed out that the difference in mean age of the vaccinated and non-vaccinated groups and the biphasic peak observed in the vaccinated group indicated that probably the Sudden Infant Death Syndrome was not associated with vaccination. The Sub-Committee suggested that Professor Knowelden be asked if he could provide a report of the Sheffield Study of the Sudden Infant Death Syndrome.

6.4. **Nature and rates of adverse reactions associated with DTP and DT immunisation in infants and children** C L Cody, MD, L J Burack, MD, J D Cherry, MD, S Michael Marcy, MD, & C R Manclark, PhD - (PEDIATRICS Vol 68 650-660 1981) ARVI/82/12D

Dr Smith observed that the number of convulsions reported in this study was too small to make a significant comparison between triple and diphtheria/tetanus vaccines, although the number of minor reactions reported was large enough to make a significant comparison.

The Chairman commented that the number of convulsions within 48 hours of DTP (9 in 15,000 injections) was high in relation to the expected random rate in infants and young children.

7. **Adverse reactions to rubella vaccine**


7.1. Dr Barnes said that the paper was tabled for the information of members of the Sub-Committee; however, the number of cases reported and followed up was too small for firm conclusions to be drawn. It was noted that one of the vaccines quoted was not at present used in this country
although the RA27/3 vaccine, also mentioned, was in use in this country.

7.2. A paper on persistent rubella infection and rubella associated arthritis (J K Chantler, D K Ford, A J Tingle (The Lancet June 12 1982 Pages 1323-5)) was also tabled for information. The Chairman suggested that these papers be brought to the attention of the Rubella Vaccination Sub-Committee of the JCVI.

8. Measles Vaccine and SSPE


The Chairman said that this paper might be of interest to members.

Dr Smith said that he had sent Dr Christine Miller a copy of the paper, Dr Miller had replied that there were now 100 or more cases on the UK register and that none of them had apparently received immunoglobulin. The Chairman suggested that the paper be brought to the notice of the Measles Vaccination Sub-Committee of the JCVI.


Dr Barnes said that this paper described the surveillance up to 1980 which was quoted by Dr Bellman when he spoke on this subject at the last meeting. The Sub-Committee noted the contents of this paper.

10. Adverse reactions reported on yellow cards from 1 February to 31 May 1982 ARVI/82/16

Dr Barnes introduced this paper which included one case of infantile spasms and four cases of convulsions following the use of DTP vaccine; five cases of convulsions following administration of measles vaccine. Members noted the
excessive number of injection site reactions associated with diphtheria/tetanus vaccine and also with DTP vaccine. It was requested that these reactions be divided into those arising from booster doses and those occurring during the basic course of immunisation.

11. Any other Business

The Chairman suggested that as well as finalising the report on polio vaccines, adverse reactions to diphtheria and tetanus vaccine might be considered at the next meeting.

12. Items of information

MAIL 34 was circulated to members for information.

13. Date of the next meeting

The amended date of the next meeting is the 29 October 1982 at 11 am in Market Towers.