Minutes of the meeting held on Friday 7 June 1985 at Market Towers

Present: Professor R W Gilliatt (Chairman) Professor J E Banatvala Professor D Hull Dr C L Miller Professor D L Miller Dr D Reid Dr J W G Smith Dr S J Wallace

DENSS
Dr D W Zutahi (Medical Secretary) Dr M Duncan (Medical Secretary) Mr J P Digings Mr K L Fowler (Secretary)

SHRD
Dr R Covell

1. Confidentiality and announcements

The Chairman reminded members that the proceedings, papers and information before them were confidential and should not be disclosed. He welcomed Mr Digings to the meeting.

2. Apologies for absence

Apologies were received from Sir John Badenoch, Dr Bussey, Dr Fine, Professor Glynn, Professor Lloyd and Dr McGuiness.

3. Minutes of the meeting held on 1 February 1985

The Chairman signed the minutes as a true record of the meeting after a number of typographical errors had been corrected and the following amendments made:

(i) Page 1: Professor D L Miller was added to the record of those present at the meeting.

(ii) Page 10: Item 9.2, line 3, delete second half of first sentence and replace after; "but that the excess of cases related to DTP vaccine was not due to a failure to observe contra-indications to vaccination".
(iii) Page 10: Item 9.3, line 3, delete "vaccination" and replace by "dose of vaccine". Line 6 delete "vaccination" and replace by "dose".

(iv) Page 10: Item 9.4, reword as follows: "Professor Miller said that the study had found that the relative risk for neurological illness following whooping cough was greater than that associated with DTP vaccination, during the month before onset of illness. This ratio was six to one for the disease compared with a vaccination course comprising three doses. He said that he had continued a study carried out by Dr Cherry on deaths of infants from respiratory disease of all causes. When the rate for the period 1970-77 was extrapolated over the periods of the major whooping cough epidemics of 1978-79 and 1982-83 the gradual decline was interrupted at the time of these epidemics. The cumulative excess of infants' deaths from acute respiratory conditions between 1977 and 1983 was 295. Only 55 deaths were recorded in this age group, ie under the age of one, from whooping cough in the 1977/79 epidemic.

(v) Page 10/11: Item 9.5, delete the whole of this paragraph apart from the first four lines ie up to the words ending ..... DT vaccines".

4. Matters arising from the minutes

4.1 Page 2: Item 5.1: It was agreed that the second sentence of the Sub-Committee's comment should be amended as follows: - "One exception would be when the eczema is associated with a severe form of immune-deficiency".

This paper concerning Guillain-Barré syndrome and swine influenza vaccine was noted by the Members with interest.

5. BCG Vaccine

5.1 BCG immunisation and osteomyelitis: letter from Dr Ian Sutherland

5.1.1 The Committee noted the letter from Dr Sutherland and expressed their gratitude for the information he had provided from the 1983 survey of tuberculosis notifications on cases of bone and joint tuberculosis in school children who had received BCG vaccine. Professor Miller said he would write to Dr Sutherland requesting further relevant information.

5.2 BCG immunisation and pregnancy: letter from Dr George Comstock

The Chairman said that the information in Dr Comstock's letter was in accord with our current knowledge and the present policy on BCG in pregnancy. He said he understood that trials were being undertaken in Southern India and we were awaiting a reply on our request for information about these trials.

5.3 BCG school programme

5.3.1 Dr Zutshi reported that the JCVI had recommended that the BCG vaccination programme for school children should be maintained at the present for a few further years with the intention of stopping before 1990 unless the further notification survey in 1987 shows that the present downward trend in notifications etc., has not been maintained. It also recommended that plans should meanwhile be developed to ensure that BCG vaccination continued to be offered to all those at special risk.
6. Pertussis Vaccine

6.1 Pertussis and pertussis vaccine: Gold R. in Canada Diseases Weekly Report for 23.2.85, pages 29-32

Readers were unclear as to how some of the risk rates both for the vaccine and the disease quoted in Table 1 on the second page of the paper had been estimated. Some of the information was derived from the National Childhood Encephalopathy Study, however the figures for complications from the disease did not correlate well with observations made in this country. Professor Miller agreed to write to Dr Gold seeking clarification about the sources of his information so that it could be determined as to what extent these estimates may be applicable to the situation in Britain. Members also noted that the contra-indications for pertussis vaccine quoted in this paper were less strict than those quoted by the Joint Committee on Vaccination and Immunisation's Memorandum 'Immunisation against Infectious Disease'.

6.2 Contra-indications to whooping cough immunisation - myths or realities. Nicoll A. Lancet 1985; ii: 679-681

Professor Hull said that this paper was written as a consequence of Dr Nicoll making a teaching video concerning immunisation. The article stressed that when the recommendations concerning contra-indications were made these should be of a positive nature and advice should be given about myths which were inhibiting uptake of immunisation. Professor Hull said that there was a problem in anticipating what myths would arise and therefore it was important to study the market response. Dr Miller said experience at an immunisation clinic had shown that the main myths concerning contra-indications to vaccination related to eczema, food allergy, and distant relations with a history of a fit. Dr Zutahi reported that the JCVI had asked the Joint JCVI/BPA working Party to consider this report.

6.3 (a) Whooping cough, disease, vaccination, vaccine damage - ARVI/85/20
Paper by Mrs Rosemary Fox, Secretary of the Association of Parents of Vaccine Damaged Children, March 1985

(b) Preliminary comments on Mrs Fox's paper ARVI/85/21

6.3.1 Dr Zutahi reported that a copy of this paper had been sent to him, subsequent to a request to him from Mrs Fox for a copy of the most recent edition of the Memorandum 'Immunisation against Infectious Disease'. He confirmed that this paper was being circulated on request by Mrs Fox to interested parents.
6.3.2 The Chairman informed the Sub-Committee that the JCVI had asked ARVI to comment on Mrs Fox's paper. The JCVI had considered that although Mrs Fox's paper had showed some shift in her position towards its views, it was important that this paper was not thought to have been received by the Department without comment lest such inaction might be regarded as acceptance of Mrs Fox's paper.

6.3.3 After detailed consideration of Mrs Fox's paper, the Sub-Committee noted the comments on this paper supplied by Professor Miller and his colleagues and by Dr Smith. It discussed an outline response incorporating these comments which the Chairman had prepared. It was agreed that the Chairman and Dr Zutshi should complete this draft reply and that after further consultation with Professor Miller and Dr Smith it should be sent to Sir John Badenoch. The ARVI response could either be sent to Mrs Fox or used as a basis of a JCVI response to Mrs Fox, as the Chairman of the JCVI wished.

6.3.4 The Sub-Committee wished to minute its thanks to all those who prior to the meeting, had participated in the preparation of the response to Mrs Fox's paper.

7. Adverse events following immunisation - MMWR 1985; 34; pages 43-47 ARVI/85/22

The Chairman said this was an interesting paper describing the efforts in the USA to obtain reports of suspected adverse reactions to vaccine in a similar manner to the CSM Yellow Card reporting system, and giving the reporting rates between 1979 and 1982. Members noted the difficulties and drawbacks of a voluntary reporting system.


Dr Zutshi said that parts of this report were concerned with the question of the sudden infant death syndrome (SIDS) and immunisation. The report described 988 deaths among infants between the ages of one week and 12 months, occurring during the years 1976-79. Information was obtained from hospital records, general practitioners, health visitors and in some cases from a home interview a few weeks after the death. Since most of the deaths occurred
before the 28th week, the data on the deaths associated with vaccination was rather scant. An analysis was based on all the case control pairs in which the immunisation status was known. There were more vaccinated controls than cases in each of the clinical categories of recognised terminal illness and unexpected death. There was "nothing in the case control comparisons to suggest that infant death, unexpected or after a recognised terminal illness, occurred more frequently within a few days of immunisation, nor that triple vaccine rather than antigens other than pertussis had such an association. Professor Hull questioned whether the tables fully reflected the number of controls used and whether further information was available in the report. Professor Hull and Dr Zutshi agreed to look at the original report and to report back to the Sub-Committee.

9. Summary of suspected adverse reactions associated with vaccines
reported on Yellow Cards since 21 December 1984 to 20 May 1985

9.1 Dr Zutshi said that during this period a total of 380 suspected adverse reactions associated with vaccine had been assessed, coded and registered.

9.2 Eighty-five suspected adverse reactions to DTP vaccine were registered. These included one death (142822) and one case of encephalitis (141879). These together with 12 cases of convulsions and one case of infantile spasms would be followed up. In at least two of the children who had convulsions an infection was present which might have caused the fever and the convolution. The Sub-Committee considered that the suspected adverse reaction of brachial neuritis following DTP immunisation (144615) was probably due to the tetanus component rather than the diphtheria component. The Sub-Committee decided that it would be unsatisfactory to offer advice about the treatment of the local mass described in report 145112. Members were unaware of any evidence which would confirm the suggestion in 146765 that a drug interaction had occurred between Augmentin and DTP vaccine.

9.3 There had been one report of a suspected adverse reaction to monovalent pertussis vaccine (142876). Dr Wallace commented that "the symptoms were more likely to be those arising from a painful injection site reaction rather than cerebral irritability."
9.4 Seventy-two reports of suspected adverse reactions to diphtheria and tetanus vaccine had been received. The majority of these were injection site disorders associated with booster doses. There was one report of an infant, a young child who died within 12 hours of receiving a dose of DT and OPV (140679). This death had been attributed to SIDS, but the Sub-Committee considered the cause of death was presumably acute laryngo-tracheo bronchitis. The Sub-Committee in noting the report of joint swelling following a booster dose of DT vaccine considered it might be a forme fruste of the serum sickness syndrome (149084). It was decided to search the CSM register for any similar cases.

9.5 Seventy-four suspected adverse reactions were reported with tetanus vaccine including 68 injection site disorders.

9.6 There were two reports of suspected adverse reactions to poliomyelitis vaccine. Further information was needed on the report of the case of a baby with agenesis of the brain in an otherwise normal skull and in particular whether hydrocephalus was present.

9.7 There were 34 reports of suspected adverse reactions following measles vaccination. These included three reports of convulsions. Six occurred within the first 24 hours and three of these within an hour of immunisation.

9.8 There were seven reports of suspected adverse reactions to rubella vaccine, including a woman of 30 who appeared to have had a central demyelinating lesion or a Guillain-Barré syndrome (144839).

9.9 Fifty-one reports of injection site abscesses associated with BCG vaccine had been received. Forty-eight of these had occurred in a group of 547 children vaccinated by one doctor. The Sub-Committee expressed its concern about these reports and again stressed the need for efficient education and training of doctors and other health personnel who carry out BCG vaccination. The Sub-Committee wished its concern to be brought to the attention of the JCVI.

Dr Zutashi reported that a proposed letter to District Medical Officers (through District General Managers regarding the future of the School BCG vaccination programme and also a proposed item on BCG abscesses for "Current Problems", drew attention to the necessity for adequate training of those involved in BCG vaccination and the correct technique of administering the vaccine. The Sub-Committee also urged that the suggested follow-up study of the incidence of infection site abscesses and keloid scars should be considered by the BCG Sub-Committee.
9.10 There were 14 suspected adverse reactions reports following influenza vaccine including one report of tinnitus and deafness. Dr Zutshi agreed to check the CSM register for other similar reports and to present his findings to the Sub-Committee.

9.11 There were three suspected adverse reaction reports associated with hepatitis B vaccine.

9.12 Thirteen reports of suspected adverse reactions associated with typhoid vaccine either used alone or in combination with other vaccines had been received. There were also two reports associated with cholera vaccine.

9.13 Eight reports of suspected adverse reactions to house dust mite desensitising agents and fourteen associated with grass pollen vaccines had been received.

Members expressed concern at the number of reports from these agents and asked if at some future occasion previously reported adverse reactions to desensitising agents could be collated and further studied.

10. **Further information on suspected adverse reactions associated with vaccines**

Further information was available on the following suspected adverse reactions.

(i) 128123 Absent left hand associated with rubella contact and rubella vaccination at about eight weeks of gestation. Follow-up indicated that the mother had not received rubella vaccine but only rubella immunoglobulin. It was considered that the missing left hand was probably caused by an intra-uterine band rather than by rubella infection or vaccination.

(ii) 113178 Febrile convulsion following first dose of monovalent pertussis vaccine. On assessment, two years later, the patient was considered to be doing well without any apparent sequelae. A slight speech problem had been noted when examined following immunisation and a hearing test had revealed a slight low frequency loss on the left. A member remarked that a significant increase in speech problems had been observed following febrile convulsions.
(iii) Possible fit following first dose of pertussis vaccine. Follow-up two years later showed that this patient seemed to have made a complete recovery.

(iv) Seven patients had been followed up between 12 months and 29 months after immunisation. Four (106212, 111130, 116518 and 123368) had made a complete recovery and developed normally although one was cyanosed due to a coincidental tricuspid valve atresia. Another (106212) had likewise recovered completely and uneventfully when assessed 17 months later. A few days later this child had a febrile convulsion associated with tonsilitis but during the following 18 months she had not had any further convulsions. The sixth child (114012) had no developmental problems but had further convulsions when aged 14 and 20 months. She had completed her diphtheria, tetanus and polio immunisation uneventfully. The seventh child (110585) appeared to have delayed speech development. Some two weeks before immunisation there was concern as to whether he had excessive head lag but this had resolved at the age of six months. Dr Wallace said that amongst children who had febrile convulsions there was an excess with delayed neurological development.

11. Tetanus vaccine

11.1 Adverse reactions to reinforcing doses of plain and adsorbed tetanus vaccine - Paper by A E Jones et al

Dr Smith said that a paper published by Professor Collier some five years ago suggested that there were more reactions from adsorbed vaccine compared with plain vaccine produced by the manufacturer when used for booster doses. At that time trials had not been carried out on all available vaccines and this study was therefore carried out by Dr Jones and her colleagues. It observed that the reactivity of tetanus vaccines when given to boost immunity tend to be variable and there is not a good indication for recommending plain vaccine for school leavers as was suggested originally.
11.2 Diphtheria and tetanus boosters - Article in the Lancet ARVI/85/27
1985 pages 1081-1082, Vol 1

This paper was noted with interest by members. Dr Smith drew attention to the paper by Bainton et al (BMJ: 1979, i: 858) not considered in this leading article. This study showed that reinforcing immunisation at school entry appeared to be necessary to maintain adequate titres of diphtheria antitoxin in children up to 15 years of age. On the other hand lasting immunity to tetanus was readily established in most children by primary immunisation alone, and the prime benefit may be to prolong immunity through adolescence into adulthood. There was little effect on the titres of antibodies to poliomyelitis.

12. Childhood immunisation acceptance rates in England and Wales by Regional Health Authorities ARVI/85/28

This item was noted with interest.

13. Items for information

13.1 Disclosure of interests (Table Paper 1)

The Sub-Committee noted this paper which had been produced to assess a situation which had arisen following a parliamentary question asking whether members of the CSM would disclose their connections with the pharmaceutical industry.

13.2 The Secretary stated that a paper would be prepared assessing all aspects of the disclosure of interests. Any changes in procedure which might be considered necessary would take effect in the new appointment period to Committees which begins in January 1987. The PQ in question had referred to Committees and not to members of Sub-Committees but the Secretary agreed to report any further developments.
14. Any other business

14.1 Data Protection Act

The Chairman enquired how this Act affected CSM data. The Secretary replied that the adverse reaction computer records are subject to the Act and will have to be registered, but the exact terms of registration, especially regarding disclosure of information was not yet known. The Chairman asked that further information be reported to the Sub-Committee when it became available.

14.2 Professor Miller informed the Committee that while he had been successful in obtaining an MRC grant to follow-up the children in the NCES, the project had been funded at a reduced level, without the research assistant who would obtain the details of the 2,500 cases and controls from the computer records and be responsible for recording the information on each child in the same way. Members of the Sub-Committee were disturbed by this information, as the practicability of the whole project seemed to be threatened.

15. Date and time of next meeting

The next meeting will be held on Friday 4 October 1985 at 11.00am in Room 1611/12 Market Tower.