JOINT COMMITTEE ON VACCINATION AND IMMUNISATION

MINUTES OF THE MEETING HELD ON MONDAY 9 OCTOBER 2000

Agenda Item Number 2

JOINT COMMITTEE ON VACCINATION AND IMMUNISATION
Minutes of the Meeting of Monday, 9 October 2000,
held at Partnership House, Waterloo Road, London SE1.

ATTENDING

Members:
Professor Michael Langman (Chairman)
Professor Keith Cartwright
Professor Jonathan Cohen
Dr David Goldblatt
Professor Paul Griffiths
Dr Christopher Harling
Dr David Joynson
Professor Simon Kroll
Professor Neil McIntosh
Professor Lewis Ritchie
Mrs Gillian Rogers
Dr Michael Roworth
Dr Richard Smithson
Professor Brent Taylor

Ex Officio Members:
~~Dr~~ Ian Jones
Dr Angus Nicoll
Dr Geoffrey Schild

Observers:
Dr Natasha Crowcroft (for Dr Elizabeth Miller (PHLS, CDSC))
Wg. CDR Andy Green (MoD)
Dr Angela Williams (MRC)
Dr Jan van Wijjngaarden (Ministry of Health, the Netherlands)
Ms Jo Yarwood (Health Promotion (England))

Invited to attend:
Dr Mary Ramsay (PHLS, CDSC)
Dr Nigel Gay (PHLS, CDSC)

Department of Health
Dr Mary O'Mahony
Dr David Salisbury, **JCVI Medical Secretary**
Dr Jane Leese
Dr Hugh Nicholas
Nick Adkin, **JCVI Administrative Secretary**
Ed Davis
Carole Fry
Helen Campbell

Dr Arlene Cook
Debby Webb
Robert Freeman (minute secretary)
Jeff Porter
Claudette Gyampoh
Olabisi Ogboye
Monica Francis

Medicines Control Agency
Dr Mair Powell
Dr Lincoln Tsang
Dr Katharine Cheng
Jim Slattery

Scottish Executive
Dr Elizabeth Stewart
Alan Oliver

National Assembly for Wales
Dr Mike Simmonds
Gaynor Legall

DHSS Northern Ireland
Dr Moira Briscoe (for Dr Elizabeth Mitchell)

1. ANNOUNCEMENTS AND WELCOME

1.1 This was the first meeting formally chaired by the new Chairman of the JCVI, Professor Michael Langman, and he welcomed new members of the Committee attending their first meeting: Dr Michael Roworth, Professor Neil McIntosh, Professor Brent Taylor, Professor Paul Griffiths, Professor Jonathan Cohen, Dr Christopher Harling, Professor Simon Kroll and Dr Angus Nicoll.

1.2 Also attending their first meeting were Dr Mary O'Mahony (new Head of the Department of Health's Communicable Disease Branch); Dr Elizabeth Stewart (new medical officer from the Scottish Executive); Dr Mike Simmonds and Gaynor Legall (respectively, new medical officer and new administrator from the Public Health Unit, National Assembly for Wales); Dr Moira Briscoe (attending for Dr Mitchell, DHSS, Northern Ireland); Dr Natasha Crowcroft (for Dr Miller, PHLS, CDSC); Dr Angela Williams (new MRC representative); Dr Tsang, Dr Powell, Dr Cheng and Mr Slattery (MCA); Ed Davis, Jeff Porter, Claudette Gyampoh and Bisi Ogboye (administrators from the Department of Health).

1.3 Apologies had been received from: Professor Roy Anderson and Drs Barbara Bannister and Diana Walford (from the Committee); Dr Liz Miller (PHLS,

CDSC); Dr Liz Mitchell (DHSS, Northern Ireland); Dr Devlin (Republic of Ireland); and, Loraine Gershon (Department of Health).

1.4 A full list of the membership of the Committee was tabled for information; Gillian Creighton had recently married and was now Mrs Rogers.

1.5 The Chairman mentioned those members whose terms of appointment on the Committee had ended, namely Drs Karl Nicholson, Stephen Conway, Marie Ogilvie, Robert Aston and Colin Kennedy and asked that a note of thanks for their contribution to the work of the Committee be included in the minutes of the meeting.

1.6 Members were reminded that the proceedings of the Committee were confidential and should not be discussed outside of the Committee. Any possible conflicts of interest should be declared at the start of meetings. Information about conflicts of interest etc. was contained in the information package provided to all members. No conflicts of interest were declared at this meeting.

1.7 The following papers were tabled:

JCVI: Membership List;
Revised Agenda for the meeting;
'Risk of Measles Epidemic' (National Assembly for Wales, CMO Letter (2000)19, 18 September 2000);
Immunisation Information Programme, Health Promotion England (Agenda item 6.5) (JCVI(00)30);
'Comments on "Measles, mumps, rubella vaccine: Through a glass, darkly" by Wakefield and Montgomery' (Miller, Andrews) (see Agenda item 9.3);
Minutes of the BCG Panel Meeting held on 3 April 2000 (Agenda item 10.1) (JCVI(00)69);
Minutes of the Influenza Panel meeting held on 25 February 2000 (Agenda item 11.1) (JCVI(00)71);
Influenza Risk Groups (Agenda item 11.7)(JCVI(00)77(a));
Monitoring influenza and other acute respiratory infections in 2000/01 (Agenda item 11.8).

2. JCVI MEMBERSHIP

Oral Report by Nick Adkin

Two Committee posts were presently vacant, Consultant in Communicable Disease Control and paediatric neurologist, and the terms of appointment of a further three members of the Committee ended at the end of December 2000. Recruitment for all these posts was in hand.

3. CONFLICTS OF INTEREST

Oral Report by Robert Freeman

The Committee was required to keep a Register of Members' Interests; this was in the public domain. Members were reminded to keep the Secretariat informed of any future changes that should be reflected in the Register. The question of Declarations of Interest by ex-officio members was being considered by the Secretariat in consultation with the Cabinet Office. The Secretariat would write to all ex-officio members about this matter. Members were also reminded to provide full contact details to the Secretariat where this had not yet been done.

4. MATTERS ARISING

There were none that were not covered elsewhere on the Agenda.

5. MINUTES OF LAST MEETING HELD ON FRIDAY 21 JANUARY 2000

JCVI(00)25(a)

MINUTES OF THE MEETING HELD ON FRIDAY 2 MAY 1999

JCVI(00)25(b)

The minutes of the 2 May meeting were unchanged from those presented at the January meeting but were included as information for new members. The January minutes were agreed as a true record.

6. COVERAGE AND OTHER REPORTS

6.1 Cover Report and Immunisation Statistics — JCVI(00)26

Report by Dr Mary Ramsay and Helen Campbell

A shortage of vaccine had led to a decline in diphtheria booster coverage at school entry. However, stocks of pre-school DT had become available from April 2000 and there was now sufficient vaccine both to enable catch-up of those children who had not been immunised and to provide routine vaccine thereafter. How best to achieve this catch-up would be raised with Immunisation Co-ordinators at their Conference being held on 3 November. Amongst the general concerns about low MMR uptake, there was particular concern about London where there was now a large cohort of unimmunised children.

6.2 Immunisation Coverage - Northern Ireland — JCVI(00)27

Report by Dr Moira Briscoe

MMR vaccine uptake appeared to have improved a little in Northern Ireland.

6.3 Immunisation Coverage - Wales JCVI(00)28
Report by Dr Mike Simmonds

The successful use of a pilot "myth buster" education resource had led to a small increase in MMR uptake in North Wales. It was planned to use this resource throughout Wales, including in the South which remained the worst area for uptake.

6.4 Immunisation Coverage - Scotland **JCVI(00)29**
Report by Dr Elizabeth Stewart

MMR uptake appeared stable at present, despite an anti-vaccine campaign.

6.5 Health Promotion England JCVI(00)30
Report by Jo Yarwood (tabled)

With the demise of the Health Education Authority at the end of March 2000, immunisation work had moved to a new organisation, Health Promotion England. An overview of the work of HPE was tabled. It was reported that there had been an increase in mothers' positive views about immunisation on the back of the successful meningitis C immunisation programme.

6.6 Vaccine Associated Suspected Adverse Reactions JCVI(00)30(a)
Report by Helen Campbell

The papers reported reactions identified by parents under the vaccine damage payments scheme and were a useful monitor of parental attitudes. The main parental concern remained the alleged association between measles containing vaccines (MMR especially), autistic spectrum disorders, autism and developmental and learning difficulties. In addition, claims had been submitted regarding developmental disorders and autism following pertussis vaccine.

7. THE MENINGOCOCCAL GROUP C IMMUNISATION PROGRAMME

7.1 Vaccine Supply
Oral Report by Debby Webb

and

7.2 Update on the Meningitis C Campaign
Oral Report by Dr David Salisbury

7.1.1 A year ago the Government had announced a campaign to introduce the new meningococcal group C conjugate vaccine with the aim of completing catch-up immunisation of all under age 18 years by the end of 2000. 17.7 million doses of vaccine had been distributed since then and the programme was on target to be completed on schedule. The papers provided to the Committee gave a full report on research on the vaccine and adverse reactions. It was particularly noted that - with the exception of primary care in June/July - once the first two weeks of the programme had passed vaccine supply had been excellent with no delays in supply

from the manufacturers. The school-based programme had resulted in a dramatic fall in disease to very low levels in those age groups immunised. In primary care the most dramatic impact had been in the under ones with an effect being seen even before three doses of vaccine had been given. There had been a less obvious impact in the remainder of the primary care age groups and immunisation of 3 to 5 year olds was lagging behind. These age groups had been harder to target and a further effort was needed to immunise them.

7.1.2 An article by a freelance journalist had appeared in The Observer newspaper over the August bank holiday. He had based his article on ADR reports from the MCA and, despite the intensive briefing he had been given, he had misrepresented the deaths reported following meningococcal C immunisation as being deaths caused by the vaccine. The Department of Health and the Chairmen of the Committee on Safety of Medicines and JCVI had become involved in writing to the paper and in providing information for health professionals and the public. The most up-to-date data on the impact of the new vaccine on disease had been publicised the following week and had received a lot of positive reporting.

7.1.3 Three meningococcal Group C conjugate vaccines were now licensed. As the last two vaccines were licensed for children aged over 1 year only, it had proven difficult at times to ensure the appropriate vaccine was allocated for the appropriate part of the programme. Chiron and NAVA were seeking variations to their licences to be able to use their vaccines in children from two months of age.

7.1.4 ***The Committee agreed that the type of information provided following this campaign was a good example of its future information needs.***

7.3 Impact on Disease JCVI(00)31
Report by Dr Arlene Cook

The residual problem of disease in people aged 20 and over was particularly noted. However, the Committee felt that the main programme should be completed before this issue was considered further. A paper was requested for the next meeting.

7.4 The epidemiology of meningococcal disease in England and Wales, 1999-2000 - the impact of conjugate MenC vaccination JCVI(00)32
Report by Dr Mary Ramsay

In 15-17 year olds vaccine coverage data from March was available. Uptake was high in the school groups but declined with age. Uptake in the same age groups not at school was low. There had been only four documented true vaccine failures showing a vaccine efficacy in 15 to 17 year olds of at least 96%; efficacy in infants after only one dose was about 70-85% and this would be significantly higher after three doses, although one child had been ill after two doses.

7.5 The Programmes in Scotland, Wales and Northern Ireland
Oral Reports by Dr Elizabeth Stewart, Dr Mike Simmonds and Dr Richard Smithson

The programme in Northern Ireland had been hard work but had gone very well. Vaccine uptake in the higher school years had been up to 90% but out of school it had been only 20 to 30%, figures almost identical to the MR campaign. Contrary to expectation, there had been good uptake in the Further Education Colleges. Reports would be available at the next meeting from Wales and Scotland.

7.6 Update on Safety Profile of meningococcal C Conjugate Vaccine JCVI(00)33
Reports by Dr Peter Arlett and Dr Katharine Cheng

7.6.1 A safety review of the meningococcal Group C conjugate vaccine for the period up to the end of February 2000 had been presented to the CSM in June. The CSM had agreed that there was an overwhelming balance in favour of the vaccine, but that certain ADRs (eg. headache, nausea, vomiting and malaise) should be added to the data sheets for older teenagers; this had been done at the end of June.

7.6.2 A Working Party had been set up which had briefed CSM on the safety of the vaccine and a full review of safety would be held once the catch-up programme had been completed. The Working Party had reviewed data available and had concluded that an association between MenC vaccine and seizures had not been proven. There had been 14 deaths reported. (2 further deaths had since been reported: 7 of the deaths were SIDS, 2 were meningitis B, 3 were in children with underlying conditions, 1 was pneumococcal septicaemia, 1 was infantile encephalitis, 1 bronchiolitis and 1 child collapsed one month after immunisation with no cause of death being found). The Working Party believed that the deaths were all explained by other causes and that the vaccine was most unlikely to be implicated. By 21 September 2000, there had been 8,300 reports of 17,000 ADRs (1 ADR per 2,000 doses). The profiles were the same for each brand of vaccine.

7.6.3 Although headaches had been commonly reported as ADRs, the Committee noted that headaches were common to other vaccines and they were likely to represent the result of the injection rather than the vaccine. Post-marketing surveillance did not particularly identify headaches in teenagers as an ADR. However, the Committee recognised the particular concerns of the public about a new vaccine which protected against a 'brain condition'. The Committee did feel that the MCA statement that there was "no evidence that the vaccine caused meningitis" was far too light: the vaccine categorically did not cause meningitis. The MCA Meningitis Working Party would consider this issue further, although it was noted that the Terms of Reference of the Working Party were to look at how (in the light of The Observer incident) people got information from the MCA.

7.7 Statement from the Chairman of the Committee on Safety of Medicines (CSM) and the Chairman of the Joint Committee on Vaccination and Immunisation (JCVI) on Meningitis C Vaccine JCVI(00)34

7.8 Press Release on impact of new vaccine JCVI(00)35

These had received good media coverage

7.9 Meningococcal C Conjugate (MCC) Vaccine Studies JCVI(00)36
Update report from the Vaccine Evaluation Consortium: September 2000
Paper by Dr Elizabeth Miller

7.9.1 Despite the success of the meningitis C vaccine there was still a lot of work to do on other vaccines such as meningitis B and pneumococcal. With the potential for 'overcrowding' in the immunisation schedule, the Consortium was looking at reducing the use of currently used vaccines - eg. through the use of combinations or sequential administration - to allow new vaccines to be introduced. An initial response from the Consortium would be available in one year. ***The Committee agreed that this was important work which needed to go forward.***

7.9.2 It was pointed out that the special needs of premature babies should be borne in mind by the Consortium. It was also mentioned that one other study should be added to this list, one funded by the Wellcome Trust looking at meningococcal colonisation in 16 and 17 year olds.

7.10(a) Recommendations for meningococcal vaccine for asplenic individuals
Oral Report by Dr Jane Leese

7.10(b) Guidelines for the Prevention and treatment of infection in patients with an absence [absent] or dysfunctional spleen JCVI(00)36(a)
BMJ: February 1996

Meningococcal vaccine was not currently routinely recommended for asplenic patients. Whilst there was no new evidence of an increased risk of disease in asplenic patients, it had been suggested that, as we now had a conjugate vaccine available, which was likely to give better and longer lasting protection in such people than the polysaccharide vaccine, it should be routinely recommended. Although the increased risk was probably tiny, asplenic patients were at a greater risk of bacterial disease. They would make an adequate immune response to the vaccine. ***The Committee agreed that, although uptake may not be high, the vaccine should be recommended for asplenic patients. They would still require A and C or quadrivalent vaccine for travel.***

7.11 Outbreak of W135 meningococcal disease among pilgrims returning from Saudi Arabia and their contacts JCVI(00)37(a)
Report by Dr Mary Ramsay

7.12 Serogroup W135 meningococcal disease in travellers returning from the annual Hajj pilgrimage JCVI(00)37(b)
Report by Dr Mary Ramsay

There had been 46 cases of W135 meningococcal disease reported between March and July 2000. Nine of these people had been on the Hajj and 20 were close contacts; 17 people had no history of close contact although all but 2 of these had been Asian Muslims. W135 was a virulent strain which was common in other parts of the world - including parts of the US - and it was agreed that people other than Hajj pilgrims, such as occupational workers, were also likely to be at risk. A quadrivalent vaccine (A, C, Y and W135) was available and was used in the USA, Italy and Switzerland. Two quadrivalent vaccines were licensed in the UK and the Department of Health was consulting manufacturers about increasing supply of this vaccine. ***The Committee accepted the recommendation that the quadrivalent vaccine be recommended as the preferred vaccine for pilgrims to Saudi Arabia, particularly for the main Hajj, from 2001.***

8. VACCINE SUPPLY SUB GROUP

8.1 Minutes of the JCVI Vaccine Supply Sub Group held on 2 December 1999 JCVI(00)38
Report by Helen Campbell

There were three areas for discussion: pertussis (8.2 to 8.8); OPV (8.9 to 8.13); and, thiomersal (8.14 to 8.18).

Pertussis

8.2 Update on Pertussis Surveillance, November 1999 JCVI(00)39

8.3 Serological evidence of pertussis in patients presenting with cough in general practice in Birmingham JCVI(00)40

8.4(a) Estimating the burden of *Bordetella pertussis* infection presenting to paediatric intensive care units and wards in London to inform vaccination policy in the UK JCVI(00)41(a)
Paper by Dr Natasha Crowcroft

8.4(b) Medical certificates of cause of death underestimate deaths from pertussis JCVI(00)41(b)
Report by Dr Natasha Crowcroft

8.5 Modelling the impact of pertussis vaccination: what effect would the addition of booster doses have on the incidence of infection in infants JCVI(00)43
Paper by Dr Nigel Gay

8.6 Immunogenicity and Reactogenicity of acellular diphtheria/ tetanus/pertussis vaccines given as a pre-school booster : effect of simultaneous administration of MMR JCVI(00)44
Paper by Dr Elizabeth Miller

8.7 Options appraisal for increasing protection against pertussis JCVI(00)45(a)
Report by Dr David Salisbury

8.8 Influence of vaccination coverage on pertussis transmission in France JCVI(00)45(b)
The Lancet, November 1999

8.2.1 Studies had identified that there was a high rate of hospitalisation especially in under ones as a result of pertussis. This was not reflected in the routinely available data. Pertussis in adults was also being under-reported. Studies in Paediatric Intensive Care Units of those babies too young to be immunised, had shown that 11% of babies admitted under 5 months had pertussis although only 2 had been suspected of the disease on admission. All but one of these children had had older siblings. This data confirmed that diagnoses were being missed. Recorded deaths were also an under-estimate. Data from 1970 to date showed that the rate of pertussis infection had decreased but that the decline had ceased since 1990. Cases in the population overall had continued to decline but they were as high in the under 3s as in the 1970s. Serological evidence suggested that the speeding up of the immunisation schedule was the most likely cause of this situation, despite improvements in population coverage.

8.2.2 Vaccine produced sufficient antibody responses to diphtheria and tetanus but studies showed persisting levels of pertussis disease in those immunised and in those too young to be immunised which suggested further steps were needed to improve the levels of protection against pertussis. Since most disease transmission to babies appeared to come from individuals under 15 years, and particularly 2-4 years, a booster at 1-4 years would help reduce transmission, providing extra protection for both those immunised and those too young to be immunised. Booster immunisation at school leaving would, therefore, be less effective and boosters for adults even less, although French studies had showed that often grandparents were a cause of the disease in babies.

8.2.3 The US included 5 doses of pertussis in their primary schedule, France had added a booster dose and Scandinavian countries had two early doses and another dose at 9 to 12 months (although it was not known if the effect of a third dose or a booster). There was no real supporting evidence for neonatal immunisation. Different schedules in different countries made studying the effect of these extra doses difficult. However, when acellular pertussis vaccine was given at 12 months in the US, there was a higher rate of reactions at the fifth dose (the US was considering dropping the fourth dose). It was also noted that the inter-epidemic interval had not changed suggesting that immunisation was protecting against severe disease but not infection.

8.2.4 On vaccine availability, the Netherlands had contracted SKB to provide a single acellular pertussis vaccine. A licensed acellular pertussis vaccine for older children would be available in the UK within a few weeks. DTaP vaccine was currently given at 2, 3 and 4 months although the Vaccine Supply Group had

recommended that we should continue to use wholecell pertussis vaccine if available.

8.2.5 It was agreed that – whilst the evidence could be stronger - there was a significant burden of disease, that transmission of disease in children too young to be protected was the main concern and that a pre-school booster would be helpful and would be the best way to protect these children. There were two existing immunisation visits to which a pertussis booster could be added: MMR at 12-15 months; or DT, MMR, polio at 3½-5 years. The pros and cons of various options were set out in the paper. Concern was expressed over adding a pertussis injection alongside MMR in the current climate. ***The evidence supported the introduction of a pertussis booster with the pre-school DT and the Committee supported this recommendation.*** A booster at school-leaving may also be helpful.

JCVI AND THE CHALLENGES AHEAD
Paper by Professor Michael Langman

C.1 This paper looked at the potential future role and tasks of the Committee.

C.2 The Committee was responsible for evaluating the use of all new vaccines. The Committee made medical and policy recommendations; implementation of JCVI's recommendations then fell to the UK Health Departments, with Ministers deciding how, or whether, to take forward the policy. However, the interface between policy and implementation was important and members felt that the Committee needed to be kept up to date should be able to give advice on implementation.

C.3 ***It was agreed*** that members should be encouraged to put forward items for discussion by the Committee. The more timely supply of papers, divided between "papers requiring decisions", "papers for background information" and summary sheets was essential. Putting more information in the papers as to what was required of the Committee would also be helpful; the Chairman said that the papers prepared about the acellular pertussis booster discussion were a good example of how papers could be best presented. It may be helpful for a recommendation to be comprehensively worked up by the Secretariat, with other options provided with notes on why these were not being recommended to the Committee. This would help the decision making process and allow members to consider issues in more depth.

C.4 ***It was also agreed*** that one or two additional meetings per year would be helpful, perhaps as separate childhood and adult vaccine meetings. Dates for meetings should be planned well in advance

C.5 The Committee had previously considered the issue of 'horizon scanning' as part of their remit. The Terms of Reference for the Committee had been reviewed five years ago and deliberately changed to allow JCVI to consider new vaccines before they were ready for use. Some vaccines, eg. meningitis C and pneumococcal, had come high on the list in a previous horizon scanning exercise whilst others, such

as hepatitis B, had come low. Doing this sort of exercise more regularly would be helpful.

C.6 ***In consideration of public interest about immunisation issues, it was agreed that making a statement after each meeting for public consumption or at least producing an annual report was important.*** Although the Committee had the valuable HPE research on parental attitudes, it was also felt that a lay member would provide an additional dimension to the Committee's discussions. The Scottish Executive supported the idea of a lay member. It was agreed, however, that 'commercial in confidence' issues made open meetings impossible. The Chairman also felt that the Committee should be proactive wherever possible and less defensive.

C.7 The Chairman and the Secretariat would consider members' views on these points and report back. Members were invited to put any further views in writing to the Secretariat or Chairman.

Oral Polio Vaccine

8.9	**Workshop on Oral Poliovirus Vaccine (OPV) and Intussusception, 15-16 June 2000, Atlanta, USA**	JCVI(00)46
8.10	**Investigation into the relationship between intussusception and oral polio vaccine in the UK** Report by Dr Elizabeth Miller et al	JCVI(00)47
8.11	**Live attenuated Polio Vaccine and the risk of intussusception** Report by Dr Hershel Jick	JCVI(00)48
8.12	**Summary of Intussusception Study in Cuba**	JCVI(00)49
8.13	**A descriptive study of the potential association between intussusception and oral polio vaccination among children in Ontario and Quebec, Canada**	JCVI(00)50

8.9.1 In the USA, rotavirus vaccine had been licensed and introduced and then withdrawn from the market following the discovery of an increased risk of intussusception linked with the vaccine. This event had raised concerns about whether other live oral vaccines, especially oral polio vaccine, might also be linked with an increased risk of intussusception.

8.9.2 A US study into OPV had suggested that there was an increased risk of intussusception up to 2 weeks after the second dose of vaccine. A UK study had tried to replicate this finding and had found initially that there may be an increased risk, but that it was after the third dose. Further work in the UK, including a further analysis following the January JCVI meeting using an expanded data base, had found no statistical link between OPV and intussusception. The US meeting had looked at all the

studies - the one US study showing an association, the 4 UK studies, a Canadian study showing no association, and preliminary data from Cuba (one third of this data was still to be analysed) which also showed no association. Overall, this thoroughly researched evidence supported there being no link between OPV and intussusception; these findings would be published in the MMWR and CDR.

8.9.3 ***The Committee agreed that this data was reassuring and that, unless other contrary evidence became available, it showed no link between OPV and intussusception.***

8.9.4 It was noted that the findings on OPV did not affect the position on rotavirus vaccine, a very different product where the link with intussusception was much stronger.

Thiomersal

8.14 **Assessment of neurologic and renal impairment associated with Thiomersal-containing vaccines** JCVI(00)51
Report by CDC

8.15 **Joint Statement of the American Academy of Family Physicians (AAFP), the American Academy of Pediatrics (AA), The Advisory Committee on Immunization Practices (ACIP), and the United States Public Health Services** JCVI(00)52

8.16 **Weekly Epidemiological Record**
Thiomersal as a vaccine preservative JCVI(00)53

8.17 **The Global Vaccine Safety Advisory Committee Sub-Group Meeting, 25 August 2000** JCVI(00)54

8.18 **Thiomersal in Vaccines**
The Lancet – April 2000 JCVI(00)55

8.14.1 This issue had had considerable exposure in the media in the US and had been seized on by anti-vaccine groups. The thiomersal content of some regimens of childhood vaccines given in the US had exceeded some limits for environmental exposure to mercury. However, there was no objective evidence that thiomersal actually caused harm. The US had advised that hepatitis B vaccine should not be given to neonates but that it should be given at an older age; this had led to a fall in uptake. The change to acellular pertussis vaccine and non-thiomersal containing hepatitis B vaccine had reduced exposure to thiomersal to very low levels.

8.14.2 Studies had been conducted to see what effect, if any, thiomersal in vaccines might be having. A wide range of ICD codes and outcomes such as speech defects and developmental delays had been investigated. Whilst one set of studies in California had suggested a dose effect for certain non-specific neurological outcomes, a second study at Harvard had shown no association between thiomersal and adverse outcomes, even

in pre-term infants, supposed to be at the greatest risk from mercury. Autism was not a significant association in the US studies. The ACIP statement was balanced and the move to non-thiomersal containing vaccines sensible. CPMP – the European Committee for Proprietary Medicinal Products – had also advised that manufacturers should move to producing vaccines that did not contain mercury.

8.14.3 However, thiomersal could not just be simply removed from vaccines. It was unlikely that non-thiomersal containing wholecell DTP vaccines would become quickly available and, on the basis of the US studies, the WHO had decided not to change its policy but to fund further studies, possibly through CDSC using the GPRD database. Acellular DTP did not contain thiomersal, neither did BCG.

8.14.4 ***The Committee agreed that the present evidence did not confirm any risks from thiomersal*** although data were hard to interpret. The Committee nevertheless supported the general principal that thiomersal be removed from vaccines.

9. MMR

9.1 **Report on the Strategy Development Group Sub-Group on Research into Inflammatory Bowel Disorders and Autism** JCVI(00)56
Report by the MRC

9.2 **Testimony before Congressional Oversight Committee on Autism and Immunisation** JCVI(00)57
Dr Andrew Wakefield

9.3 **Measles, Mumps and Rubella Vaccine** JCVI(00)58
Report by Dr Andrew Wakefield

9.4 **Autism and the Gastrointestinal Tract** JCVI(00)59
The American Journal of Gastroenterology, September 2000

9.5(a) **Detection and Sequencing of Measles Virus from Peripheral Mononuclear Cells from Patients with Inflammatory Bowel Disease and Autism** JCVI(00)60
Hisashi Kawashima et al

9.5(b) Correspondence from Dr Afzal and Dr Minor JCVI(00)61

9.5(c) Correspondence from Dr David Brown JCVI(00)62

9.6 **A Case-Control Study of MMR and other measles-containing vaccines and inflammatory bowel disease** JCVI(00)63
Results from the Vaccine Safety Datalink Project

MMR and Autism

9.7(a) MMR and autism : further evidence against a causal association JCVI(00)64
Report by Dr Elizabeth Miller and Paddy Farrington

9.7(b) American Academy of Paediatrics: MMR and Autism JCVI(00)65
Report of meeting held on 12-13 June 2000

9.7(c) Correspondence from Dr Eric Fombonne JCVI(00)66

9.1.1 Most of these papers were presented for information. Following Dr Wakefield's testimony in the US, there had been much media attention in the UK. However, the scientific basis for his presentation had not yet been published. A review of his paper (JCVI(00)58) had been prepared by CDSC and was tabled for the Committee; both these papers would be passed to the CSM.

9.1.2 ***The Committee agreed that the testimony and report from Dr Wakefield gave no new insights or evidence which changed its views on the safety of MMR vaccine.***

9.8 Potential for sustained measles transmission in England: an evaluation using district level vaccine coverage data JCVI(00)67
Report by Dr Nigel Gay

9.8.1 In order to maintain control of measles transmission in the UK, it was necessary to maintain low levels of susceptibility. This paper looked at the progress in measles control since the 1994 MR campaign and the current vaccination status of those aged under 10 years. Those who had been born since 1990 had little acquired immunity, only vaccine immunity. The COVER data might be incomplete, but it did show that susceptibility rates were above the levels needed to keep measles under control. Many health authority areas were already above the threshold at which transmission could occur and the situation was particularly bad in London. It was also noted that Congenital Rubella Syndrome was on the increase in Scotland and mumps was on the increase in Northern England.

9.8.2 Acting before measles could take off again would not be easy, but a proactive approach similar to that taken in Wales would be helpful for the whole of the UK. Options included asking Immunisation Co-ordinators to identify and target those children not immunised or to find local, proactive solutions. It may also be helpful to share the problems with journalists to appreciate the need for action. The situation in Japan - which had ceased using MMR vaccine because of adverse events associated with the Japanese manufactured mumps component of the vaccine - was outlined. It was also reported that there had been an outbreak of measles in Japan recently with 30 deaths; further information on this was coming from WHO.

9.8.3 ***The Committee agreed that, in the face of clear evidence of increased population susceptibility to measles, it would be neglectful not to act to pre-empt an***

increase in measles cases. It was agreed that officials should address this issue urgently.

9.9 Update on MMR and Idiopathic thrombocytopenia (ITP) JCVI(00)68
Report by Dr Elizabeth Miller

The evidence available showed that when there was a history of ITP, MMR was not contraindicated. The main issue was that of ITP following a first dose of MMR and the policy to follow at the second dose. In this context it was noted that vaccine associated cases tended to be mild. ***The Committee agreed that these were licensing issues to be clarified with MCA/CSM.***

10. BCG

10.1 Minutes of the BCG Panel Meeting held on 3 April 2000 JCVI(00)69
Report by Dr Jane Leese

There had been problems with the manufacture and supply of BCG vaccine and PPD such that it had been necessary to suspend the routine school's immunisation programme from September 1999. This had recently restarted in the London area. The Department was re-tendering the contract for BCG vaccine and PPD. The BCG Panel had discussed policy on neonatal immunisation, in particular in relation to children of second generation immigrants from countries with high rates of tuberculosis. Neonatal BCG was recommended for these groups. Although the Panel had not been convened to review the necessity of continuing the school's immunisation programme they had considered the issue and had agreed that the UK needed a secure neonatal programme before any further thought could be given a change in policy. ***The Committee agreed with the conclusions of the BCG Panel.***

10.2 Guidelines for the implementation and monitoring of local neonatal BCG immunisation programmes JCVI(00)70
Report by Helen Campbell

A survey of health authorities had found that procedures for neonatal BCG immunisation were variable, policies were unclear and monitoring was inadequate. Clear guidance and good monitoring were required to help improve uptake in the target groups. The Department of Health was planning to issue guidance and to introduce vaccine uptake targets with effect from the beginning of 2001. ***The Committee endorsed the work to try and resolve the problems identified by the survey.***

11. INFLUENZA

11.1 Minutes of the Respiratory Panel meeting held on 25 February 2000 and subsequent consultation of JCVI members JCVI(00)71
Report by Dr Jane Leese

11.2 **Major changes to the policy on influenza immunisation** JCVI(00)72
CMO's Update 26 - May 2000

11.3 **Health Service Circular** JCVI(00)73
Winter 2000/01: Capacity Planning for Health and Social Care
May 2000

11.4 **Influenza Immunisation:** JCVI(00)74
Joint CMO/CNO/CP/GPC Letter
1 August 2000

11.5 **Implementation of the 2000/01 influenza immunisation programme** JCVI(00)75
Report by Ed Davis

11.6 **Publicity Information Pack** JCVI(00)76

11.7 **Influenza Risk Groups** JCVI(00)77
Report by Dr Jane Leese

11.8 **Monitoring influenza and other acute respiratory infections in 2000-01**
Oral report by Dr Jane Leese

11.1.1 Influenza immunisation had become an increasingly important issue over the past two years. In 1998, influenza immunisation had been extended to include all those aged 75 and over in addition to the existing risk groups. A Working Group had then been set up by the Respiratory Panel to consider whether extending immunisation to all aged 65 and over would give good value for money. The Panel had agreed that it would. A paper was then circulated to JCVI members who had endorsed the Panel's recommendation. Ministers had agreed the policy change, to be implemented this year. On health care workers, the Panel had said that there was no new information on which to base any change in immunisation policy. Ministers had accepted this view but had decided that, with increasing winter pressures on the NHS, health care workers currently involved with patient care in the NHS should be offered vaccine.

11.1.2 Extra funding had been provided to implement the 65 plus immunisation policy. Health authority influenza co-ordinators had been appointed, targets had been set and an advertising campaign had been undertaken. Despite some media reports, there had been a large increase in the amount of vaccine available and only one manufacturer had so far experienced any significant delay in supplying vaccine to the UK.

11.1.3 The National Institute for Clinical Excellence had asked that common, clear and simple definitions of the influenza risk groups be developed. Although the Respiratory Panel was divided on the validity of such definitions, on the grounds that they could not be 'evidence based', they had agreed to go ahead. They were in favour of more 'inclusive' rather than 'exclusive' definitions. Committee members

were asked to let Dr Leese have any comments on the tabled draft definitions within one week of the meeting.

11.1.4 During 1999 RSV had co-circulated with influenza. ***The Committee endorsed that it would be necessary to monitor RSV as part of routine surveillance this winter, in order to assess the effectiveness of the new influenza immunisation programme.***

11.1.5 The Committee noted that no consideration was being given at present to introducing an age-related immunisation policy for pneumococcal vaccine.

12. PNEUMOCOCCAL SURVEILLANCE IN CHILDREN

JCVI(00)78

Report by Dr Elizabeth Miller

This issue was part of the horizon scanning discussed earlier in the meeting. Data confirmed the benefits of the routine use of pneumococcal vaccine in at risk children. This issue would come before the Committee again in the future.

13. POLIO

13.1 Polio Virus Laboratory Containment Report

Oral report by Helen Campbell

13.2 Global Polio Eradication

JCVI(00)79

Report by WHO

13.1.1 Four countries still had high levels of polio: India, Pakistan, Bangladesh and Nigeria. Other areas with polio included other parts of Africa such as Sierra Leone and Ethiopia. The situation in all these countries had been exacerbated by poverty and/or warfare. Importation of wild virus was the sole risk to the UK. The biggest concern remained India where there had been 170 cases last year; although this was a ten-fold reduction on the situation 10 years ago. India had improved her surveillance and now only 2 states were left with a significant number of cases. Nigeria and Pakistan remained challenges. All these countries had big population movements to and from the UK.

13.1.2 The European WHO had asked all countries within the region to look at the issue of laboratory containment for wild polio virus in preparation for global eradication of the disease. A joint JCVI/CDP group was taking this work forward. A survey of all biological laboratories would be conducted early in 2001 to identify all laboratories holding infectious or potentially infectious samples and action will be needed to assure that appropriate containment facilities are employed.

14. ANAPHYLAXIS MANAGEMENT JCVI(00)80
Report by Professor Chamberlain

The Resuscitation Council had recommended a dosage of adrenaline in cases of anaphylaxis which was different to other guidance. The paper provided for the Committee was the guidance which had been agreed by the three groups involved; the dosage was now consistent with that in "Immunisation against Infectious Disease" and the BNF. ***The Committee was content with the recommendations but recommended that it should be made very clear that adrenaline should be given through the intramuscular route not through the intravenous route.***

BSE AND VACCINES

15.1 Report of Ad Hoc Working Party of the CSM on TSE and Safety of Vaccines JCVI(00)81

15.2 Vaccines and Variant CJD JCVI(00)82
Vaccine - April 2000

15.1.1 All vaccine manufacturers had been asked by the MCA to check again what they had done with regard to the guidance from CSM on minimising risk of BSE in production and to give estimates of the degree of certainty that all necessary actions had been taken. The conclusions of this survey were far more reassuring than had been expected. The CSM had concluded that significant risks from manufacturing processes in the UK were extremely unlikely.

15.1.2 The possible risks associated with use of bovine blood or blood products in vaccine manufacture were given particular consideration. It seemed extremely unlikely that UK manufactured vaccines posed risks through the use of bovine blood products. The main reasons were:

a. Attempts to transmit BSE by use of blood taken from infected cattle had failed;
b. Manufacturers had complied with CSM advice in 1989 to source bovine materials outside the UK from BSE-free areas.

15.1.3 The particular position of the MRC-5 cell line held by NIBSC was considered. NIBSC had sourced albumin included in establishing the cell line from countries outside the UK since 1980.

15.1.4 General examination of the epidemiological background in cases of vCJD had, in addition, shown no features to indicate possible transmission from vaccines. ***JCVI were reassured by these and other findings that UK licensed vaccines did not pose risks.***

16. YELLOW BOOK

Oral report by Dr Jane Leese

A new edition of the 'Yellow Book', "Health Information for Overseas Travel", was about to go to print.

17. GREEN BOOK

Oral Report by Dr David Salisbury

Work on a revision of the 'Green Book', "Immunisation against Infectious Disease", had been delayed by the large number of policy changes in the pipeline. However, the aim was still to get the book published during this financial year. The Royal College of Paediatrics' "Blue Book" was being sent to the Department for checking soon.

18. HEPATITIS B

Oral Report by Dr Hugh Nicholas

18.1 From 1 April 2000 all pregnant women should be being offered screening tests for hepatitis B. A leaflet had been prepared giving information for patients and the Department of Health had worked with the Royal College of Midwives to produce guidelines for midwives. Discussions with the Antenatal Screening Task Force on how the programme should be monitored were ongoing.

18.2 Monies from the Modernisation Fund had been made available for a second year to improve the uptake of hepatitis B immunisation among IDUs. There was evidence of increased sharing of injecting equipment and laboratory reports of acute cases of hepatitis B among injecting drug users were increasing. Hepatitis B would be emphasised in the Department's forthcoming Sexual Health Strategy, and the role of GUM clinics in providing immunisation further explored.

18.3 The Advisory Group on Hepatitis (AGH) was reviewing the use of booster doses of hepatitis B vaccine both in immunocompetent persons including health care workers, and in immunocompromised individuals and those with chronic renal failure. It had also considered whether foster carers should be added to the risks groups for whom immunisation was recommended. The number of children from 'at risk' backgrounds were increasing, and the Group felt that all short term foster carers (who may be required to take any child at short notice) should be offered immunisation.

18.4 The Department had issued further guidance on the management of hepatitis B infected health care workers in June based upon the advice of the AGH. This requires that hepatitis B infected health care workers who are e-antigen negative and who perform exposure prone procedures should be tested for HBV DNA. Those with higher levels should have their working practices restricted. The Group was now considering further the management of hepatitis C infected health care workers.

18.5 The Advisory Group on Hepatitis had also been looking at the indications for immunisation against hepatitis A. A recent report from the Advisory Committee on the Microbiological Safety of Food entitled *'Foodborne Viral Infections'* had recommended that JCVI keep the question of routine immunisation of food handlers under review. The AGH felt that there remained insufficient evidence to recommend hepatitis A vaccine for food handlers.

18.6 There had been several large outbreaks of hepatitis A involving a significant proportion of drug misusers and the homeless, and the AGH considered that IDUs should be added to the groups for whom immunisation should be recommended. The current recommendation for hepatitis A immunisation and homosexual men would also be strengthened.

18.7 Asked about universal immunisation against hepatitis B, it was recalled that JCVI had considered this three years ago. The Committee, noting that the UK had a very low prevalence of hepatitis B, had felt that more could be achieved by better implementation of the selective programme and that universal immunisations should not be recommended for the present. In any case, a universal programme would be unlikely to have any major impact on the number of acute hepatitis B infections for perhaps 10-15 years as most infections in the UK occurred in early adulthood. Hence, whatever decisions were made concerning a universal programme, the targeted programme would need to continue.

19. ARTICLES FOR INFORMATION

JCVI(00)83

These were noted.

20. ANY OTHER BUSINESS

There was no other business.

21. DATES OF FUTURE JCVI MEETINGS

January 2001 and Friday 4 May 2001.

It was agreed that 12 or 19 January 2001 would be the date of the next JCVI meeting; the Secretariat would confirm the date.