ADVISORY GROUP ON HEPATITIS

Minutes of the meeting held on 9 October 1984 in Room 84, Hannibal House

Present:	Sir Robert Williams	(Chairman)
	Dr M Contreras	
	Dr J Craske	
	Dr D M S Dane	
	Dr T H Flewett	
	Dr R Lane	
	Dr S Polakoff	
	Dr R S Williams	
	Dr S E J Young	
	Professor A J Zuckerman	
	Dr M Sibellas	- Medical Secretary
	Mrs R C Gorvin	- Administrative Secretary
	Dr J Barnes	DHSS
	Mr C Howard	DHSS
	Mr T W S Murray	DHSS
	Dr A Smithies	DHSS
	Miss B F Weller	DHSS
	Dr S N Donaldson	- Northern Ireland
	Dr S R Palmer	- Welsh Office
	Dr W Prentice	- Scottish Home and Health Department
	Dr J C M Sharp	- Communicable Disease (Scotland) Unit

Introduction

The Chairman welcomed Dr Sharp who was attending the meeting to speak to his paper AGH(84)8.

1. Apologies for absence

Apologies were received from Professor Kennedy, Dr Lambert, Dr Oliver, Dr Graveney and Dr Duncan.

2. Minutes of the meeting held on 1 May 1984

The following amendments were agreed:

Present: replace Dr D Gambier by Dr S R Palmer;

Item 5, paragraph 2, line 10: add 'Central' before 'Blood';

Item 7.2 to read: "Dr Polakoff reported a cluster of five hepatitis B patients possibly resulting from a registrar operating during the incubation period of an acute hepatitis B infection. The association is being investigated by following up patients who had operations during relevant periods. The registrar has recovered clinically and has not developed persistent HB antigenaemia."

3. Matters arising

Professor Zuckerman reported that paediatric doses of hepatitis B vaccine were available on request.

4. Guidance for Health Care Personnel dealing with patients infected with hepatitis B virus - final draft — AGH(84)5

There was a detailed discussion on the final draft, which was agreed subject to the following amendments:

Paragraph 2, line 3 - after "However ..." insert "it should be noted that".

Paragraph 2, line 8 - delete "However ..." to end of paragraph.

Paragraph 3.3 - to read "The blood of patients with acute hepatitis B should be regarded as highly infective."

Paragraph 6.3, line 2 - amend "bleeding" to "blood".

Paragraph 6.3 - insert at end of paragraph "Care should be taken when dealing with broken glass".

Paragraph 9.3 - delete the first sentence; add "and syringes" after "needles" in the second sentence.

5a. Progress report on the development of hepatitis vaccines at the London School of Hygiene and Tropical Medicine — AGH(84)6a

b. Affinity of Antibody Responses in Man to Hepatitis B Vaccine determined with Synthetic Peptides - Extract from the Lancet 28 July 1984 — AGH(84)6b

c. Determination of the Affinity of Antibodies to Hepatitis B Surface Antigen in Human Sera - Extract from the Journal of Immunological Methods 72(1984) 41-48 — AGH(84)6c

Professor Zuckerman spoke to these papers. He reported that an agreement relating to hepatitis B and other micelle vaccines had been reached between Merck, Sharp and Dohme (MSD), the British Technology Group and the London School of Hygiene and Tropical Medicine. The technology had been transferred to the Merck Institute of Therapeutic Research after the secondment of a Merck scientist to the London School. The micelle vaccine would be available in two forms - plasma-derived and yeast-derived. Preliminary results were encouraging and it was hoped that it would be cheaper than the currently licensed vaccine. The initial target population for immunisation would be dialysis patients; other groups would include the 5-15 per cent non-responders to current vaccines, immuno-compromised patients and healthy individuals over the age of 40.

Considerable progress had been made on the synthetic amino-acid sequence (reported in the Lancet and the Journal of Immunological Methods) and the cyclical form was now under development as a vaccine. The synthetic peptide was also being evaluated as a method for quality control of each batch of hepatitis B vaccine. Professor Zuckerman said that the figures showing a 240-340-fold benefit from micelles were MSD's and were possibly optimistic. However, a lower dose would be required than for the current vaccine although the precise dose had yet to be established. The purity of the present recombinant yeast vaccine was about 80 per cent; the micelle vaccine would be purer. Antibody to yeast had been looked for carefully and had not been observed.

With regard to hepatitis A vaccines, Professor Zuckerman said that the largest vaccine producers were changing to a killed vaccine from the live attenuated vaccines. One laboratory was using a diploid cell line for production. A strain of hepatitis A virus isolated at the London School had been adapted to growth in MRC 5 cells. It was expected to have vaccine preparations available for evaluation within 18 months.

6. a. Adverse reactions to Hepatitis B vaccine AGH(84)7

b. Sales of Hepatitis B vaccine

Dr Sibellas spoke to this paper by the Department. There had been four reports so far of adverse reactions to hepatitis B vaccine, all of which had been of a transient nature. There was a possibility of under-reporting but the incidence of very few serious side effects of the vaccine mirrored the USA experience. Dr Flewett reported adverse reactions in two ambulance men who received vaccine in the arm and gammaglobulin in the leg and suffered vomiting and feverishness. These cases would be reported through the Yellow Card System to the Committee on Safety of Medicines. Dr Polakoff said that the PHLS was planning a study of adverse reactions in collaboration with occupational physicians. Dr Contreras expressed concern about the case of pancreatitis reported as an adverse reaction and it was agreed that the report would be followed up.

With regard to the sales of hepatitis B vaccine, Dr Sibellas reported sales of 14,157 doses in 1983 and 7,416 doses up to 31 July 1984. There was no shortage of the vaccine but the cost remained high. The shelf life of the vaccine was two years.

7. a. National Surveillance of infants at risk of acquiring Hepatitis B

Dr Polakoff reported on a study carried out between October 1982 and August 1984 involving the follow-up of 252 ante-natal patients.

Seven at-risk infants were reported late and were not given anti-hepatitis B immunoglobulin (Anti HBsIG); 132 infants were started on an HBsIg course, and the number of infants given whole or part of a course of HBsIg before they reached one year was 57. Of the 57, four were infants of mothers with acute hepatitis B in the last trimester; three out of the four were HBsAg positive at one year (one received the first dose after 48 hours). Of 53 infants of carrier mothers: five (9 per cent) were HBsAg positive at one year and two (4 per cent) were actively immune. A hepatitis B vaccine course was offered to parents of the 46 susceptibles at one year - 27 accepted, four refused, 12 did not respond, and records were not returned for three. Of the 27 given HB vaccine, 19 had two doses: specimens taken after one year showed that a further five had developed evidence of HBV infection. One was HBsAg positive

(five per cent) and four were actively immune (21 per cent). If the published attack rate of 90 per cent among untreated infants of 'high risk' carriers was assumed, then the protective effect of HBsIg so far was about 84 per cent. However only about 25 per cent of the protected infants developed active immunity.

The study showed that the system of identification and delivery of anti-HBsIg to the newborn of 'high risk' carrier mothers was usually successful. HBsIg was highly effective in preventing persistent HBsAg carriage in infancy, but more than half remained susceptible and required HB vaccine at one year plus. Results of controlled trials of passive/active immunisation of infants at high risk were published almost a year ago. Subsequently, Merck, Sharp and Dohme (MSD) HB vaccine was licensed for infants of less than six months in the USA. Dr Polakoff said that HB vaccine should be licensed for young infants in Britain without delay to allow passive/active immunisation in the neonatal period.

Dr Polakoff's paper on the options in Britain for future protection of newborn of HBsAg mothers would be presented to the JCVI at the meeting on 19 October together with the Advisory Group's recommendation that the most practical option was an initial dose of immunoglobulin at birth followed by three doses of vaccine. Dr Flewett said that it would be cheaper to use the vaccine alone rather than vaccine plus immunoglobulin. Dr Polakoff said that American studies showed 90 per cent efficacy from the use of combined vaccine and immunoglobulin but the effect in general use was not yet known. Dr Barnes said that he had made enquiries about the possibility of the DHSS providing hepatitis B vaccine centrally but had received a negative response from the Department's Supply Division.

7. b. PHLS Study of Hepatitis B in the NHS

Dr Polakoff reported on the PHLS hepatitis surveillance of the risk of transmission between doctors and dentists and their patients. A study had been made of an association between a cluster of five patients who developed acute hepatitis B some months after surgery by a team which included a registrar who operated or assisted during the incubation period of an attack of hepatitis B. All six infections were of subtype ad.

Postal enquiries showed the following:-

	Clinical hepatitis B		
	No	Yes	NK*
49 patients (1.9.83. - 3.11.83) Registrar operating/assisting	31	3+	13
51 patients (4.11.83. - 24.1.84.) Registrar on sick leave	45	0	6

*No reply, no information or patient died without evidence of hepatitis, but before possible incubation period completed.

+All reported before postal enquiry.

The registrar became hepatitis B surface antigen negative soon after onset and made a good recovery.

The surveillance has now ended and a report will be completed and offered for publication in the near future.

8. Viral Hepatitis A Outbreaks, Scotland 1983 AGH(84)8

Dr Sharp spoke to this paper which described the investigation of an outbreak of food borne viral hepatitis A following a private business banquet in a hotel at Aberdeen Airport in November 1983. Twenty-four persons developed viral hepatitis - six banquet guests, 15 canteen staff and three hotel diners. The only common food eaten by all 24 was raspberry mousse. Of the 8/10 banquet guests who had eaten mousse, six had become ill and were IgM positive, while the two who remained well were IgM negative but IgG positive. The supplier of the raspberries was traced but there was no way of tracing which of 21 farms had produced the particular raspberries supplied to the hotel. The mechanism and extent of contamination of the raspberries, possibly at the farm of origin, remained unknown. Dr Sharp said that it had been concluded that the raspberries in the mousse were almost certainly the cause of the outbreak but that there had been no universal contamination of the batch involved. Dr Williams pointed out the similarities of this incident with the outbreak at the Apothecaries Hall in 1980.

Dr Sharp also described an outbreak of viral hepatitis in which a total of 42 confirmed or suspected cases were notified to the Western Isles Health Board, most of which were associated with the local school at Daliburgh, South Uist. The results of the investigation verified that there had been a smouldering person to person spread of infection taking place over a 4-5 month period and was largely confined to members of one extended family with some spill-over to other schoolgirls. Preventive measures included use of immunoglobulin and improvement of handwashing and drying facilities at the school.

9. Update on AIDS AGH(84)9

Dr Craske reported that the most significant developmentin the last six months had been the identification of a retro-virus in Paris and in the USA. The French virus, originally named lymphocytic associated virus (LAV) had been shown to be serologically identical to the American virus by several groups or workers. This virus was the most serious candidate so far found for the aetiological agent of AIDS. A reliable immunoassay procedure had been developed at the Middlesex Hospital Medical School and showed a prevalance of HTLV-III antibodies in 17 per cent of the homosexuals at risk. The relationship between exposure and infection was not yet known. The incubation period of AIDS could be up to six years, with the average about four years. The number of cases of AIDS was rising rapidly, doubling every six months. Cases were mostly in London and among male homosexuals. There was a relatively low prevalence of HTVL-III antibodies in intravenous drug abusers, indicating that the retrovirus had not spread widely in this community.

Dr Craske said that it was unlikely that hepatitis B vaccine would transmit HTLV-III infection owing to the stringent virus inactivation procedures used in its preparation, but it was likely that the virus could be transmitted by blood and blood products. There was no epidemiological evidence that albumin or immunoglobulin were likely to transmit AIDS. Dr Contreras pointed out that 1.6 per cent of her male donors were homosexual and the risk of AIDS was reduced by

discouraging donation by homosexuals. Dr Smithies said that a new AIDS leaflet was to be published shortly which would advise that practising homosexuals should not donate. Dr Lane said that the development of a heat treatment should result in a reduced risk and policy on the licensing and importation of factor VIII might then be reviewed.

10. a. Delta Agent Infection in Drug Abusers - CDR84/23 AGH(84)10

b. Alarm over new form of Hepatitis - The Times 3 September 1984 AGH(84)11

The Advisory Group noted these items.

11. PHLS Surveillance of Anti-HBe Immunoglobulin prophylaxis: October 1975 - September 1981 AGH(84)12

Dr Polakoff spoke to this paper on the long-term follow-up of the outcome of prophylaxis with specific hepatitis B immunoglobulin to find out if an attack of clinical hepatitis had followed. The majority who had been exposed to accidental inoculation, contamination of skin cuts or abrasions or splashes into the eye or mouth with material known to contain HBsAg or body fluids of HBsAg positive individuals were health service staff. During October 1975 to September 1981, records had been received for 6,152 recipients and replies to enquiries were received for 84 per cent.

Attack rates were found to be generally low and the highest attack rate, 5.7 per cent, was found among sexual contacts of patients with acute hepatitis B. The two-dose schedule showed no apparent advantage and assessments of incidence for individuals who received prophylaxis on the same day or the day after exposure showed no apparent advantage for those treated promptly. The present results suggested that although prophylaxis should continue to be given as promptly as possible, it should not be withheld when the interval from exposure was longer than 48 hours. It was intended that the results of the study so far would be published.

12. a. Supplies of Hepatitis B Immunoglobulin AGH(84)13

Dr Lane reported that the supply of hepatitis B immunoglobulin had improved. The blood transfusion service had been approached and there had been an improvement in volume of plasma and potency. It was intended that the routine supply of hepatitis B immunoglobulin would be maintained through the established channels of the Central Public Health Laboratory, Colindale, so that supplies could be monitored and accumulation of the immunoglobulin on hospital shelves could be avoided. However, the Blood Products Laboratory was now prepared to make supplies available direct to meet the requirements of specialised users such as St Thomas' Hospital, provided that the recommendations for use of immunoglobulin were adhered to in practice, and documentation was properly maintained by the users.

12. b. Blood donors: compensation for injury

Dr Smithies reported that the Treasury had approved the proposals to extend an existing scheme of injury compensation to include any claims which might arise from the immunisation of voluntary donors with hepatitis B vaccine given to increase the level of hepatitis B immunoglobulin in their blood. Any such claims would be examined by a panel of assessors similar to that agreed for the scheme for plasmapheresis volunteers.

13. Post exposure Prophylaxis of Hepatitis B - Extract from MMWR 1 June 1984 Vol 33/No. 21 — AGH(84)14

14. Hepatitis B Vaccine in patients receiving Hemodialysis - Extract from the New England Journal of Medicine 23 August 1984 — AGH(84)15

These papers were for information.

Dr Flewett suggested that difficulties in some renal dialysis units should be taken note of and the Rosenheim advice might be reviewed or extended.

Dr Sibellas said that this matter would be discussed with the appropriate Division in the Department.

15. Any other business

There was none.

16. Date of next meeting

To be arranged for Autumn 1985.