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Your reference

Members of the Advisory Group on Hepatitis

Our reference

Date

24 September 1987

Dear Member

MINUTES OF THE MEETING OF THE AGH HELD ON 28 JULY 1987

I attach for your information the unconfirmed minutes of the above meeting. Also attached is a copy of the revised hepatitis B guidelines for proposed inclusion in the new Memorandum and a copy of an article from the New Zealand Medical Journal.

Yours sincerely

GRO-C

C P GALVIN  
JCVI Secretariat

NOT FOR PUBLICATION

JOINT COMMITTEE ON VACCINATION AND IMMUNISATION

ADVISORY GROUP ON HEPATITIS (AGH) MEETING ON 28 JULY 1987  
AT 2.00pm IN ROOM 67 HANNIBAL HOUSE

Members Present:

Professor D G Grahame-Smith - Chairman  
Dr D M S Dane  
Dr R Lane  
Dr Sheila Polakoff  
Dr R S Williams  
Dr J Craske

Dr J W G Smith - JCVI  
Dr J B Selkon - JCVI  
Dr R G Penn )  
Mr L T Wilson ) - Secretariat  
Mr C P Galvin )  
Miss D D Cato )

Dr A D McIntyre - SHHD  
Dr Palmer - Welsh Office  
Dr S M Donaldson - DHSS, NI

Dr F Rotblat )  
Miss B Weller ) - DHSS  
Mr C Howard )  
Mr N M Hale )  
Mr R L Cunningham)

1. Announcements and Apologies

Mr Wilson said that Dr Flewett had retired from the Birmingham PHLS Regional Virus Laboratory and so from the Advisory Group. Dr Elizabeth Boxall had been invited to replace him, but was unable to attend this meeting. Other apologies for absence were received from Professor Kennedy and Professor Zuckerman, Dr Contreras and Dr Young and from Dr Kurtz (HEA), Dr Barnes and Dr Graveney. Sir John Badenoch and Dr Selkon and Dr Smith had been invited as JCVI members but Sir John had sent his apologies.

There were also two numbered tabled papers:

- (a) A letter from Professor Zuckerman which had been numbered JCVI(AGH)87(6).
- (b) A paper from Dr Polakoff numbered JCVI(AGH)87(7).

In addition, Dr Selkon had brought a further Paper in the form of a draft letter to the Lancet with attachments. This had been tabled and would be numbered JCVI(AGH)87(8).

## 2. Intradermal Hepatitis B Vaccine

JCVI(AGH)87(4)

As Professor Grahame-Smith was unavoidably detained at Market Towers, Dr J W G Smith took the Chair until he arrived. Dr Smith suggested that the item on vaccine to be used by the intradermal route should be taken first. Dr Smith referred to the papers circulated about this item and said he understood that no licence had been issued for the vaccine to be given by that route. At his request, Mr Hale confirmed for the Department that this need not inhibit the Group from giving a recommendation on its use. There was discussion on the amount of evidence on safety and efficiency, but Dr Selkon pointed out that the vaccine to be given by the intramuscular route was licensed before comprehensive proof on its safety and efficiency was available. Dr Smith said the Group needed to address the problem on whether antibody responses to intradermal vaccine reflected adequate immunity. This divided itself into two questions.

- NOT True //
- (a) Whether the presence and level of the necessary antibodies was enough to allow the Group to accept the vaccine - members were content on this point.
  - (b) Was there sufficient weight of evidence of an adequate antibody response.

On (b), Dr Selkon referred to various papers which had been circulated, including those from the United States and Munich; he also tabled an extract from "The New Zealand Medical Journal" of 12 February 1986, Vol 99, No. 795 (note: a full copy of the article to be circulated to members. Dr Selkon went through the tabled draft letter to "The Lancet", which provided further useful evidence.

Dr Williams remarked that there seemed to be as much evidence in support of intradermal vaccine as there was for any other vaccine and that it would provide a much cheaper means of immunising large groups.

After discussion, the Group agreed that intradermal vaccination should be offered as an alternative to intramuscular vaccination particularly for mass vaccination programmes. Additional points made were that it was essential that the vaccinator should be adequately competent to give injections by the intradermal route for any vaccination programme.

There should be follow-up tests for antibody levels, certainly in the case of intradermal and preferably also for intramuscular vaccination. It was recognised however that this would put pressure on the PHLS Laboratories. Preferred date for follow-up tests was two to four months following the third dose. In reaching this decision the Group took into account Professor Zuckerman's letter tabled as JCVI(AGH)87(6).

It was also agreed that the advice to be issued on booster doses should be based on the last paragraph of the datasheet (page 67 of the papers) and that it should contain a mention that the duration of the immunity was at present uncertain but that it appeared to be at least five years. Precise advice on booster doses could not be formulated at present but where those individuals followed up showed unsatisfactory antibody levels, this fact should be given to them in case they met with an accident.

3. Revised Guidance on Hepatitis for the Memorandum  
'Immunisation against Infectious Disease'

JCVI(AGH)87  
(1)/(2)/(3)

The Group considered in detail the draft guidance for the Memorandum (pages 2-14) in particular, paragraphs 15.3.2 - 15.3.5. The amendments suggested by the Group are reflected in the further draft attached.

4. Other matters considered

The Group agreed that in recommending vaccination by the intradermal route, some mention would need to be made of the possibility of pigmentation changes and the appearance of small nodules at the site of vaccination.

The new guidance issued by the Royal College of Nursing (which recommended only intramuscular vaccine) was produced by Miss Weller and noted by the Group.

The possibility of a national contract for the vaccine, producing lower prices, was mentioned; Dr Selkon said he believed the new recombinant vaccine would be available from 7 August.

5. There being no other business, the meeting was adjourned. No date was fixed for the next meeting.

## IMMUNISATION AGAINST INFECTIOUS DISEASE

## 1 VIRAL HEPATITIS

## HEPATITIS B

15.1 Introduction

15.1.1 Viral hepatitis B usually has an insidious onset with anorexia, vague abdominal discomfort, nausea and vomiting, sometimes arthralgia and rash, which often progresses to jaundice. Fever may be absent or mild. The severity of the disease ranges from inapparent infections, which can only be detected by liver function tests, to fulminating fatal cases of acute hepatic necrosis. Among cases admitted to hospital the fatality rate is about one per cent. The average incubation period is 40-160 days but occasionally can be as long as 6-9 months.

15.1.2 The number of overt cases of hepatitis B identified in the UK appears to be low, averaging nearly (2200) reported cases a year. The incidence of hepatitis B surface antigenaemia (HBsAg) is not known with certainty but is in the order of about one in 500 of the general adult population; often such

individuals do not give a history of clinical hepatitis. A small proportion of antigen carriers develop chronic hepatitis. Sometimes there is impairment of liver function tests; biopsy findings range from normal to inactive hepatitis, with or without cirrhosis. The prognosis of the liver disease in such individuals is at present uncertain. About 80 per cent of patients with hepatic cell carcinoma have associated antigenaemia.

15.1.3 Certain occupational and other groups are known to be at increased risk of infection (see paragraph 15.3) although in comparison with most other countries the incidence of the disease is low in Britain.

15.1.4 There are two types of immunisation product, a vaccine which induces an immune response and a specific immunoglobulin which provides passive immunity and can give immediate but temporary protection after accidental inoculation or contamination with antigen positive blood.

## Vaccine

15.2.1 There are two types of hepatitis B vaccine each containing 20 micrograms per ml of hepatitis B surface antigen (HBsAg) adsorbed on aluminium hydroxide adjuvant.

One vaccine is purified from human plasma by a combination of ultra centrifugation and biochemical procedures. The product is inactivated by a threefold process; each of these processes has been shown to inactivate hepatitis B virus and a range of other viruses.

The other type of vaccine contains hepatitis B surface antigen produced by yeast cells using a recombinant DNA technique.

15.2.2 The vaccine should be stored at 2-8°C but not frozen. Freezing destroys the potency of the vaccine.

15.2.3 The vaccine is effective in preventing infection in individuals who produce antibodies. Ten-fifteen per cent of those over the age of 40 do not respond though a smaller proportion of younger people are non-responsive and overall the vaccine

is about 90 per cent effective. Routine post-vaccination screening for antibody response should be done some 2-4 months after the course of injections.

Non responders should be considered for a further booster dose but as even then the response is likely to be poor such patients should note that HBIG may be necessary if exposure to infection occurs (see 15.8 below).

Patients who are immunodeficient or on immunosuppressive therapy may respond less well than healthy individuals and require larger doses of vaccine.

The duration of immunity is not precisely known but is of the order of three to five years.

Advice on the need for further booster doses cannot yet be formulated but individuals who are at high risk may wish to determine periodically their antibody level. If this falls below 10iu/l, the need for a booster dose should be considered.

### 15.3 Recommendations

15.3.1 The vaccine should be offered to those at special risk as described below though this list should not be seen as being exclusive.

15.3.2 The vaccine need not be given to individuals known to be hepatitis B surface antigen (or antibody) positive or to patients with acute hepatitis B since in the former case it would be unnecessary and in the latter ineffective. Intimate contacts of individuals suffering from acute hepatitis B should be treated by passive immunisation (see 15.8 below).

Screening for antibodies prior to vaccination may sometimes be considered in a population where the antibody prevalence is expected to be high.

15.3.3 Vaccination should be considered for the groups of individuals discussed in the succeeding paragraphs under the headings "Health Care Personnel", "Patients and Family Contacts" and "Other Indications for Immunisation".

#### 15.3.4 HEALTH CARE PERSONNEL

Doctors, dentists, nurses, midwives and others including students and trainees who have direct contact with patients or their bodily fluids or with frequent contact with blood and needles.

Groups at highest risk in this category are

1. Those directly involved over a period of time in patient care in residential institutions for the mentally handicapped.
2. Those directly involved in patient care over a period of time, working in units giving treatment to known carriers of hepatitis B infection.
3. Health care personnel on secondment to work in areas of the world where there is a high prevalence of hepatitis B infection if they are to be directly involved in patient care.
4. Laboratory workers, mortuary technicians.

In the event of accidental inoculation with infectious material from a patient with hepatitis B, health care workers should be offered combined active immunisation with hepatitis B vaccine and passive immunisation with hepatitis B immunoglobulin. If they have already been vaccinated, they should be given a booster dose of vaccine unless they can be shown to have adequate protective levels of antibodies (see also paragraph 15.8 Hepatitis B immunoglobulin).

#### 15.3.5 PATIENTS AND FAMILY CONTACTS

1. Patients on first entry into residential institutions for the mentally handicapped where there is a known high incidence of hepatitis B.

2. The immune response to the current hepatitis B vaccines is poorer in immunocompromised patients and those over 40. For example, only about 60 per cent of patients undergoing treatment by maintenance haemodialysis develop anti-HBs. It is suggested therefore that patients with chronic renal damage be immunised as soon as it appears likely that they will ultimately require treatment by maintenance

and  
HIV ✓  
✓

haemodialysis or receive a renal transplant.

3. The spouses or other consorts of carriers of hepatitis B if the potential vaccinee is negative for hepatitis B surface antigen, surface antibody.

4. Infants born to:

(a) Mothers who are persistent carriers of hepatitis B surface antigen, particularly if hepatitis e antigen (HBeAg) is detectable or its antibody (anti-HBe) is not. The nature and size of the risk at birth varies from persistent carriage in 80-90 per cent of infants of HBeAg positive mothers to the rare occurrence of acute hepatitis B in infants of anti-HBe positive mothers. It is most important to identify the infants at risk and antenatal patients in high risk categories should be screened. These include:

(i) All ethnic groups other than Caucasian though Caucasians from Southern and Eastern Europe should also be considered.

(ii) All those with a personal or family history of occupation suggestive of an increased risk of exposure to hepatitis B virus (HBV).

(b) Mothers HBsAg positive as a result of recent infection particularly if HBeAg is detectable or anti-HBe is not.

The optimum timing for immunisation in conjunction with the administration of hepatitis B immunoglobulin at a contralateral site is immediately at birth or as soon as possible thereafter and preferably within 12 hours. It is sensible to make arrangements for such immunisation well in advance.

5. Whenever immediate protection is required immunisation with the vaccine should be combined with simultaneous administration of hepatitis B immunoglobulin at a different site. It has been shown that passive immunisation with hepatitis B immunoglobulin does not interfere with an active immune response. A single dose of hepatitis B immunoglobulin (usually 500 IU for adults; 200 IU for the newborn) is sufficient for healthy individuals. If infection has already occurred at the time of the first immunisation, virus multiplication is unlikely to be inhibited completely, but severe illness and, most importantly the development of the carrier state of HBV may be prevented in many individuals, particularly in infants born to carriers mothers.

### 15.3.6 OTHER INDICATIONS FOR IMMUNISATION

Consideration should also be given to members of the following groups and it should be noted here that if the recommended precautions to protect against HIV infection were taken the risk of spread of HBV would be considerably reduced.

#### 1. Police and Emergency Services

The statistics of the incidence of hepatitis B do not show that in general members of the police, ambulance, rescue services and staff of custodial institutions are at greater risk than the general population. Nevertheless, there may be individuals within these occupations who may be at higher risk and who should be considered for vaccination. Such a selection has to be decided locally by the occupational health services.

#### 2. Travellers

Those going to work in areas of the world where hepatitis B is endemic especially those involved in the care of patients. Travellers who are likely to be in such endemic areas for a lengthy period could also be considered for vaccination.

3. Morticians and embalmers.

4. Individuals who frequently change sexual partners, particularly prostitutes and male homosexuals.

5. Inmates of long-term custodial institutions.

6. Parenteral drug abusers.

#### 15.3.7 RECOMMENDED DOSAGE FOR PRIMARY IMMUNISATION

The basic immunisation regimen consists of three doses of vaccine with the first dose at the elected date the second dose one month later and the third dose at six months after the first dose.

The vaccine may be given intramuscularly or intradermally (but this only in adults and children over 10 years of age).

In patients with haemophilia the intradermal or subcutaneous route may be considered,

The intramuscular injection should be given in the deltoid though the anterolateral thigh is the preferred site for infants.

DOSAGE SCHEDULE

GROUP	INITIAL	1 MONTH	6 MONTHS
Newborn infants and children under 10 years	0.5ml intramuscular (10 micrograms)	0.5ml intramuscular (10 micrograms)	0.5ml intramuscular (10 micrograms)
Adults and children over 10 years	1.0ml intramuscular (20 micrograms)	1.0ml intramuscular (20 micrograms)	1.0ml intramuscular (20 micrograms)
	0.1ml intradermal (2 micrograms)	0.1ml intradermal (2 micrograms)	0.1ml intradermal (2 micrograms)
Immunocompromised and dialysis patients	2.0ml intramuscular (40 micrograms)	2.0ml intramuscular (40 micrograms)	2.0ml intramuscular (40 micrograms)

#### 15.4 ADVERSE REACTIONS

Adverse reactions to hepatitis B vaccine observed to date have been generally limited to soreness and redness at the injection site if given intramuscularly.

Injection intradermally may produce a temporary nodule at the site of injection sometimes with local pigmentation changes.

It is important that adverse reactions should be reported to the Committee on Safety of Medicines (by the 'Yellow Card System').

#### 15.5 PREGNANCY

Hepatitis B infection in pregnant women may result in severe disease for the mother and chronic infection of the newborn. Vaccination should not be withheld from a pregnant woman if she is in a high risk category.

#### 15.6 EFFECT OF VACCINATION ON CARRIERS

The vaccine produces neither therapeutic nor adverse effects on carriers of hepatitis B.

#### 15.7 CONTRA-INDICATIONS

Vaccination should be postponed in individuals suffering from serious infection.

## 15.8 HEPATITIS B IMMUNOGLOBULIN (HBIG)

15.8.1 A specific immunoglobulin is available for passive protection against hepatitis B. It is used in the following circumstances:-

a. Persons who are accidentally inoculated or who contaminate the eye or mouth or fresh cuts or abrasions of skin with blood from a known carrier of HBsAg. Individuals who sustain such accidents should wash the affected area well and seek medical advice. Advice about prophylaxis after such accidents should be obtained by telephone from the nearest Public Health Laboratory. Advice following accidental exposure may also be obtained from the Hospital Control of Infection Officer or the Community Medicine Specialist (Environmental Health).

b. Children born to mothers who develop acute hepatitis B in the last trimester of pregnancy or who are highly infective HBsAg carriers should be immunised in the neonatal period, beginning as soon as possible after birth and not later than 48 hours.

c. Sexual consorts and, in some circumstances, a family contact judged to be at high risk, of individuals suffering from acute hepatitis B and who are seen within one week of onset of jaundice in the contact.

15.8.2 There is no epidemiological evidence associating the administration of intramuscular immunoglobulin, both normal and specific, with seroconversion for antibodies to HIV. Not only does the processing of the plasma from which these immunoglobulins are prepared render them safe but the screening of blood donations is now routine practise.

15.8.3 Supplies Public Health Laboratory Service either from the CPHL [Tel 01-200 4400] or via the Local Public Health Laboratories. Hepatitis B immunoglobulin is held in Scotland by the Blood Transfusion Service.

Tel. Aberdeen	(0224) 681818
Dundee	(0382) 645166
Edinburgh	(031) 2292585
Glasgow	(0698) 373315/8
Inverness	(0463) 232695

Hepatitis B immunoglobulin is held in Northern Ireland by the Regional Virus Laboratory, Royal Victoria Hospital, Belfast. [Tel. 0232 240503].

Note: Supplies of this product are limited and demands should be restricted to patients in whom there is a clear indication for its use.

## 15.9 HEPATITIS A

15.9.1 Hepatitis A is usually transmitted by the faecal oral route usually after the ingestion of contaminated food or drink. The disease is usually milder than hepatitis B and is very seldom fatal. A chronic carrier state is unknown and chronic liver damage is extremely unlikely. The incubation period is about 15-40 days. Outbreaks occasionally occur in this country although most cases occur sporadically. Persons travelling to developing countries may be at greater risk of contracting hepatitis A.

15.9.2 Human normal immunoglobulin (HNIG) offers protection against infection with hepatitis A and is normally used under the following circumstances:-

- a. to control outbreaks of hepatitis A in households and in institutions
- b. for persons travelling to areas of poor sanitation.

15.9.3 Human normal immunoglobulin may interfere with the development of active immunity from live virus vaccines. It is therefore wise to administer live virus vaccines at least three weeks before the administration of immunoglobulin. If immunoglobulin has been administered first then an interval of three months should be observed before administering a live virus vaccine.

15.9.4 Supplies The Public Health Laboratory Service,  
or in Scotland the Blood Transfusion Service.