PROPHYLAXIS OF HEPATITIS B INFECTION

N.R. GRIST
University Department of Infectious Diseases, Ruchill Hospital - Glasgow, U. K.

INTRODUCTION

Prophylactic measures for the control of hepatitis B are as follows:

1. *Interruption of transmission of infection* by rational measures based on the known properties and behaviour of hepatitis B virus which spreads mainly by apparent and inapparent parenteral routes from infected blood and potentially from other blood-contaminated body fluids.

2. *Passive immunisation* to provide temporary protection by injecting high titred specific immunoglobulin (anti-HBIG) shortly before or as soon as possible and not later than 48 hours after exposure to infection. Advice on dosage (currently 500 mgm for an adult) will be given by the supplier (mainly Public Health Laboratories in England and Wales, or the Scottish Blood Transfusion Service).

3. *Active immunisation* by inactivated hepatitis B vaccines which have been shown by field trials to be safe and effective (Szmuness *et al.*, 1980; Szmuness, 1981; Deinhardt *et al.*, 1981; Crosnier *et al.*, 1981). Although these vaccines are not yet freely available for use in this country, it is to be expected that they will become so during the next few years. Ideally they are given before exposure to infection, but the long incubation period of hepatitis B provides a possible opportunity for some benefit if given shortly after exposure to infection.

4. *Passive-active immunisation* against hepatitis B by administration of anti-HBIG under conditions of continuing exposure to risk of infection which

may then produce symptomless but actively immunising infection under the umbrella of dwindling passive protection; or by injecting vaccine and anti-HBIG at different sites at the same time (Deinhardt *et al.*, 1981).

Experience over the next few years will show the relative merits of several types of vaccine which are under development and the best ways to use them (Zuckerman, 1982). Application of the above prophylactic measures to problems arising in obstetric practice are considered below.

Acute hepatitis B in pregnancy

In the first and second trimesters, acute hepatitis B entails an approximately 6% risk of infection of the infant (Schweitzer, 1975; Boxall, 1980). This risk depends on whether the mother still has viraemia (for which antigenaemia is the available marker) at the time of delivery. If the mother gives a positive reaction in tests for hepatitis B surface antigen (HBsAg) at this time, the baby should be passively protected by anti-HBIG as soon as possible within a few hours after birth.

Acute hepatitis B during the third trimester or within two months postpartum entails a high risk (approximately 70%) of infection of the baby. In the first of these situations the infant should be protected by injecting anti-HBIG as soon as possible after birth, and it is advisable to isolate the baby from the mother who should not breast feed her infant until she has clinically recovered and become HBsAg-negative. If maternal hepatitis develops in the early months after birth, the baby may already have been infected during the presymptomatic period of maternal viraemia but should be given the benefit of an injection of anti-HBIG.

Hepatitis B carrier mother

If the HBsAg-positive mother is HBe-antigen negative and an ethnic European, the risk of transmission of infection to her infant is small, especially if she has HBe antibody which in any case will probably prevent the infant becoming a chronic carrier (Derso *et al.*, 1978; Chin *et al.*, 1981). Specific immunoprophylaxis is not essential in these circumstances.

If the carrier mother is of some other ethnic origin, especially S.E. Asian, and in any case if she is HBe-antigen positive, the risk of transmission of infection is high with the possibility that the child will become a chronic carrier with longterm risks to health and also helping to maintain the world reservoir of infection. Vigorous prophylactic action is justified, though without guarantee of success. The baby should receive anti-HBIG as soon as possible

within 48 hours after birth. This should be supplemented by additional injections for 6 months either monthly (Reesink *et al.*, 1979) or at intervals of three months (Beasley *et al.*, 1981). This will reduce the chance of the infant becoming a chronic carrier even if infection does occur (Beasley *et al.*, 1981). It may also be effective to give both anti-HBIG and vaccine, when available (Maupas *et al.*, 1981; Szmuness, *et al.*, 1981).

Mother is consort or close contact of hepatitis B (acute case or carrier) or of drug addict

The mother's hepatitis B status should be determined by tests for the antigen and antibody. If non-immune, she should be advised on hygienic precautions to minimise the risk of acquiring infection during pregnancy and the first few months after delivery. In addition, she should be given passive protection by anti-HBIG. Vaccine may also ultimately have a useful role in these circumstances.

Hepatitis B infections in staff

An acute case of hepatitis should be off duty until clinically recovered with clearance of HBsAg and development of antibody. This is the usual outcome, and staff can expect to resume their duties and career after convalescence.

Staff found to be chronic antigen carriers present a more difficult problem, largely because of exaggerated fears of the implications. In this country most carriers are negative in tests for HBe antigen and positive for the corresponding antibody, thus having no significant infectivity for others except perhaps by blood donation. Staff in this category require advice, reassurance, and can continue normal duties.

The unfortunate minority, about 20%, who are HBe antigen positive carriers, present a more difficult problem. They require advice on hygienic precautions to avoid infecting others, though it must be recognised that they are not infectious in the same sense as measles – if hepatitis B were more "catching" it need not have evolved a mechanism of normal transmission from blood-stream to blood-stream! Nevertheless, although these carriers are not "lepers" (to name another poorly-transmissible but feared infection), it is clearly wise to limit their professional activities so as to avoid the possibility of their blood infecting patients, instruments (unless subsequently sterilised) or medicaments. This may interrupt a career, but the carrier should be kept under long-term observation with annual blood tests since ultimately a transition to antigen-negative and antibody-positive status is to be expected.

Protection of staff from hepatitis B

The first essential is to minimise exposure to risk of infection by the standard common-sense, organisational and procedural arrangements which should be good practice in well-run establishments (Tedder, 1980). The success of these "ordinary" measures is witnessed by the virtual disappearance of laboratory-acquired hepatitis since 1974 in British clinical laboratories (Grist, 1981) and the good record of dialysis units in this country in recent years (Polakoff, 1981). Although there is little doubt that the prevalence of antibodies and incidence of infection are higher in staff with clinical contact than in the general population, evidence that hepatitis B is not easily transmitted from hospital patients with acute hepatitis, provided that proper precautions are taken for handling blood, secretions and excretions, has been recorded by Papaevangelou *et al.* (1981).

Specific prophylactic measures comprise administration of anti-HBIG as soon as possible and certainly within 48 hours after percutaneous or mucosal contamination of non-immune staff with HBsAg-positive material, particularly if HBeAg-positive. Exposure to HBe-antigen negative material, particularly if e-antibody positive, in small amounts entails no significant risk. Blood should be collected from the exposed person before giving anti-HBIG in order to establish whether he is already a carrier or immune and therefore at no risk, and in any case in order to provide a baseline for follow-up observations. Administration of anti-HBIG should not be delayed for the result of these tests. The sensitivity of modern testing is such that the appearance of antigen can be detected before the onset of illness and before the development of more than low-level infectivity, at which stage the victim can be withdrawn from occupational or other situations involving unacceptable risk of further spread of infection.

In due course vaccination against hepatitis B will be valuable for staff in the highest risk groups, and the limited time before vaccines become available and demanded should be used to collect valid data on the incidence of hepatitis B and the prevalence of antibody in the various occupational groups in order to facilitate rational assessment of priorities for the use of vaccine which is, initially, both expensive and in short supply.

Rational policies for vaccination

Examples of groups for which the possible value of prophylactic vaccination deserves consideration and evaluation are as follows:

Patients: pregnant contacts of cases and carriers; newborn babies of cases or carriers or in households with cases or carriers; patients requiring repeated transfusions, access to circulation, injections of blood products, or other frequent tissue penetrations; patients receiving prolonged in-patient treatment or chronic institutional care; immunodeficients; in patients with malignant disease.

Health care staff: various categories of medical, dental, nursing, laboratory and ancillary staff; first aid workers.

Other groups: drug abusers, homosexuals, prostitutes, the sexually promiscuous, the armed forces, police, prison staff, rescue services, travellers to endemic areas, family contacts of carriers, women of child-bearing age especially those in endemic areas who are non-immune.

Clearly it will be neither necessary nor feasible to vaccinate all members of the above groups, but it is important to collect objective data on which national policies and priorities for the sensible allocation of resources to control the problem of hepatitis B can be decided.

SUMMARY

The prophylaxis of hepatitis B by interrupting transmission of the virus, by passive and active immunisation is discussed with particular relation to problems arising in obstetrics. Better information about the incidence of the infection and the clincal disease is urgently required to provide a rational basis for optimal use of the vaccines which will soon become available.

REFERENCES

Beasley R. P., Hwang L. Y., Lin C. C.: Lancet, *2*, 388, 1981.
Boxall E. H.: *Maternal transmission of hepatitis B.* In: "Recent Advances in Clinical Virology", A. P. Waterson (ed.), Churchill Livingstone, Edinburgh, *2*, 17, 1980.
Chin K. C., Chaudhuri A. K. R., Follett E. A. C.: Journal of Infection, *3*, 246, 1981.
Crosnier J., Jungers P., Couroucé A.: Lancet, *1*, 455, 1981.
Derso A., Boxall E. H., Tarlow M. J., Flewett T. T.: British Medical Journal ,*1*, 949, 1978.
Deinhardt F., Zachoval R., Frösner H., Frösner G.: *Passive-active immunization against hepatitis B.* In: "Proceedings of the European Symposium on Hepatitis B", S. Sherlock and S. Krugman (eds.), Rahway, Merck Sharp and Dohme International, 1981 (in press).
Grist N. R.: Medical Laboratory Sciences, *38*, 103, 1981.
Maupas P., Chiron J. P., Barin F.: Lancet, *1*, 289, 1981.
Papaevangelou G. J., Roumeliotou-Karayannis A. J., Contoyannis P. C.: Journal of Medical Virology, *7*, 143, 1981.
Polakoff S.: Journal of Hygiene, *87*, 443, 1981.
Reesink H. W., Reesink-Brongers E., Lafeber-Schut B. J. T., Kalshoven-Benschop J., Brummelhuis H. G. J.: Lancet, *2*, 436, 1979.
Schweizer I. L.: *Infection of neonates and infants with the hepatitis B virus.* In: "Progress in Medical Virology", J. L. Melnick (ed.), S. Karger, Basel, *20*, 27, 1975.

Szmuness W.: *Hepatitis B vaccine (Merck) studies co-ordinated by the Laboratory of Epidemiology, The New York Center.* In: "Proceedings of the European Symposium on Hepatitis B", S. Sherlock and S. Krugman (eds.), Rahway, Merck Sharp and Dohme International, 1981 (in press).
Szmuness W., Stevens C. E., Harley E. J.: New England Journal of Medicine, *303*, 833, 1980.
Szmuness W., Stevens C. E., Oleszko W. R., Goodman A.: Lancet, *1*, 575, 1981.
Tedder R. S.: British Journal of Hospital Medicine, *23*, 266, 1980.
Zuckermann A. J.: British Medical Journal, *284*, 686, 1982.