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DE briefing

BRITAIN

Viral hepatitis consists of at least two distinct disease entities. Although they are both virus infections of the liver which may lead to clinical 'yellow jaundice', they are caused by different viruses and have contrasting aetiologies and epidemiologies.

The first, which is now generally referred to as hepatitis A (formerly 'infectious hepatitis'), is normally transmitted by the faecal-oral route, in the same way as most of the enteric infections which cause 'food poisoning'. It has a characteristic incubation period of four weeks. It occurs most commonly in children and adolescents, within residential institutions and in conditions of poor sanitation and over-crowding. Infected shellfish can be a cause of the infection, for example in Southern Europe, and there have been water-borne outbreaks of the disease causing sudden and explosive epidemics. There is an increased incidence among travellers to high endemic areas of hepatitis A. The disease has a relatively low case fatality – probably about one in 500 – and does not lead to chronic liver damage.

Hepatitis B (formerly referred to as 'serum hepatitis'), on the other hand, is transmitted in Britain mainly by direct intradermal injection with infected blood or blood products and hence tends to occur less frequently. It usually has a longer incubation period of from six weeks to six months and occurs mainly in specific high risk groups in circumstances where adequate safeguards have been neglected. These groups include recipients of blood transfusions; patients and staff in renal dialysis units; health care personnel, especially those engaged on laboratory work; residents and staff living in institutions, especially those for the mentally handicapped; and patients who must receive frequent injections. Drug addicts also constitute a high risk group and there is a frequent incidence of infection with hepatitis B among promiscuous individuals, particularly homosexuals; this suggests that transmission may sometimes be venereal rather than as a result of penetration of the skin. In addition, menstrual blood from infected patients is a potential source of infection in institutions and in the home. Tattooing and piercing ears can in unskilled hands cause serious outbreaks of infection.

Hepatitis B has a much higher case fatality than hepatitis A, possibly as high as 5 per cent (Tolsma and Bryan, 1976). Infection may also be associated with progression to chronic liver disease, including chronic active hepatitis, cirrhosis and primary liver cancer. Hence hepatitis B presents quite different epidemiological problems from hepatitis A, and must also be regarded as a very much more potentially serious disease.

The possibility that other types of viral hepatitis may exist, apart from A and B, is discussed later under the heading of blood transfusion.

Viral hepatitis in Britain

Viral hepatitis was made a notifiable disease as 'infective jaundice' throughout England and Wales in 1968.[1] However, its epidemiology remains obscure for three reasons. First, notifications are seriously incomplete; a study in the United States has suggested that only 10 per cent of actual infections are recorded as such (Tolsma and Bryan, 1976). Second, and in part explaining that statistic, there is a very poor correlation between laboratory-confirmed cases of infection and reported cases of clinical disease. Most infections are asymptomatic or subclinical, and in the case of hepatitis B this leads to the problem of the chronic carrier state persisting in people who are unaware that they have ever contracted the infection. Third, notifications of hepatitis in Britain do not routinely differentiate between hepatitis A and hepatitis B.

Nevertheless, Table I shows that on the basis of crude numbers of notifications there appears to have been a steady and substantial decline in hepatitis in England between 1968 and 1974. Furthermore, Figure I shows that the proportion of notifications relating to children under the age of 15 dropped from about 60 per cent in 1968 to less than 40 per cent in 1975. This suggests that the decline has been mainly in hepatitis A, which would also account for the rising fatality ratio. Some observers, however, believe that the decline represents no more than a downturn in a long-term cyclical pattern of incidence

1 This was exactly forty years after it had been made the subject of compulsory notification in Denmark. However, in France, Italy and Spain, where the incidence is substantially higher than in Northern Europe, it is still not generally notifiable.

of hepatitis A, and a slight increase in notifications in 1976 as compared with those for 1975 tends to support this view (Polakoff, 1976).

The cyclical pattern in the incidence of infectious hepatitis in other countries is illustrated in Figure II. It is clear from this, however, that the characteristic length of the cycle may vary from country to country (Krejs *et al*).

There were 11,690 notifications of infective hepatitis in England in 1972. For the year 1972–73, the Epidemiological Research Laboratory of the Public Health Laboratory Service at Colindale, London, reported 681 cases of confirmed hepatitis B. This specific diagnosis was based on the identification of hepatitis B surface antigen in blood samples taken from the patients.[2] This antigen, previously called Australia antigen, acts as a marker for the presence of the virus and can be identified by a number of tests, which are discussed below in relation to blood transfusion.[3] For 1974–75, the number of confirmed cases of hepatitis B reported to Colindale had risen to 913, although total notifications had fallen to 7,407 in 1974. This increase was probably due to better reporting rather than to a real rise in the incidence of hepatitis B. Table II shows the age–sex breakdown for the reported cases, indicating a clear peak among adolescents and young adults.

However, notified and reported cases represent only a small proportion of all infections. Therefore, the best indication available of the overall prevalence of hepatitis B comes from the routine screening of new blood donors. This screening is undertaken to exclude, so far as possible, the carriers of various diseases from the panel of voluntary blood donors. The proportion of positive results for the presence of hepatitis B surface antigen in recent years implies a prevalence of between 1 in 500 and 1 in 1,000 among this apparently healthy group of the population. The rate is at the higher end of the scale in London, with its more cosmopolitan population, and at the lower end among the more stable communities for example in Scotland (Barbara *et al*, 1976; Payne *et al*, 1974). However, since voluntary blood donors are self-selected and are likely to exclude some of the high risk groups, it is probable that the overall prevalence of the antigen would be at least 1 in 500. Nevertheless, this still represents a very low prevalence compared to that in Southern Europe, where the figures may be nearer 1 in 20, or tropical Africa, where the carrier rate may be as high as 1 in 5 of the apparently healthy population.

As most of these 'carriers' of the hepatitis B surface antigen are presently unaware that they have or have had hepatitis, its significance can only arise either from the possibility of their developing chronic liver disease in the future or else from their acting as a source of infection for others. The long-term problem of chronic liver disease is still the subject of research, and the benefit from preventing the asymptomatic carrier state on these grounds is therefore still uncertain. The problem of carriers as a source of infection, on the other hand, is best discussed later in the section on specific 'at risk' groups. This follows a brief general discussion of methods of prevention and treatment.

2 Apart from the discrepancy in the exact period covered, the figure of 681 cases of hepatitis B cannot be directly related to the total reported notifications of 'infective jaundice' for two other reasons. First, not all confirmed cases of hepatitis B would be known to Colindale. Second, some of the 681 cases might for one reason or another not have been included in the original notifications.

3 A more specific measure of infectivity may depend on identification of other antigens associated with the core of the hepatitis B virus. However, the more complex tests for these antigens are not yet practicable for routine use in general laboratories.

Figure I *Registrar General's notifications infective jaundice: percentages among children and adults*

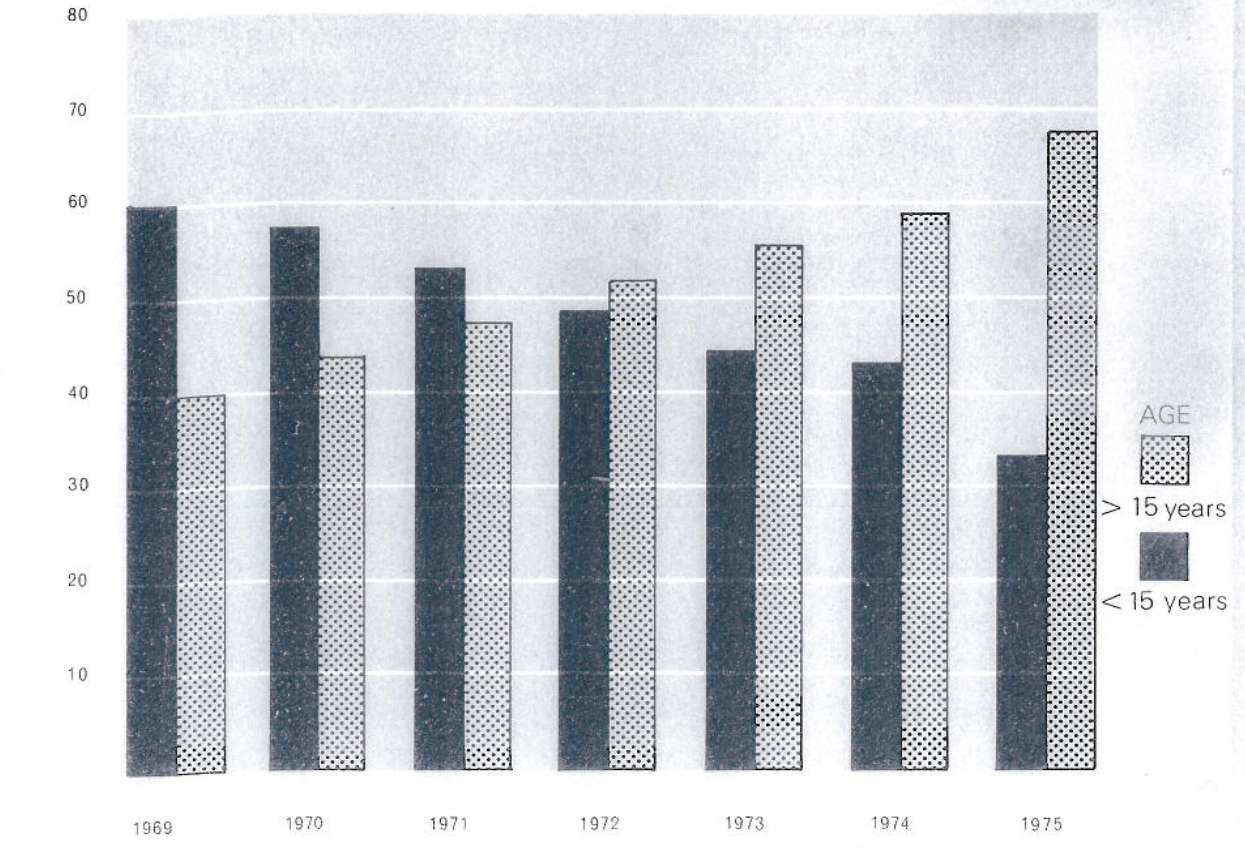


Table I *Corrected notifications of infective jaundice and deaths assigned to infectious hepatitis, England, 1969 to 1974*

Year	Corrected notifications*	Notified morbidity per 100,000 population	Deaths	Fatality ratio†	Mortality per 100,000 population
1969	21,560	47·0	188	0·9	0·41
1970	18,383	40·0	166	0·9	0·36
1971	12,621	27·4	148	1·2	0·32
1972	11,690	25·2	138	1·2	0·30
1973	7,850	17·0	121	1·5	0·25
1974	7,407	16·0	123	1·7	0·26

*Excluding original notifications from Port Health Districts.
†Deaths per 100 notifications of infective jaundice.

Source State of the Public Health, 1974, HMSO.

Note The Department of Health is probably justified in assuming that for the practical purposes of compiling this table the terms 'infective jaundice' and 'infectious hepatitis' could be regarded as synonymous.

The prevention of hepatitis A depends primarily on the same public health measures which should be used to control other diseases transmitted by the faecal-oral route. These include the provision of efficient sewage disposal systems, food hygiene, personal cleanliness and health education generally. As with several of the enteric diseases, special attention has to be paid to the role of seafood which has been reared in water contaminated with sewage.

There is no specific treatment for hepatitis A, although a measure of protection (and consequent amelioration of symptoms if infection nevertheless develops) may be gained by the injection of human immunoglobulin prepared from the general blood donor pool. Because hepatitis A is widespread, this globulin contains antibodies which will give some short-term passive immunity to infection. Its use is justified only for persons known to have been or likely to be exposed to infection, for example to protect travellers to high risk areas such as India during times of flood or other disasters.[4] There are no immediate prospects of the development of a vaccine which could confer active immunity against hepatitis A.

The prevention of hepatitis B depends on the health care policies which will be discussed in respect of specific risk groups in the next section of this paper. Once again, some limited protection can be gained by the use of hepatitis B specific human immunoglobulin. This must be prepared from donors whose blood specifically contains hepatitis B surface antibody rather than from the pool of blood donors as a whole. As with hepatitis A, this specific immunoglobulin should be used only selectively, for example in laboratory workers known to have been contaminated with infected blood or other materials. The development of vaccines which would confer active immunity against hepatitis B is still at an experimental stage, although they have already been administered to human volunteers on a very limited scale.

Recently, there has been some evidence that the use of interferon may prove to be of value in the treatment of hepatitis B carrier state, although its effects have been generally demonstrated so far to be transient (*Lancet*, 1976.) The present very high price of interferon would no doubt be reduced if large scale production were justified by the proof of its efficacy in this or other fields.

4 Some Eastern European countries routinely administer immunoglobulin to all schoolchildren, as a 'preventive' measure. There appears to be no scientific justification for this practice and it does not prevent a higher incidence of hepatitis A than is commonly recorded in Western Europe.

Hepatitis B risk groups

Renal dialysis units

During the 1960s there were a number of outbreaks of hepatitis B in renal dialysis units in Britain, some of which resulted in fatalities among the medical and nursing staff as well as the patients. These focused attention on the high risk of infection resulting from the widespread handling and use of blood and through regular access to the circulatory system of the dialysis patients. Since these outbreaks, Britain has had an outstanding record in the control of infection in these units. This has been achieved by rigorous screening for the presence of hepatitis B surface antigen in the blood used, in staff and in patients. The screening of blood is discussed in more detail below in relation to blood transfusion and the same principles apply to dialysis units. The screening of staff, however, raises special issues. It has meant the exclusion of doctors, nurses and other health care personnel from work in renal dialysis units if they were carriers of hepatitis B and this exclusion could be a potential cause of hardship.

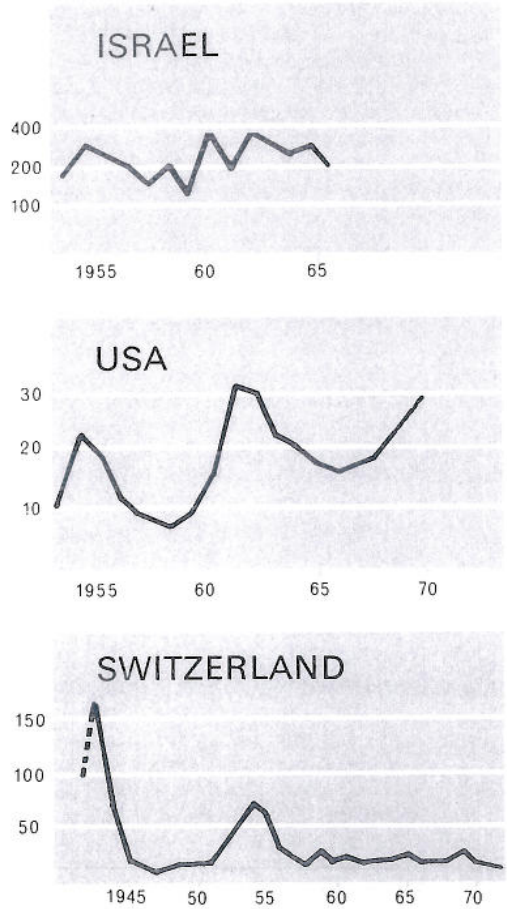
The problem in respect of potential patients who are found to be carriers is even more difficult. Units were naturally reluctant to accept them because of the risk of infection in other patients and among the staff. Nevertheless, dialysis in isolation from other patients together with rigorous sterilisation procedures and immaculate care in handling both the potentially infectious patients themselves, as well as any equipment or materials contaminated by their blood, has made it possible for

Table II *The age and sex of patients with acute hepatitis B infections confirmed by HBAg tests. July 1974 to June 1975 inclusive*

Sex	Age (years)									
	<1	1–14	15–24	25–34	35–44	45–64	≥65	Adult	Not specified	Total
Male	3	10	210	149	71	75	22	8	51	599
Female	2	6	151	59	17	22	8	1	30	296
Not stated	0	2	2	2	2	1	1	0	8	18
Total No	5	18	363	210	90	98	31	9	89	913
%	0·5	2·0	40·0	23·0	9·9	10·7	3·4	1·0	9·7	

Source Public Health Laboratory Service

Figure II *Infectious hepatitis: secular changes of incidence in Israel, USA and Switzerland*



Ordinate gives yearly incidence per 100,000 population.

Source Krejs *et al*; op cit

such patients still to be dialysed without risk to others. Perhaps for humanitarian reasons, no attempt has been made to cost the very extensive protective procedures involved. In some other countries, an alternative policy has been adopted for the dialysis of carriers of hepatitis B. They have specific 'dirty' dialysis units in which all staff and all patients are carriers. Potential dialysis patients who are found to have hepatitis B surface antigen are automatically referred to these 'dirty' units. Although this policy provides job opportunities in renal dialysis units for hepatitis carriers which do not exist in Britain, it is generally regarded as a far less satisfactory way of controlling the problem than Britain's policy of 'all-clean' units.[5]

Blood transfusion service

Blood transfusions previously represented another major risk of infection with hepatitis B. In the United States in 1970, for example, it was estimated that transfusion caused 14 cases per 1,000 units of blood transfused (Tolsma and Bryan, 1976). In a study of post-transfusion hepatitis in North London in 1969–71, although the incidence of hepatitis was smaller there was a morbidity and mortality equivalent to 27 cases of hepatitis, including 8 deaths, per 10,000 units of blood transfused in patients receiving blood only (MRC Working Party on Post-transfusion Hepatitis, 1974). In order to minimise such infections, all blood donations in Britain are now routinely screened for the presence of hepatitis B surface antigen.

There are several screening tests available, but the two which are now most routinely used are reverse passive haemagglutination and radioimmunoassay. The former is considerably less costly than the latter in terms of capital investment, materials used and technicians' time. However, radioimmunoassay is more sensitive: one study has shown that it picked up 11 per cent more positive cases than reverse passive haemagglutination. A rational policy therefore seems to be to use the more expensive and more sensitive test to screen new donors, as well as for blood to be used in dialysis units, for example, but to restrict the surveillance of donors who have previously given blood to the use of the less expensive procedure. For these established donors, it has been estimated that a switch to the more sensitive but more costly radioimmunoassay would involve an additional expenditure of about £50,000 to prevent one or two cases of post-transfusion hepatitis. Such an expenditure could not be justified on economic grounds.

In practice, the combination of the radioimmunoassay test for new donors and the reverse passive haemagglutination test for established donors has facilitated a progressive reduction in the number of cases of hepatitis B caused by blood transfusion in Britain. For example, in 1975 the North London Blood Transfusion Service received reports of only three suspected cases, from a total of more than 150,000 donations of blood.[6] This contrasted with 30 suspected cases in 1970, before routine screening of blood donations was introduced (Barbara *et al*, 1976).

At present, research is in progress into the development of an enzyme immunoassay which may provide an equally sensitive and more practical test at a lower overall cost than radioimmunoassay. This could make it economically feasible to attain even higher standards than at present in the avoidance of hepatitis B in patients receiving blood transfusions.

Nevertheless, the problem of post-transfusion hepatitis may still persist, because at least in the United States other as yet unidentified viruses apart from those associated with hepatitis A and B appear to be responsible for a large proportion of such infections (Tolsma and Bryan, 1976).

Health care personnel

All health care personnel are at risk of infection with hepatitis B because they may come into contact with blood or blood products. This may occur, for example, during surgery, while giving injections, during pathology and through dentistry. Some of this blood will be from carriers, unless these have been specifically excluded by screening.

Some hospitals do routinely screen at least all surgical and maternity patients before admission, and apply special precautions in the care of carriers. These can include treatment in isolation wards, 'barrier nursing' and the labelling of all pathology specimens as 'biohazards'. Such a screening policy has three disadvantages. First, the screening itself and, more particularly, the special nursing care given to positive cases is exceedingly costly. Second, screening may lead to a false sense of security in respect of the infective risks in handling 'negative' patients. Third, it gives the patient a sense of being labelled as a sort of 'leper' which may have profoundly disturbing effects even long after discharge from hospital.

Hence it is argued that it is better not to identify carriers (except in obvious risk groups such as drug addicts) but to ensure that proper care and precautions are taken in handling every patient and all blood and other specimens collected from them. Hospital staff should be trained to report any incident where they may have risked infection, for example, from an accidental scratch before or while handling blood. The blood concerned can then be tested for antigen and specific

5. Apart from other considerations, the establishment of specific 'dirty' dialysis units might result in less sense of urgency in avoiding infection in other 'clean' units, which would then be able to pass their 'failures' on to the 'dirty' units.

6. The number of donations is, of course, for various reasons substantially higher than the actual number of units of blood transfused. On the other hand, one donation used to produce other blood products may eventually go to many more than one recipient.

hepatitis B human immunoglobulin administered in the unlikely event of its proving positive. This policy is probably more efficient and certainly more economical than routine screening of patients. There is evidence, for example, from a study in Sweden that laboratory technicians who should be at especially high risk of infection from hepatitis B in fact suffer a lower incidence of cases than other hospital staff, presumably because they are more conscious of the risk and therefore take greater precautions (Ringertz, 1976).

Theoretically, hepatitis B carriers among health care personnel could represent an infectious risk to patients under their care. However, there is little evidence that this presents a practical problem and WHO has concluded that 'they do not routinely present a hazard, provided they take special precautions in their professional activities' (WHO, 1975). It is even possible that a policy of excluding carriers from health care work would do more harm than good, because it might lead to concealment of the carrier state rather than a frank admission that it existed and that proper precautions must therefore be applied.

Residential institutions

Residents in institutions, especially those for the mentally handicapped, have a higher risk of infection than the population as a whole. Staff working in such institutions, including particularly dentists, are also at risk of infection, and for such employees hepatitis is now classified as an industrial disease, as it is for all hospital and laboratory staff. However, until active vaccination becomes possible, there is no effective way to prevent the risk of infection, although it can be reduced if equipment for proper sterilisation of dental instruments, for example, is provided.

Travellers to high endemic areas

Britons who visit areas such as Africa and India where there is a high prevalence of hepatitis B are at some risk of infection. In these areas, the disease need not be contracted by direct contamination with blood, but may be transmitted, for example, by mosquitos. Nevertheless, hepatitis A remains a much commoner health hazard than hepatitis B for travellers to these areas.

Residents in Britain who have lived abroad in high endemic areas should also be considered high risk groups for hepatitis B.

Drug addiction and sexual promiscuity

Repeated self-injection using non-sterile syringes represents an obvious source of infection among drug addicts, and screening for hepatitis B is often therefore routine in addicts seeking treatment. Screening for hepatitis B is also now a routine in some venereal disease clinics, although the identification of infectious carriers in such circumstances may in practice do little to control the spread of infection.

Hepatitis A is an infectious disease spread by the faecal-oral route, whose natural history and epidemiology follows a more or less conventional pattern. It is probable that many people contract the infection without developing recognisable symptoms and that the adult population in Britain may therefore have a fairly high degree of acquired immunity to re-infection.[7] Although it is much commoner than the number of notifications would suggest, it does not represent a major or an exceptional health hazard in Britain.

The aetiology and epidemiology of hepatitis B, on the other hand, is exceptional. It has been specifically identified as a major health hazard for certain high risk groups only since the discovery of its 'marker' antigen about a decade ago. Thus the problems of its control have only recently come to attract particular attention and they are now the subject of growing debate.

The special risks associated with renal dialysis units and with blood transfusion have to a great extent been brought under control in Britain and this country has an outstanding record in this respect when it is compared, for example, with experience on the continent of Europe or in the United States.

Outside these two special situations, it is important not to exaggerate the risks of infection, which have only become quantifiable in the last few years. It is now technically possible to screen for carriers, and the temptation is therefore to do this. However, the only practical way to use the results of such 'case finding' would be to reduce the chance of carriers spreading infection by restricting their activities. Present epidemiological evidence does not justify such a policy, and routine screening is therefore irrational.

On the other hand, hepatitis B is much more widespread outside Britain. Thus there are at least theoretical reasons for maintaining surveillance, for example on immigrants, to ensure that the prevalence in Britain remains at its present low level. However, even within Britain now hepatitis B may be responsible for a very much larger proportion of chronic liver disease than is generally recognised, and it may eventually prove to be more significant than alcohol abuse in this respect. Thus it may be economically as well as scientifically important to tackle the control of hepatitis B in order to reduce the consequent burden of chronic illhealth in later life. If this proves to be the case, three lines of research would need to be pursued urgently. First, work needs to be done to establish more precise and more economical tests to identify the presence of the disease. These would include the enzyme immunoassay for the surface antigen which is at present being developed. In addition the significance of other 'marker' antigens needs to be investigated further because these may give a clearer measure of the infectivity of individual carriers; if so, low cost tests for the identification of these other antigens will need to be developed. Second, a vaccine needs to be made available to give active immunisation against hepatitis B for high risk groups. This requires the stimulation and extension of existing research programmes. Finally, if ultimate elimination of the disease is to be achieved, some effective way must be found to deal with the carrier state.

Enormous progress has already been made since the identification ten years ago of the surface antigen which subsequently proved to be a 'marker' for the hepatitis B virus. The problems have been clearly analysed by those working in the field and are being systematically tackled. Despite the potentially emotive connotations of 'yellow jaundice' in general and the significant risk of death associated with hepatitis B in particular, rational policies seem to have been adopted both in respect of the current control of the disease and in the evaluation of scientific and economic strategies for the future.

7 This was, of course, always the case with other infectious diseases such as poliomyelitis or tuberculosis.

Barbara J A J, Howell D R, Cleghorn T E, Cameron C H, Briggs M, Dane D S, (1976). A comparison of different methods of screening blood donations for HB_SAg. *Vox Sanguinis*. In press.

Krejs G J, Glassner M, Blum A L, (1974). Epidemiology of Infectious Hepatitis. Clinics in Gastroenterology, 3, 3, 277.

Lancet, (1976). Interferon Therapy in Chronic Hepatitis B. ii, 1122.

MRC Working Party on Post Transfusion Hepatitis, (1974). Post-transfusion Hepatitis, (1974). Post-transfusion hepatitis in a London Hospital; result of a two-year study. *Journal of Hygiene* (Camb), 73, 173.

Payne R W, Barr A, Wallace J, (1974). Hepatitis B antigen (HBAg) and its antibody (HBAb) in hospital patients. *Journal of Clinical Pathology*, 27, 125.

Polakoff S, (1976). Private communication.

Ringertz O, (1976). Data presented to a WHO Meeting on Economic Aspects of Viral Hepatitis, Copenhagen, 9–11 November.

Tolsma D D, Bryan J A, (1976). The Economic Impact of Viral Hepatitis in the United States. Public Health Reports, 91, 4, 349.

WHO, (1975). Viral Hepatitis. Technical Report Series No 570.

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