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HCV SCREENING

The attached draft submission reflects the advice of the Advisory Committee on the Virological Safety of Blood that the UK should introduce the anti HCV screening of blood donations as soon as practicable.

In view of the urgency in putting this to Ministers, I would be grateful for comments by close 18 December.

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POLICY-IN-CONFIDENCE

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HEPATITIS C ANTIBODY SCREENING TEST:
ADVISORY COMMITTEE ON THE VIROLOGICAL SAFETY OF BLOOD (ACVSB)

1 PS(L) was informed on 7 August of the intention to commence a pilot study to evaluate the two available screening tests (Ortho and Abbott) for the hepatitis C virus (HCV). This followed the advice of the ACVSB at its July meeting that the UK should introduce routine HCV screening of plasma and whole blood once the results of the pilot study were known.

2 In light of the results of the pilot study the ACVSB has unanimously recommended the introduction of routine screening as soon as practicable. This note sets out the case for the introduction of routine screening, the financial implications and the results of an economic appraisal. We are seeking Minister's approval to commence screening in the NBTS as a public health measure in line with the ACVSB's advice.

3 The other UK Health Ministers are also being asked to approve the introduction of routine testing in their transfusion services.

Background

4 HCV is considered to be the main, though not the only, cause of Non A Non B hepatitis (NANBH), which has become the most common form of post transfusion hepatitis. The disease may run a symptomless course, but in some cases it can result in chronic liver damage which may ultimately be fatal. For further details about the disease, see annex A.

5 Since the middle of 1989 an Initial Screening Test (ELISA test) has been marketed which can identify supposed carriers of HCV. However, there were problems with this ELISA test as it produced many false positives and at that time there were no means of confirming whether positive cases were infective.

6 Routine testing for HCV antibodies in all donated blood has been introduced recently in USA, Australia, Japan, France, Italy (testing on a voluntary basis), Belgium, Spain, Luxembourg, Finland, Norway, Sweden and Denmark. Many other countries are considering this move. Eire is waiting to follow action in the UK.

ACVSB Recommendations

7 The ACVSB has always taken the view that effective screening for HCV would be a useful public health measure. It would

further increase the safety of the blood supply and reduce the incidence of post transfusion NANB hepatitis and the spread of HCV in the community at large. However the Committee recognised there were deficiencies in the available ELISA screening tests from Ortho and Abbott.

8 At its meeting in July 1990 the ACVSB recommended in principle that screening should be introduced in light of recent developments in testing. However they recommended that a pilot trial should be carried out as a first step to determine if either of the two ELISA screening tests were preferable for use on the UK donor population. This trial would also provide experience of using the newly developed supplementary and confirmatory tests.

Results of Pilot Trial

9 The results of the trial were considered by the ACVSB on 21 November. The trial showed that both screening tests were satisfactory for routine use in the Regional Transfusion Centres although far less specific than established tests for other infections. The trial also underlined the importance of having supplementary tests to help determine which donors were truly positive. Details of the results are given in Annex A. In light of the results, the Committee were unanimous in recommending that we should follow the action of other nations and routine screening should be introduced as soon as practicable.

10 The Committee also recommended that the choice of screening test be left to the Regional Transfusion Centres. Samples which are repeatedly positive by a single screening test would be referred for supplementary testing to an expert centre. The donors of samples found to be positive after supplementary testing would be assumed to be carriers of infection and would be excluded from giving blood and would be counselled on the need to consult a specialist/gastroenterologist for further advice and testing. On the basis of the results of the pilot study, we would expect approximately 14,000 donations in England to be referred for supplementary testing in the first year of which perhaps 1,200 would be found positive. In the subsequent years the probability is that the number of screen positives and true positives will fall. Cost-benefit in future years could be higher or lower: costs will reduce but so will benefits as the proportion of positives in the donor population reduces.

Financial Implications of Screening

11 The ACVSB in giving their advice were concerned about public health, although clearly influenced by the threat of litigation. The economics and cost-benefit of testing are considered in annex B. The screening of blood donations using the three tests, ELISA plus two supplementary tests RIBA and PCR, would cost an estimated £5.73 million in the first year. This figure includes the cost of the test, the extra staff at the Transfusion Centres, counselling and follow-up of donors and cost of replacement of lost donors. The cost of specific treatment of positive donors, if it were to become available, would be in addition to this sum. The cost cannot be readily quantified since specific treatment is

still only at a research stage. With the expected rapid development of tests for HCV antibodies, and increased competition, reagent costs may fall as well as the need for supplementary tests. So costs in subsequent years should be less than in the first year.

Value for Money

12 Annex B attempts to summarise an economic appraisal of the possible introduction of this test. Given the paucity of information available on which to base an assessment, the conclusion about benefits must be uncertain. However based on reasonable assumptions of costs but perhaps optimistic assumptions about benefits the appraisal concludes that some form of screening programme could be cost beneficial with the cost per life-year saved in the order of £6,000. This represents questionable value for money. Moreover HCV is not unique in these respects in the health care field and financial criteria are not the only ones for deciding on public health measures.

Funding

13 No special provision has been made for HCV testing in the HCHS budget. The cost to RTCs would therefore have to be found from the general allocation. Since RTCs will be moving away from direct funding by Regions from 1 April 1991, the cost of screening would have to be reflected in higher handling charges to hospitals for blood supplies. The PHLS who would carry out the supplementary tests too would have to find the cost of some

£1-£1.5 million by charging RTCs for the service. This too would be reflected in the blood handling charges. In total the screening would add nearly £6 million to the RTCs revenue operating costs of approximately £70m pa.

Options for Reducing Costs

14 Consideration has been given as to whether costs of testing can be reduced:

a) selective testing of high risk groups is not possible; those recognised to be high risk are already excluded (eg drug misusers)

b) less frequent (eg annual) testing of donors would save on reagent costs, but add to the complexity of procedures at RTCs so increasing labour costs, increasing the chance of errors. Dual testing regimes might prove impracticable for RTCs. Since new infections could arise that might have been detected by the screening of every donation, the risk of litigation would be high.

c) restricted use of supplementary testing is a likely development in any case, with the routine use of the RIBA test but not PCR, for example, for samples repeat positive with both ELISAs. New screening tests currently under development are likely to be more specific resulting in fewer false positives that require expensive supplementary testing.

Case for Screening

15 The main arguments in favour of screening are:

- it is a public health measure which would reduce the incidence of post transfusion hepatitis and the spread of HCV in the community at large;

- it reduces the risk of litigation from those who develop hepatitis or cirrhosis as the result of a transfusion when screening tests are available;

- if treatments which are currently experimental prove to have value, it could be in the interests of the donors to discover they carry HCV infection;

- any delay is likely to be shortlived as the EC is developing common licensing requirements for blood products. Other EC countries have introduced anti-HCV screening and it may well become a requirement that the source material for blood products should be tested for HCV antibody.

Case Against

16 - The screening tests are far from perfect and even when used in conjunction with supplementary tests it is not certain that positive cases are truly infective. Even

if a patient receives infected blood he would not necessarily become infected nor develop clinical symptoms.

- Healthy donors who test positive will be converted into patients. Counselling these donors will present difficulties in view of the uncertainty whether the donor will ever suffer adverse effects. Nevertheless a positive finding is likely to induce anxiety in the donor and perhaps compromise his or her insurability.

- The outlay on screening will add to the general pressures on HA funds and mean that the newly introduced handling charges for blood will be higher than they otherwise would be. Budgets already devolved to users of blood on the basis of last year's costs will have to be topped up if supplies to patients are to be maintained.

Timing of Introduction

17 There are some operational matters that need to be finalised before routine screening can be introduced. The RTCs will need to consider how quickly they could recruit extra staff and obtain the necessary equipment to support the screening programme. The NBTS will also need to consider arrangements for counselling and referring on positive donors. There would also need to be discussions with PHLS about where within their network the supplementary testing should be carried out. The charging arrangements to recover costs would also have to be discussed

with the NBTS and PHLS. The Transfusion Services in the UK would also wish to co-ordinate preparations to introduce screening at the same time. In practice it is unlikely that routine screening could be introduced before 1 April 1991.

Conclusions

18 In view of the ACVSB's firm recommendation that routine screening should be introduced as a public health measure, the possible risk of litigation and the fact that other countries are routinely testing blood donations for the virus antibodies, any further delay in the introduction of HCV testing in the UK would be difficult to defend.

19 We therefore recommend the introduction of routine screening for HCV antibodies. We ask if PS(L) is content that screening should be introduced and that preparations should be made to introduce it as soon as practicable.

ANNEX A

HEPATITIS C VIRUS (HCV) AND BLOOD TRANSFUSION

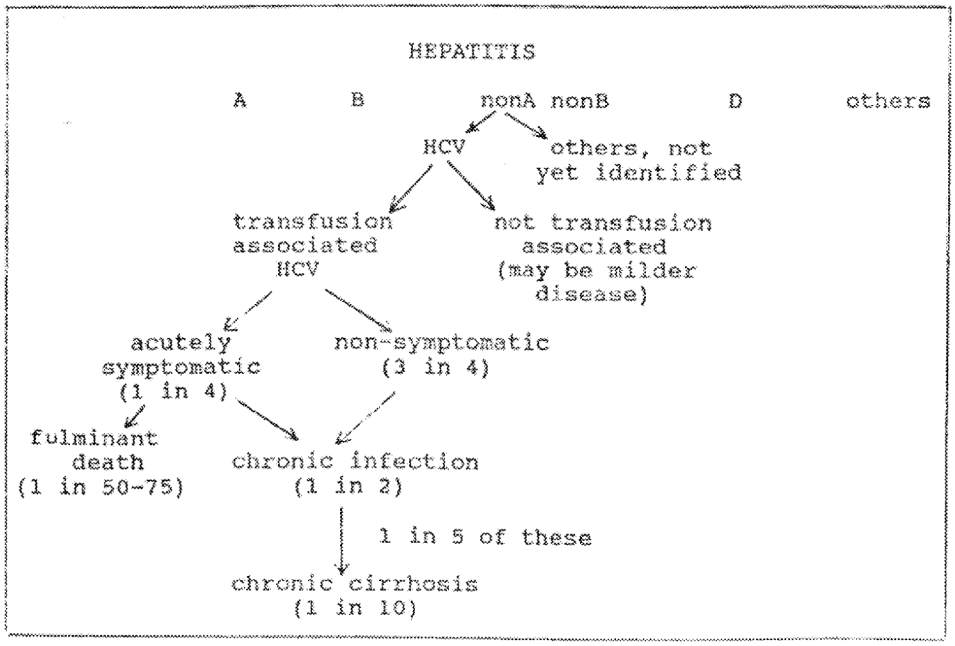
1. Viral hepatitis

Hepatitis is inflammation of the liver. This can give an acute illness, usually with jaundice, and lead on to chronic disease including cirrhosis. There are at least 5 types of viral hepatitis including hepatitis A "infectious hepatitis" which is spread by the faeco-oral route, and the important forms spread parenterally including by blood transfusion, hepatitis B and that called non A non B hepatitis (NANBH). Now hepatitis B carriers can be detected by screening and excluded, NANBH is the most common infection transmitted in blood transfusion.

Until last year there was no way of detecting who was carrying HCV infection, but some transfusion services attempted to exclude higher risk donors with surrogate tests, including for ALT, a marker for early liver damage. But in the UK this was not thought worthwhile.

2. Non A non B hepatitis (NANBH)

We now believe most people who have NANBH do not have jaundice in the acute illness, and so the disease is often unrecognised. Hence it is difficult to estimate the burden from this disease, its mortality and its frequency as a cause of chronic liver disease. In the last year since the availability of a test for Hepatitis C (HCV), thought to be the most common but not only cause of NANBH, there have been many studies on HCV epidemiology, most incomplete or as yet unpublished. In the USA only 5% of NANBH is known to be transfusion related [equivalent figure for UK not known].



3. NANBH and Blood Products

Most haemophiliacs who received unheated blood product (factor VIII) had NANBH. But it appears current heat treatment has been effective at destroying HCV and other NANB infections. Nevertheless, there are pressures to increase further the security of plasma being fractionated, and some authorities (but not the CSM) have been insisting on surrogate (ALT) tested plasma. These authorities might be expected to insist on HCV-tested plasma also, although there is scientific debate whether that is necessarily desirable on theoretical grounds [The test is for antibodies, which might be helpful in mopping up undetectable virus]. The FDA have delayed a decision on HCV testing of plasma, and the EC have yet to decide.

4. The available tests for HCV

HCV has not been isolated, properly identified or grown in culture. Part of the genome of HCV has been cloned and used to develop tests for antibody that reacts with this. The first tests were marketed only last year, and have already been superseded. At first there was no way of determining the significance of a "positive" result. But with current tests used in sequence a high proportion of those carrying HCV infection can be correctly identified.

a ELISA (enzyme-linked immunosorbent assay)

two tests now available, marked by Ortho and Abbott, more being developed
used in NBTS trial (see below)
crude screening test, high false positive rate at present
unit cost £2.50

b RIBA (recombinant immunoblot assay) or neutralisation assay

more specific test for the same antibodies
not yet marketed
for specialist use in a few centres only
unit cost £25

c PCR (polymerase chain reaction)

confirmatory test, detecting HCV sequences
highly specific, if used correctly
highly complex, for use in expert centres only
unit cost £100

5. NBTS trial

10633 regular blood donations were screened in Glasgow, Northern and N London RTCs with both Abbott and Ortho ELISA's. Those samples that repeated positive with any test were subjected to RIBA and PCR analysis. Of the 10633, ~~17~~ 18 were

positive with Abbott ELISA, ~~21~~ 25 with Ortho and ~~26~~ 25 with both (=~~69~~ 68). Preliminary results are that only 6 of these, which had tested positive with both ELISAs, were positive with RIBA and these were the only ones positive with PCR. Other work has suggested that PCR-positive blood is that which can transmit disease.

6. Practicalities of testing

The NBTS are concerned about how to deal with donors that screen positive. The trial results provide a possible schedule that might be practicable. Each RTC would use the ELISA test that fits in best with their other tests and equipment. If in their hands a sample is repeatedly positive, the donation is held back and the sample referred to a specialist centre. There might be 60 to 70 such referrals each day in England and Wales. If this also tests positive with the other ELISA, it is subjected to RIBA (and until the significance of these tests is more certain, PCR also). The RTC is informed. The "false positives" are allowed to continue to donate and blood that subsequently screens negative is used, and any that tests "positive" withheld. Donors with "true positive" samples are referred to a physician for counselling and if appropriate, treatment.

ANNEX B

SCREENING BLOOD DONATIONS AGAINST HEPATITIS C: ECONOMIC APPRAISAL

1. The EAO have attempted an economic appraisal of routine testing of blood donations for HCV antibodies, but were greatly handicapped by incomplete information on the current burden of transfusion-associated NANB and its costs. This summarises their analysis, updates it with results from the pilot survey and points out the main areas where information is deficient. The main conclusion is that the benefits for the estimated £5-6m first year cost is uncertain, but could be in the order of £6000 per QALY for the lives saved.

2. Costs

The cost of testing includes the direct costs for the RTC for procuring and administering the test; the cost for the RTC in recruiting replacement donors for those who are true positives; and counselling, diagnosis and treatment costs for the true positive donors, half of whom might be expected to receive liver biopsies.

The use of ELISA, RIBA or PCR alone or in various combinations was subject to economic analysis. The two realistic options were the cheapest. These are:

(1) ELISA screen and RIBA on all positives

(2) ELISA screen, RIBA on all positives, PCR on those positives.

For the 2 million annual donations in England these come to:

(1) £5.55m

(2) £5.73m

[The ACVSB recognises that once further experience and use of PCR has established the true significance of a positive RIBA test, dual not triple testing should become the standard practice]

Additional costs not brought into the formal economic appraisal include:

a additional treatment costs for the infected donors, which if the currently experimental interferon at an annual cost of £2-3000 becomes established as orthodox therapy for HCV carriers, could be very substantial indeed.

b indirect costs from turning these donors into patients.

3. Benefits

Difficulties here arise from ignorance of the natural history of recipients of HCV positive donations. If the pilot results are typical, and 6 in 10,000 donations will be truly positive this could give 1200 positive donations annually in England into (estimated) 2000 different recipients since fractions from each donation could go into more than one recipient. But many transfusion recipients have fatal illnesses and half the units are expected to go to patients who will die from other causes within a year. Some of the remaining recipients will be immune or not become infected. But for the analysis 520 of the original 2000 recipients a year were assumed to be affected by hepatitis, 20 acutely, the rest chronically including 100 with cirrhosis.

On the (probably false) assumption that these patients otherwise would have had a normal life expectancy and assuming that the cirrhotics all die with the average life expectation for chronic hepatitis; that hepatitis treatment costs are at current NHS levels (poor estimates available only, possible use of interferon excluded), and time off work is as for other chronic liver disease, that the non-cirrhotics have no significant loss of quality of life: the estimate is about £6000 per QALY based only on the lives saved. This is likely to be an over estimate of the benefit of screening, principally because the life expectancy of transfusion recipients is less than normal, even allowing for those who die in the first year.

Additional benefits not brought in quantified terms into this formal appraisal include:

a reduction in risk of litigation. It would be very difficult to mount a defence if it were known expert advice had been disregarded. Whilst the settlement costs are supposed to reflect costs of morbidity and premature death and hence would be covered above, there could be punitive costs and (substantial) legal costs as well.

b reduction in the pool of HCV infection in the community and subsequent reduction in chronic liver disease.

c additional benefit from the identification and early treatment of infected donors. It is hoped this would more than balance out the additional costs, but could well not.

d reduced anxiety in regular transfusion recipients with removal of the threat of HCV infection.

e the continued provision by CBLA of plasma products in the UK, and possible sale of any surplus overseas, if/when HCV testing becomes a EC or CSM requirement.

f no longer risk that purchasers who consider HCV screened blood to be safer would take blood from RTCs who make unilateral decisions to screen or even from overseas