POLICY-IN-CONFIDENCE

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

Problem

1 Screening tests for the antibody to hepatitis C virus (HCV) have now been developed. The issue is whether routine screening should be introduced in the National Blood Transfusion Service (NBTS). The expert Advisory Committee on the Virological Safety of Blood (ACVSB) has unanimously recommended the introduction of screening as soon as possible. There would, however, be considerable cost consequences for the NHS.

Recommendation

2 It is recommended that screening should be introduced as a public health measure. The other UK Health Ministers are also being asked to approve the introduction of screening in their transfusion services.

BACKGROUND AND ARGUMENT

Background

3 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.

4 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.

5 Routine testing for HCV antibodies in all donated blood has been introduced recently in a number of countries including USA, Japan, France, and the Scandinavian countries and many others are considering this move. Eire is waiting to follow action in the UK.

ACVSB Recommendations

6 At its meeting in July 1990 the ACVSB reached the conclusion in light of recent developments in testing that HCV screening could prevent a significant proportion of post transfusion hepatitis cases. However they recommended a pilot trial as a first step to determine if either of the two available ELISA screening tests were preferable for use on the UK donors and also to provide experience of using the newly developed supplementary and confirmatory tests.

7 The trial showed that both tests were satisfactory for use by the NBTS and that the choice could be left to individual Regional Transfusion Centres. It 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.

8 In light of the results the Committee took the view that with the existence of the current test procedures, to continue a policy of not screening poses an unacceptable risk to the recipients of blood. The Committee recognised that detailed cost benefits of HCV screening could not be quantified. Nevertheless their unanimous conclusion was that the UK should follow the lead of an increasingly long list of countries who have introduced HCV screening in order to significantly reduce the load of non A-non B post transfusion hepatitis. They firmly recommended the introduction of screening as soon as practicable.

Financial Implications of Screening

9 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. The cost of specific treatment of positive donors, would be in addition to this sum, but such treatment is still only at the 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

10 Annex B summarises an economic appraisal of anti HCV screening. 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 points to a cost per life-year of the order of £6,000, not

particularly good value for money in view of the optimistic assumptions. However it is possible to find other fairly common interventions whose performance is not as good. Standard yardsticks are not the whole story and in some cases there may be other arguments for adoption which weigh more heavily.

Funding

11 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 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. Details of the options considered for reducing costs are set out in Annex C together with the reasons for rejecting them.

Case for Screening

12 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 short-lived 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

13 - 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.

Management Executive view

14 The introduction of HCV will significantly increase the costs which the Regional Transfusion Centres will need to pass on to hospitals as handling charges for blood. Hospitals will have budgeted so far on the basis of the RTCs' existing costs and these Budgets will need to be topped-up if hospitals are to obtain blood at the higher cost. In view of the competing demands for extra resources the Health Authorities may question the need to impose the new screening requirement at present when the tests are as yet imperfect. Before announcing the new screening policy it will be necessary to explain the background and discuss the charging implications with RTCs, the PHLS and the user interests so that we can carry them with us.

Timing of Introduction

15 In view of the operational matters that need to be discussed and finalised, it is unlikely that routine screening could be introduced before 1 April 1991.

Conclusions

16 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.

17 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.

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ANNEX A

HEPATITIS C VIRUS (HCV) AND BLOOD TRANSFUSION

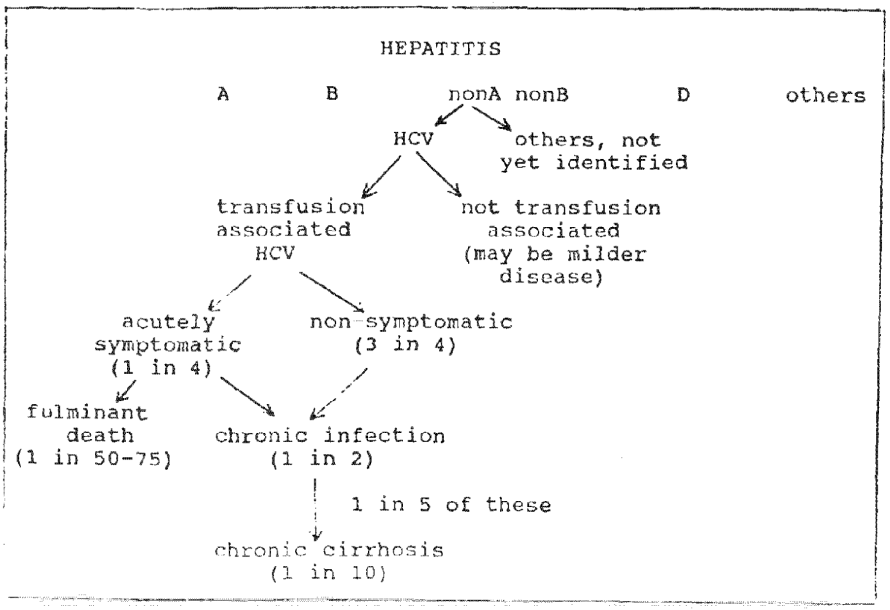
1. Viral hepatitis

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, 18 were

positive with Abbott ELISA, 25 with Ortho and 25 with both (=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. With the assistance of the Economic Advisers' office we 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 the 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

Annex C

Options for Reducing Costs

Consideration has been given as to whether costs of testing can be reduced in the following ways:-

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.