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A PRELIMINARY POSITION PAPER

Meeting to Consider the Merits of an HCV "Look-Back" Policy

Friday, 5th August 1994: West Midlands BTS Centre

OBJECTIVE:

An ad-hoc assembly of experts was convened on behalf of the Standing Advisory Committee on Transfusion-Transmitted Infection (SACTTI) to discuss the desirability and feasibility of introducing a "look back" policy to identify, test, counsel and, if necessary, refer surviving past recipients of blood components from donors later found to be anti-HCV seropositive, after September 1991, when screening was introduced in the U.K.

THOSE PRESENT:

Dr. F. A. Ala (Chair) Birmingham RTC
Dr. J. Barbara (North London BTS)
Professor J. Cash (Scottish NBTS)
Dr. J. Gillon (Scottish NBTS)
Dr. P. Hewitt (North London BTS)
Dr. V. Martlew (Mersey BTS)
Dr. D. Mutimer (Liver Unit, Queen Elizabeth Hospital, Birmingham)
Dr. A. Robinson (National Medical Director, NBA)
Professor R. Tedder (University College Hospital London, Virology Department)
Dr. L. Williamson (East Anglian BTS)

Apologies were received from:

Dr. P. Flanagan
Dr. E. Elias

DISCUSSION:

1. WHAT DATA IS CURRENTLY AVAILABLE?

A pre-publication copy of a paper from Edinburgh and SE SCotland BTS by Ayob et alia (1994), entitled "Risk of Hepatitis C in Patients Who Received Blood from Donors Subsequent shown to be Carriers of Hepatitis C Virus" was circulated to initiate the discussion.

It was noted that, of 42,700 blood donors from the first 6 months of testing, 20 were confirmed HCV seropositive by RIBA and PCR. Fifteen of these were established donors, all of whom had risk factors.

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Some 83 components were prepared from 63 anti-HCV positive previous donations of these blood donors, although only 58% of the components were actually transfused. Thirty-nine recipients were identified, but only 9 were ultimately traceable and alive.

All of these individuals were anti-HCV positive. Of 39 recipients identified, 69% had died (none survived beyond 5 years after transfusion), and 8% were not found. It was estimated that there were approximately 1.2 recipients for each individual donation.

A review of this data raised the following comments:

- The proportion of untransfused components was atypically high in this particular study.

- The proportion of recipient deaths was higher than the figure of 50%, usually cited in the literature.

- Infectivity of implicated donors was very high (even greater than reported by CLB Amsterdam (94%), and Linköping (76%) at ISBT, 1994.

- The mean age of recipients was not reported, but most survivors were said to be in their 50s.

  Comment: Although *most* blood recipients may be middle-aged or old, a very substantial proportion are children or young adults (NLBTS data).

- Infected recipients were asymptomatic, with a normal ALT, although one had progressive liver disease, currently under interferon treatment.

  Comment: Even though earlier data from several Centres (including Birmingham) suggested that HCV causes mild liver disease, further follow-up now indicates a more aggressive, progressive evolution (Mutimer, 2nd biopsy results, & Tedder).

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In addition, HCV liver disease appears to be more aggressive in old age, irrespective of the duration of infection, in post-transfusion cases compared with IVDU, and in the immuno-deficient. Absence of symptoms and normal ALT are a poor index of liver pathology.

2. WHAT IS THE EFFICACY OF TREATMENT IN THE LONG-TERM?

There is growing evidence that this is not a trivial virus, and that a significant proportion of patients benefit from receiving therapy.

The views of specialists are heterogeneous, and insufficient time has elapsed to give a confident judgement regarding the long-term benefits of therapy with recombinant Interferon-alpha, either alone, or in combination with a nucleoside analogue such as ribavirin. Hepatologists are increasingly prepared to take a pragmatic view of treatment in the individual case, however.

The evidence so far is that:

- Treatment offered as early as possible after diagnosis is likely to be most effective. The objective is to provide damage limitation within the bounds of possibility.

- The severity of liver pathology must be assessed and where there are signs of progression to moderate or severe disease, a trial of therapy with 3 million units of rIF-alpha, 3 x weekly (adjusted for bodyweight) is worthwhile for a period of 6-12 months. A 3-month re-assessment and regular monitoring will demonstrate the degree of responsiveness and determine the value of persisting with treatment.

  Patients with established cirrhosis and/or portal hypertension will not benefit, and should not be offered specific treatment.

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The relevance of HCV sub-type to disease aggression and patient responsiveness is of considerable interest, but it is still largely academic at the moment.

The combination of ribavirin and rIF-alpha may prove to give a better, more sustained response, and there is evidence that "native" IF may be more effective than rIF (Tedder).

The toxicity of therapy is low, although depression and exacerbation of auto-immune disorders may occur, and costs are no more than some £1,500 to £2,000 per patient for a 6-month course of IF.

It is still not known whether therapy, given for an adequate period and at optimal dose, will affect the longer-term natural history of the disease, and prevent relapse after treatment is discontinued.

3. Consideration of other potential competing demands on BTS or NHS systems expenditure (such as the introduction of anti-HBc testing for "tail-end" HBV carriers; HTLV-I, -II screening; screening for bacterial infection of blood components; sterilisation or quarantine of clinical FFP, etc.) was brief, as it was felt that each of these deserved individual evaluation in their own right.

4. It was generally acknowledged that we, in the Blood Transfusion Service, do have an ethical responsibility and "duty of care" towards recipients of potentially infectious blood components such that they deserve to be identified, counselled, tested and offered treatment where that is appropriate. It was felt that, despite the current uncertainties regarding long-term efficacy of treatment, and its impact upon the natural history of hepatitis C, we have a moral obligation to inform and advise surviving potentially infected blood recipients.

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5. The policies of other countries, in this context, were briefly reviewed. It was noted that, although The Netherlands, Australia and New Zealand have adopted an HCV "Look-Back" policy, the transfusion services in the USA (notably, the American Red Cross) are resisting FDA pressure to initiate it, on the grounds that it would not be efficient or cost-effective. Germany has adopted a compromise position which will only address recipients of potentially infectious blood from 1993 onwards, and France has decided to screen all blood recipients for viral markers, six months after transfusion, because their record-keeping is either unreliable or non-existent.

THE OPTIONS FOR UKBTS ARE TO:

i) Confine itself to the role of an information "clearing house", providing hospitals with the identity of implicated blood components, leaving it to them and General Practitioners, to follow-up potential recipients.

It was felt that this policy would not be effective in practice, or

ii) Trace implicated recipients through hospitals and GPs, interview and counsel surviving recipients; obtain and test a sample of blood from them; refer infected patients for specialist counselling, investigation and possible treatment by Hepatology Centres.

The latter option was generally favoured (although it was not clear how the added costs of the specialist reference centres would be defrayed). Further discussion took place as to how far back recipients should be traced. Since few, if any, recipients were likely to be traceable and alive more than 5 years after transfusion, and since sufficient archive samples were unlikely to be available to permit the identification of a sero-conversion date (most anti-HCV positive donors were probably infected in the 1970's), a retrospective analysis carried out as far back as possible, would be the most reasonable policy to adopt.

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A very approximate calculation of the probable case-load in the West Midlands might involve:

About 100 confirmed anti-HCV positive donors

85 established donors (15% new)

Assuming 2 components transfused per donation = 170

Taking 5 years at 1 donation per year = 850 donations, over 5 years.

Assuming 80% of components transfused = 680 recipients over the 5 years.

If 50% died = 340 living recipients,

And 17% not traced = 282 surviving, traceable blood recipients.

or 300 ± 20

It is likely that the overall case-load will be approximately 3,000 for England and Wales alone.

(Sero-conversions among established donors have not been included in the calculation, nor have previously regular donors who have lapsed and have only just been found to be seropositive upon their return!

In Sum: The Meeting felt that there is a serious case for considering the implcations of a "HCV Look-Back" Policy in its operational detail, and wished to refer the topic to the MSBT with a recommendation that such a policy is implemented.

FAA/MP
9.8.94