IN CONFIDENCE

Suggested 'agenda' for discussion on AIDS in relation to licensed blood products. CSM(B) July 13, 1983.

Notes:

(1) The aim of the discussion is to help the sub-committee to formulate advice to the CSM on whether any action is needed, and if so what action, in respect of AIDS and blood products licensed under the Medicines Act. These products include Factors VIII and IX, Immunoglobulin G, Albumin and hepatitis B vaccine.

(2) The names of those invited to attend in order to help the sub-committee are: Professor Bloom, Dr Craske, Dr Galbraith, Dr Gunson and Dr Mortimer.

(3) It is assumed that participants will be familiar with the problem and with at least a proportion of the many publications.

(4) This 'agenda' suggests headings for the discussion and a suggested first speaker is given. As a target for discussion, brief possible conclusions are indicated - doubtless these will be changed radically.

A. FACTOR VIII AND OTHER CLOTTING FACTORS

1. Aetiology. Current possibilities.

Dr Mortimer.

Conclusion? An infectious cause seems likely and a single new agent could be responsible. Repeated exposure to, or reactivation of, known viruses cannot be excluded. Although possible agents have been proposed (eg CMV, EBV, HTLV) their relationship to the disease remains very uncertain. The infectivity of the supposed agent(s) appears to be low, requiring for transmission intimate contact or introduction into the body tissues.

2. Epidemiology. Current position.
Assessment of risk from Factor VIII.

Dr Galbraith.

Conclusion? Recipients of clotting factor concentrates are at risk. The degree of risk cannot yet be quantified. The risk is likely to be greatest from products derived from the blood of homosexuals and i.v. drug abusers resident in areas of high incidence, and in those who repeatedly receive concentrates in high dosage.

3. Possible scientific approaches to avoiding or reducing the presence of viruses in clotting factor preparations.

(i) Screening of donors to identify high risk individuals.

Dr Gunson.

Conclusion? The new US procedures are noted and approved. They could have some effect in reducing risk, but this effect may be relatively small, since the procedures are unlikely to exclude all high risk donors, and the causative agent(s) may also be present, although less frequently, in apparently healthy donors from non-high risk groups. The advantages of requiring more stringent procedures than those now adopted in the USA are questionable, and the practicalities of doing so are clearly difficult and beyond the sub-committee's expertise.

(ii) Screening of donor blood for evidence of virus infection in addition to Hepatitis B (eg EBV, CMV), or for evidence of infection (eg Th/Ts ratio).

Dr Craske.

Conclusion? Additional measures are not at present feasible on the scale needed. Tests, which need to be speedy and simple, for known agents may become available which could be introduced into the requirements for source plasma, but only a test to detect the presence of an identified aetiological agent(s) could be expected to control AIDS.

(iii) Screening the product for infectious agents.

Dr Schild.

Conclusion? Such tests are generally insensitive, but tests too cumbersome or slow for use on donor blood may be practicable for the end-product and could, eg, lead to standards for levels of contamination. Development work is justified.

(iv) Treatment of blood products with heat or chemicals.

Dr Fowler.

Conclusion? Although the value of such measures in respect of unidentified agents can be proven only by long-term epidemiological studies, they are likely on general grounds to reduce infectious hazards but may not eliminate them.

(v) Other.

4. Consideration of the different operational "possibilities" for reducing the risks from clotting factor preparations.

(i) Withdraw Factor VIII and IX concentrates (ie use only cryoprecipitate for treatment).

Professor Bloom.

Conclusion? This step cannot at present be recommended: (a) it is probably impossible to satisfy UK needs in this way; (b) even if needs could be satisfied it would involve a major rethink of UK policy for preparing blood products; (c) the perceived level of risk at present does not justify serious consideration of this solution.

(ii) Withdraw US preparations from the UK market.

Dr Fowler.

Conclusion? Impracticable on grounds of supply.

(iii) Use US blood products as sparingly as possible.
NOTE: This possibility is largely a matter for physicians treating haemophilia, but it could in theory be decided to modify product licences, eg "not for use in children with mild haemophilia".

Professor Bloom.

Conclusion? The uncertain balance of risk/benefit considerations in various categories of patient are too finely balanced to justify action via licensing: the matter should be left to clinical judgement.

(iv) Promote UK self-sufficiency in supply of concentrate.

Dr Fowler.

Conclusion? This is highly desirable since it should reduce risk appreciably, although not completely.

(v) Use US blood products only if the source plasma was collected after the new regulations were introduced (March 23rd 1983).
NOTE: It is known that US manufacturers have stocks of 'pre March' plasma, and that the US Office of Biologics to consider this matter on July 19th.

Dr Fowler.

Conclusion? This should be adopted as soon as practicable, even though its value may be limited.

(vi) Use products treated by heat or other inactivation methods.
NOTE: Hyland are now licensed in the USA for heat-treated Factor VIII, and Armour is shortly to apply for a US licence. The cost of these products are apparently at least double that of untreated material.

Conclusion? This is desirable, but is impracticable at present, since no such products are yet available in the UK. This development should, however, be encouraged, notwithstanding the cost penalty.

When these products become available in the UK, should licences for non-treated Factor VIII from the USA and/or elsewhere be continued?

Conclusion? When these become available, the quantity that can be supplied should be established, and the advisability of this step then re-examined in the light of this information and of up-to-date knowledge on AIDS at the time.

(viii) Other.

B. HEPATITIS B VACCINE

1. Epidemiology - is there evidence of a risk?

Dr Galbraith.

2. Aetiology - are all classes of possible causative agents likely to succumb to the inactivation procedure?

Dr Schild.

Conclusion? There is no evidence of risk from hepatitis B vaccine at present. The licence should remain unchanged, ie for high-risk groups. The position should be closely observed.

C. IMMUNOGLOBULIN AND ALBUMIN

1. Epidemiology - is there evidence of risk?

Dr Galbriath.

2. Aetiology - are viruses or other possible pathogens likely to survive the Cohn process or the heating to which albumin is subjected? Is an AIDS agent in IgG likely to be neutralised by antibody?

Dr Schild.

Conclusion? As yet there is no evidence of risk and no action is at present justified. The position should be closely observed.

D. OTHER RELATED MATTERS

1. A number of organisations are involved in the question of AIDS, including the plasma fractionation laboratories and their Authorities, the National Blood Transfusion Service, the PHLS and NIBSC and their Boards, the Haemophilia Centre Directors, the JCVI, ARVI, the CSM and the DHSS departments with responsibilities related to the work of these various bodies. The MRC is also setting-up a working group. It is clearly necessary to avoid conflicting actions or conclusions by these bodies and to ensure that they can each quickly take into account new information.

Could there be advantages, therefore, in setting-up a system for ensuring prompt interchange between these various groups, either in the form of meetings of representatives, or by means of circulated information sheets from a coordinating office.

2. Although opportunities for research are possibly limited in comparison with the USA (owing to the paucity of cases in the UK) are there identifiable areas in which work should be encouraged?
eg. - epidemiological studies of the introduction and spread of AIDS in the UK,

- study of the causes of death in haemophilia patients, in part to establish the background,
- clinical and laboratory studies of at-risk groups, in part to identify early diagnostic methods,
- treatment of blood products,
- testing of blood products.

E. OTHER

J.W.G.S.
28.06.83