NOTES ON TALK GIVEN BY DR MANNUCCI ON SAFE TREATMENT FOR HAEMOPHILIA AT HAEMOPHILIA MEETING AT CARDIFF

This was basically a report of the haemophil T trial on European patients, some of whom came from

This trial was to assess the attack rate of hepatitis and as a subsidiary to see if there was a reduction in severity, chronicity, type of hepatitis, whether there was a relationship between batches and doses, how tolerable and efficacious the material was for promoting haemostasis, there were no controls and there was a prospective follow-up for twelve months. Patients were enrolled from Decembewr 1982 to December 1983. Inclusion criteria were haemophila A patients with normal liver function tests who were 'verging'. A few were vaccinated but the majority were not, against hepatitis B. Patients of any age were taken in and any bleed whether for surgical or prophylactic purposes.

Patients were excluded if they had received blood or blood products, if they had raised LFTs, were hepatitis B surface antigen positive (unless vaccinated), had been treated with hepatotoxic drugs, and did not have adequate follow-up.

The timing of the laboratory and clinical follow-up was as follows - zero time, for the first month seen every two weeks, for the second to six months, seen every three weeks, for the seventh to twelfth month seen monthly, making twenty nine visits in all. Of the LFTs the transaminases were the most informative.

The definition of post transfuson hepatitis (NANB as diagnosed by exclusion) was that the ALT must be greater than 2.5% above the upper limit on two subsequent occasions more than 21 days apart and between 14 and 180 post transfusion days.

The results showed that in 21 patients with a first exposure 4 were followed up irregularly and not included. Of the remainng 17 follow-up at six months showed that 12 had post transfusion hepatitis and 5 no post transfusion hepatitis. Of the 12 cases 1 was due to CMV and 11 were apparently due to NANB.

Of the positive patients the incubation period was 7 to 9 weeks. Only one patient actually got jaundiced. The majority had an ALT rise for a short time although one patient had two short periods of rise separated at 40 and 55 weeks. This patient had two different batches of concentrate.

The clinical and laboratory features of the NANB in the eleven patients were as follows, the median age was 2, range 0.2 to 58; the incubation period was 8 weeks mean, range 5 to 11 weeks. In the CMV case there was a slight ALT rise at 16 weeks and the CMV titre at the start was 1/80 but at 16 weeks was 1/5120. (FEB asked if he thought that this might have been a reactivation and he admitted that this could have been so rather than a primary case).

There was no relationship of the PTH to the dose given and all batches of the haemophil T were associated.

In summary, there was an attack rate of 70%. No hepatitis B was transmitted although three patients had been vaccinated. It was not

possible to assess whether there was any reduction in the attack rate but it did appear that the severity of the attacks might be reduced. The tolerance and efficacy of the factor VIII for haemosthetic purposes was good.

He also commented that as far as the AIDS antibody is concerned (using LAV antibody tests by RAPA) there is apparently no seroconversion of any patient after one year.

Of the other concentrates, Cutter like Hyland are producing a dry factor VIII whereas Behring and Alfa Laboratories produce a wet concentrate. Armour's 'superheated concentrate' is a dry preparation. Immuno are trying a low pressure steam and the NYBC a lipid solvent but this is not released. For factor IX concentrates Biotest are proceeding with their UVBPL, Kabi are proceeding with hydrophobic interaction chromotography and Behring are proceeding with a wet heat preparation.

The Alpha concentrate is apparently being tested. For the Behring concentrate of VIII prospective results appear to show a 20% NANB attack rate but the follow-up is apparently very erratic. The Armour product may be being tested but the NYBC is only experimental.

Preliminary results on a double-inactivation process (heat then chloroform) still indicates some short incubation NANB.

All factor IX concentrates have been followed up acceptably and there has been no post transfusion hepatitis.

cc Brec
PLW