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0023

NOTES OF MEETING : THE PRESENCE AND FUTURE
OF HAEMOPHILIC CARE

DATE: 18 - 19 JULY, 1988

This meeting was sponsored by Alpha and brought together people from a fairly wide catchment area. The meeting was almost entirely free from commercial hard-sell which was very refreshing. There wasn't too much new stuff, but the following notes will highlight some of the points which interested me.

1. Gossip/Private Discussion

In discussion with several people, the following points come to light.

- The US Red Cross have withdrawn solvent detergent products pending a full audit of all Red Cross plasma collection facilities for the procedures of exclusion of HIV and HBsAg positive donations. This follows the recently reported cases where known HBsAg and HIV-antibody positive donations were sent for fractionation.

- Current US prices range from 12 cents per unit for Cutter product to 60 cents/unit for Hyland product.

- Alpha are currently developing a product which will include solvent/detergent treatment and final dry-heat treatment. C Heldelrand advised me that the objective of the dry-heat treatment is to inactivate parvovirus, although they don't intend doing any in vitro studies on parvovirus inactivation. Dry-heating will be at 60 °C but heating period has not yet been defined. He believes that a product lacking stabilisers gives significantly more virus inactivation.

- Cutter's choice of 68 °C for dry-heating is apparently reported to be due to a transcription error. (Companies moguls had specified 60 °C but development work done at 68 °C in error).

- Frank Hill advised me that

  - None of his virgin patients on 8Y have immunological abnormalities.

  - None of his virgin patients on 8Y have sero-converted to parvovirus, whereas several of his patients previously treated with unheated BPL material have serological evidence of parvovirus.

  - Two patients have developed anti-HBc antibodies, suggesting subclinical HBV infection.

File Haemophilia Director

LAB00501.048

2. Points raised in the formal presentation are as follows:

2.1 J Goldsmith

Review of current data indicates that AIDS develops in 18Z of patients. 5 years after seroconversion. This rate of AIDS development is virtually identical to that for homosexuals.

2.2 P Jones

In his HIV patients, 3 died of lymphoma. Each of these patients developed lymphoma in 1886 · He wondered if this might be product-related.

Apparently 2 other cases in London and it was agreed that proper histological examination should be undertaken.

2.3 A Giles

Currently investigating FXa + phospholipid in haemophiliac dogs with inhibitors. This looking promising and a clinical trial in humans planned for Autumn.

Speculated that Va - Xa cross-linked may also prove valuable.

2.4 B Hollinger

Reported study of 579 haemophiliacs.

- 53Z had ALT and or AST abnormalities.
- HBV markers and anti-Delta also studied.

HBV MARKERS		PERCENTAGE OF GROUP WITH DELTA ANTIBODY
No HBV Markers	12 Z	0 Z
Anti HBs Only (Vaccinated)	30 Z	0 Z
Anti HBs + Anti HBc	46 Z	6 Z
Anti HBc Only	2 Z	9 Z
All HBsAg	9 Z	32 Z
HBsAg + HBeAg	2 Z	7 Z
HBsAg + Anti HBe	6 Z	47 Z
HBsAg Only	1 Z	14 Z

Stated that in an NIH study, Delta survived liquid heating at 60 °C/10 h - I wonder if this is correct.

Believes that all anti HBc positive donations should be tested for anti-delta. Anti-delta positive donations should not be sent for fractionation.

2.5 P Mannucci

Talk 1 - HB Vaccination

Tabulated HB vaccine status of patients in published clinical trials.

PRODUCT	TRIAL REPORT	NO. OF VACCINATED PATIENTS
Alpha	Kernoff, 1985	0/11
	Colombo	1/11
Behring	Schimpf	16/26
Alpha	Kernoff, 1987	1/11
Immuno	Mannucci, 1988	14/28
TOTAL		32/89 (35%)

Talk 2 - Trial Protocols

Reviewed ICTH criteria for clinical trials and concluded that these standards should be met. Still does not believe that BPL trial data acceptable.

Jim Smith commented that these criteria had never been formally published or approved. Mannucci, however, argued that these criteria had been published in recent paper by Schimpf.

Talk 3 - Review Of Clinical Trial Data

Nothing new here but still concludes that dry-heat treatment is ineffective in inactivating NANB. He thinks that clinical data on NYBC process is totally inadequate to sustain their claim for virus safety.

In discussion, Mannucci claimed that 2 cases of HBV associated with Behring product. No data presented.

Similarly, Dr F Stoerkel (Germany) gave an anecdotal report of a case of NANB in a virgin patient who had elevated ALT + AST 4 weeks after treatment with Behring product and now has chronic transaminitis.

2.6 H Thomas

Reported on clinical evaluation of Alpha interferon in patients with chronic hepatitis.

In chronically HBV infected patients, interferon was given thrice weekly at a dose of around 10^7 units/m^2. Optimum therapy period was 3 months. Hepatitis was resolved in around 40% of treated patients. Following points are relevant:

- Ineffective in HIV positive patients.
- Ineffective in neonally acquired hepatitis.
- Successful outcome more likely if treatment initiated as early as possible in the development of the chronic infection (before HBV genome integrates into host's DNA).
- Interferon encourages expression of HLA antigens in liver cells and this facilitates killer T cell activity. Thus, jaundice encouraged and patients become quite ill before recovery occurs.

5-10 x 10^6 units/m^2 inhibits replication of delta virus but this is reversed as soon as treatment stopped.

Interferon is also being given to Northwick Park Hospital patients with NANB. Low doses (2-3 x 10^6 u) given regularly for at least 2 years. ALT levels have returned to normal in all patients.

2.7 D Brettler

Gave an updated account of the clinical evaluation of Monoclate. Still no evidence of major immunological benefit in pre-treated HIV infected patients.

Inhibitors have developed in 3/30 virgin patients. This is, apparently, much higher than expected.

2.8 E Gomperts

32 virgin patients currently enrolled in trial of Hyland monoclonal product.

2.9 A Giles

Still only 2 patients being treated with recombinant product, basically due to low level of gene expression.

Currently studying modified (deleted) FVIII in dogs. Seems quite promising. Apparently use Tween to stabilise molecule because albumin causes anaphylactic reaction in dogs.

2.10 T Stagnaro (Alpha)

Interestingly, listed affinity/chromatography in his list of future systems of product manufacture. Claimed that yield from monoclonal processes is:

125 - 175 iu/litre for Hyland
100 - 125 iu/litre for Armour

DR B CUTHBERTSON
22/04/88