REPORT ON XIX TH CONGRESS OF ISBT

AND XXI ST CONGRESS OF ISH

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WP REF:ISBT/ISH (Disk 2)

2. AIDS

2.1 Blood Products

2.1.1 FVIII and Haemophilia

Jones (177) reported that there were 8 cases of confirmed AIDS amongst his patients with a further 4 cases awaiting confirmation. This represented an incidence of 8-10% which was considerably higher than either the rest of the UK or the USA (1-2%). He was also seeing unusual carcinomas (eg of the jaw) which had not been previously reported in this situation. He claimed that the degree and type of treatment in Newcastle was no different to many other Centres and he was unable to postulate any reason why Haemophiliacs in Newcastle should be effected so differently.

Bloom (178) noted that the proportion of haemophilia B patients seroconverting was about 1/10th of that for haemophilia A. He speculated that the α1-thymosin present in FIX concentrates may be acting as an immunostimulant.

The timescale from exposure to seroconversion ranged from 6 days to 1 year and the mean timescale for developing full blown AIDS was 3 years. Only 1.6-4% of haemophiliacs had developed full blown AIDS suggesting that haemophiliacs may be lagging

behind other high risk groups and that many more cases may develop in the coming months. In Cardiff 43/153 patients had seroconverted (cf 44% for UK as a whole); 2 had already died from AIDS, 1 was dying and 7 were showing clinical symptoms of the disease. Bloom proposed that virgin haemophiliacs should be treated with "2nd generation" heated concentrates (eg 8Y) while severe haemophiliacs should continue to be treated with "1st generation" heated products.

Bloom noted that the incidence of transfusion AIDS in Australia was 10 times greater than the UK. He also mentioned that 2 "amateur nurses" had seroconverted while involved in the home treatment of haemophiliacs. This was contrasted with 1 seroconvertion and one possible case of AIDS from 2563 exposed health care workers (incl 876 needlestick).

Kasper (199) noted that 5 haemophiliacs had seroconverted after the start of clinical symptoms (ie 3, 5, 5, 9, and 19 months). There were 2 cases where passive transfer of antibody may have occurred. The US National Haemophilia Foundation is not recommending recall of product lots containing positive donations. Non heat treated products are still being sold in some parts of the World.

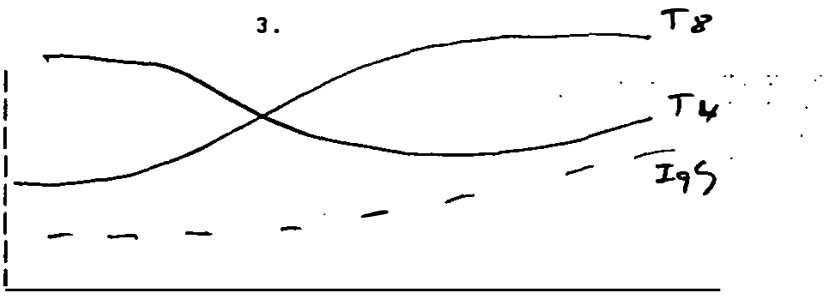
Allain (350) reviewed a prospective study of seroconversion in a cross section of haemophiliacs. 105 patients were selected who had no clinical or immunological abnormalities at the beginning of 1984. All were treated with unselected non-heated product and screened again after 12 months.

Type of Patient	Total No.	No. -ve	No. +ve at 1984	No. +ve at 1985
Haem A	63	22	19	41
Haem A + Inhib.	18	12	1	6
Haem B	24	10	7	14

i.e. a total of 34 haemophiliacs (58%) seroconverted during the 12 month period of study. A similar study with transfused patients (chronic anaemia) showed 2/18 seroconverting (13%) over the same period. This was related to a single infected donation.

Monitoring of T_4 and T_8 cells and IgG over the period gave the following typical profile for a patient who seroconverts.

3.



Garsia (350) gave a similar report on Australian haemophiliacs. From a total of 161 haemophiliacs studied 72 has seroconverted. These were in the following groups.

Haem A	severe	51	
Haem A	mild	15	
Haem B		1	(6%)
VW disease		4	(25%)

There have been no cases of seroconversion since heated products were introduced and Garsia postulated that seroconversion without AIDS may represent immunisation rather than latent infection.

2.1.2 Other Blood Products

Archer (545) described 60 cases of seroconversion following treatment with blood products (excluding haemophilia). Of these cases 15 had developed AIDS and a further 9 had lymphadenopathy. Complete records were currently available for 51 of these cases and 22 had been definitely associated with positive donations (from 16 +ve donors).

Padvelski (426) reported that the Ortho Ion exchange process for IgG manufacture had been examined for retrovirus fractionation using Feline Leukaemia Virus. Two ion exchange steps are used DEAE-Sepharose 6B followed by QAE-sephadex A-50. In the former step 84% FeLV was bound to the ion exchanger while 16% passed through. Further virus was removed on the second step and there was no detectable FeLV in the final IgG product.

Zuck (135) reviewed the safety of IgG. Virtually all product lots examined by FDA contained HIV-antibody.

ie

Year of manufacture	Ab+ve lots
1982	2/2
1983	5/5
1984	6/6
1985	12/13

Zuck felt that each manufacturers process would have to be assessed for safety and then described the FDA study (Transfusion 26, 210, 1986) considering that this showed such a high margin of safety that similar process would be safe.

In a survey of receipts of IV products 133 immunocompetent patients had been followed for 4-24 months. There was evidence of passive transfer of Ab but not seroconversion (on the grounds that Ab disappears from circulation).

938 patients receiving IM products had been surveyed 2 of whom had seroconverted (1 from a high risk group and the other had a needlestick injury).

3.5% of AIDS cases (USA) had received IM IgG but only 7 of these had no other risk factors (ie 2%) this compares with 3.6% of all AIDS cases having no risk factors.

Zuck also noted that HIV may be inactivated in IgG during storage in the liquid state (see next issue of Transfusion).

2.2 Donor Screening

Sayers (511) examined the problem of false +ves in a group of 85065 donors. When tested using by the Abbot method (HTLVIII EIA) there were

1.08% initially reactive
0.47% repeatedly reactive
0.20% confirmed by Western Blot

60% of the false +ves were female and 9/15 repeatedly reactive (but WB -ve) were found to have HLA antibodies reactive to a cell line with the same phenotype as that used to prepare the Abbott HTLVIII EIA.

It was suggested that test methods should not depend for viral growth on cells expressing class II antigens.

437 donors repeatedly reactive by Abbott EIA were then tested by the Genetic systems method (LAV EIA), only 23 were reactive. The Genetic Systems method also identified all Wester Blot +ve donors (ie 21/437).

Perkins (49-54) reported CDC data on the testing of 51000 donors. 0.23% were EIA +ve, 94% of these were confirmed by Western Blot and 54% had given a +ve culture. However virus had also been cultured from Ab -ve individuals.

Kasper (199) noted that following the policy of excluding high risk donors 1/400 donations were repeatedly +ve (nearly all male), false +ves were present with a male/female ratio of 1.

Kasper noted that viraemia could occur without detectable Ab (eg in 4/10 Ab -ve wives of haemophiliacs) she therefore queried the effectiveness of Ab screening.

Kuhnl (349) claimed that the Abbott Western Blot kit was the most sensitive confirmatory test and that comparisons between donors in the Federal Republic of Germany (781,982 unpaid) and west Berlin (42,982 paid) were suggesting a much higher positive rate amongst paid donors.

Rossiter (349) noted that the incidence of +ves varied according to different manufacturers tests ie

Abbot	3.7%	(1/27)
Bio-Enzybead	2.2%	(2/90)
Genetic Systems	0	(0/10)

This was blamed on pipetting and technical errors and it was suggested that duplicate testing may be required!

Clark (349) described the preparation of ready-to-use Western Blot strips at CSL for use throughout Australia. CSL antigen was initially prepared from H9 cells but gave a weaker response to p41 antigen than NIH material. Weaker +ves were not fully detected with this material.

ie	p24	gp 41
+ve serum	85/90	75/90
Strong +ve(A)	30/30	30/30
Weak +ve	28/30	28/30
-ve serum	4/29	1/29

A second antigen preparation was made from LAV infected CEM cells and this was better than the HTLVIII preparation. It was suggested that the H9 preps were compromised by cellular contamination.

	Titre	
	p 24	gp 41
NIH	10^5	10^5
CSL 1	$1\text{-}2 \times 10^5$	$0.5\text{-}1 \times 10^5$
CSL 2	$1\text{-}2 \times 10^5$	$1\text{-}2 \times 10^5$

Levy (167) had earlier argued that glycoproteins gp 120 and gp 160 were important for ELISA and confirmatory tests and that up to 10% true +ves could be missed. The CSL team were currently working on gp 120 but had not yet started on gp 160. This CSL kit includes: 30 strips.
-ve control strip
+ve control serum
-ve control serum

These will be supplied free of charge to authorised laboratories.

Vyas (350) described a study of IgG and IgM circulating immune complexes and the culturing of HTLVIII from the serum of healthy homosexual males.

		HTLVIII Ab -ve	HTLVIII Ab +ve
IgG immune complexes	-ve	173	127
	+ve	4	22

		IgM immune complexes -ve	IgM immune complexes +ve
IgG immune complexes	-ve	246	27
	+ve	19	7

Positive viral cultures had been obtained from 4/7 Ab -ve individuals. Vyas concluded that the Ab screening methods were not sufficiently sensitive and suggested that a nucleic acid hybridisation assay was required.

2.3 General

Levy (167) suggested that HIV was a Lentivirus but that there were many virus isolates with different variable regions.

Barrie-Sinoussi (no abstract) described the recent African strain which had low cross-reactivity with p25 & p26 but not with gp of LAV 1 and LAV 2. The viral genome had no homology with LAV 1 and was therefore probably an "ancestor" of LAV 1. HIV replicates exclusively in T_4 cells but only 4-10% of T_4 cells are replicating and expressing virus in culture.

Only 50-60% of sexual contacts become infected with HIV suggesting that a high dose of virus may be needed to cause infection.

Possibilities for prevention and treatment include:

1. McAb to receptor.
2. Vaccine.
3. Antivirals active at the level of reverse transcriptase to stop replication.
4. Immunomodulators.

Various options for developing a vaccine were reviewed. Major uncertainties are:

1. Do viral antigens induce neutralising Ab.
2. If so, which antigens are requries.
3. There is substantial variability amongst different isolates.
4. The virus may continuously mutate throughout the illness.

Desmyter (167) summarised the situation in Central Africa. The incidence of AIDS in cities is 50-100/10^5 pop/yr (This compares with 2 for USA and 0.2 for Europe). The sex ratio is 1 with the mean age being 40 for males and 30 for females. Seroprevalence is now 5-15% of city populations. Many different strains of virus have been isolated with up to 30% variation in amino acids, probably because the virus had been present for a long time in Zaire and had had more time to diverge. Mortality from AIDS was 33% of cases within 1 year. Restrospective cases have been discovered going back to 1975 (air stewardess, Ab +ve but now healthy).

Retrospective Ab screening in Kinshasa shows:-

	% +ve
1970	0.25
1980	3.0

a 12-fold increase from 1970 - 1980. This was considered to be compatible with slow heterosexual transmission. On this basis extrapolation backwards in time suggests that the disease first appeared in Africa in 1940.

A high proportion of false +ves are found in Africa possibly because of interference from malaria (Abbott test). It was suggested that if LAV II and HTLV IV were not confined to Africa then the serology of screening tests would become much more complicated.

Evatt (47-48) claimed that the loss of T_4 cells explained most clinical abnormalities in AIDS but the presence of large amounts of circulating immunoglobulin is still a paradox. He noted that the virus appears to exhibit extensive genetic drift (see Science 231, 850, 1988).

The incidence of seropositivity in the USA is:

haemophilia A	74%
haemophilia B	35%
female prostitutes (Miami)	40%

There has been no evidence of child-to-child transmission with paediatric cases being due to perinatal maternal transmission (74% high risk group, 15% haemophilia wives) or exposure to blood products.

13% of USA haemophilia wives are now seropositive with the seroconversion rate still increasing.

Of 1758 exposed health care workers 26 are seropositive (1.5%) but 23 of those are in high risk groups. For the 3 remaining cases:-

Case 1; No information (anonymous).
Case 2; Female, needlestick injury.
Case 3; Lab worker with severe cut while pooling platelets (Dec 83) and needlestick (Aug 84) became Ab+ve April '85.

In a specific study of needlestick injuries there are 2 cases seropositive from 1000 cases entered into the study. In 40% of these cases proper precautions were not followed.

Keller (351) provided an update on the use of isoprinosine for the treatment of AIDS and ARC. It has taken 3-4 months of steadily increasing the dose to discover the appropriate dose (4 patients died during this period). For AIDS patients the dose is now 3-3.5 g/day with perhaps up to 4g/day being required. For ARC the dose is 2.5 - 3.5 g/day. Patients have shown a general clinical improvement with some encouraging laboratory results:-

	AIDS	ARC
T_4 cells	+16%	-23%
NK cells	+82%	
PHA response	+83%	+63%
NK activity	+64%	+81%

Keller suggested a larger clinical trial was warranted.

Imbach (135) noted that IV IgG had reversed the T_4/T_8 ratio in 2 haemophiliacs who were HTLVIII +ve.