IN CONFIDENCE CBLA 88/10

SCREENING OF NBTS BLOOD DONORS

Exclusion of Carriers of Sporadic Hepatitis Virus (Non-A Non-B) by Routine Determination of Serum Alanine Transferase

Proposal

That the Blood Products Laboratory comes into line with all other major fractionators of human plasma by including serum alanine transferase estimation in the specification for source plasma collected by blood donor centres.

Background

All blood and plasma donations are tested at source for antigen to hepatitis B virus and antibody to HIV.

During the past five years, attempts have been made to limit NANBH in haemophiliacs and in a search for putative markers for HIV carriers, donor screening programmes in USA were variably extended to include hepatitis B core antibody, alanine transferase, β_2-microglobulin and interleukins. It is reported that American Red Cross will introduce HTLV1 screening during 1988.

Of the above markers, ALT has been retained almost uniformly by the industry.

No direct markers of NANBV are available. The virus(es) have not been identified.

Rationale

Carriers of non-A non-B virus and convalescents from NANBH may retain disordered liver function associated with a low grade viraemia or recurrent viraemia believed to result from pro-viral DNA replication reactivated by other intercurrent viral and bacterial infections.

This type of liver dysfunction causes elevation of serum ALT levels.

There are other causes of raised ALT levels including excess alcohol consumption.

It is argued that exclusion of donations where ALT is 2.5 x the upper limit of the normal range will exclude some NANB virus carriers, if not all.

Implications for Donors

A percentage of otherwise acceptable blood donations will be lost by introducing ALT testing, but that percentage has not been comprehensively established throughout NBTS although estimates range between 2 and 5 per cent.

Pros and Cons

Plasma products from BPL are now subjected to processes believed to inactivate or attenuate NANBV. Assurance is based on clinical observation and the margins of safety in the process are unknown.

Until virus inactivation procedures were introduced, NANBH was transmissible by most batches of factor VIII and factor IX and by intravenous normal human immunoglobulin.

The process inactivation strategies are augmented by a general policy aimed at limiting the challenge i.e. the viral count gaining access to pooled plasma. Hepatitis B and HIV are so controlled - ALT testing is believed to assist empirically with reduction of NANBV.

Cellular products of blood, i.e. red cells and platelets, can transmit NANBV and are not suited to viral eradication except by exclusion of donors 'at-risk'.

It is accepted that the scientific basis for introducing ALT screening of donors is far from satisfactory.

The drive for ALT testing is strongly augmented by Manufacturer's Liability and demands of patients to eliminate NANBH as a certain sequel to treatment, with the development of severe liver disease in up to 60% of sufferers.

Now that HIV transmission in blood products has been reliably controlled, NANBV eradication has become the gold standard by which coagulation factor concentrates are judged.

Considering factor 8Y, BPL are now distinguished from the remaining field by the preferred use of dry-heat virus inactivation and the uniform use of plasma unscreened for ALT. To this extent, BPL operates outside the 'State of the Art' practised in USA and Europe.

BPL can introduce new stringent procedures to add assurance to dry-heat virus inactivation. A loss of 10-20% of factor 8 yield may be predicted - in product terms, shelf value of lost product for each percentage point of factor 8 yield is £150,000. Alternatively an increase in plasma utilisation per annum of 20% will increase BTS costs by £4 million.

Committee on Safety of Medicines is to meet in February to establish the criteria for granting licences on biological products from human plasma including procedures for elimination or attenuation of viruses.

BPL is currently unable to export excess intermediates because the source plasma is not ALT tested. Excess final products in the future may be so affected.

BPL currently has approximately 500 tonnes of FFP which is not ALT tested and which will meet process requirements until 1989/90.

ALT testing of all 2.5 million NBTS blood donations per annum is estimated to cost between £0.1 and £0.25 M.

An estimated 2-5% of donations will be unnecessarily rejected by ALT screening.

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