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Our ref: PI86-11

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Dr. A. Smithies,
Medicines Division,
D.H.S.S.,
Health Services Division,
Hannibal House,
Elephant & Castle,
LONDON. SE1 6TE.

Ack.
Sent note.

Dear Dr. Smithies,

Please find attached a summary report on the recent incident affecting batches GZ29, 30, 31 and 32. My principal reason for producing this summary was to define the choronology of events - when we met last week I did not have my day-book and could not be certain of all the dates involved.

I can now confirm that all four batches of finished product were negative for HTLV-III Ab by the Wellcome kit as used by BPL. I understand from Philip Mortimer that the RIA system in use at Colindale detects a low level of antibody in at least one of these products.

Yours sincerely,

GRO-C

T.J. Snape
Head of Quality Control.

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RISK OF AIDS WITH ARTIFICIAL INSEMINATION

To the Editor: On September 14, 1984, the Privacy Committee of New South Wales advised the Department of Health in New South Wales that a moratorium should be imposed on the use of male homosexuals as sperm donors in artificial-insemination programs.

Male homosexuals were known to be donors in the programs. Also, in the light of the knowledge about the acquired immunodeficiency syndrome (AIDS) at that time, the health risk to recipients in these programs was uncertain. No screening programs for antibodies to the human T-cell lymphotropic virus Type III (HTLV-III) were then available. A moratorium was initiated in October 1984 and lifted in April 1985, when screening for antibodies to HTLV-III was introduced for sperm donors as well as for blood donors.

In July 1985, four women in an artificial-insemination program in New South Wales were found to have antibodies to HTLV-III, and lymphadenopathy developed in one of them. The source of their exposure was identified as a semen donor who had participated in the program before the moratorium. It is reassuring that other programs for artificial insemination are now introducing the screening of semen donors for antibodies to HTLV-III (June 20 issue).*

The Privacy Committee is an independent statutory committee that acts as ombudsman for privacy and investigates and advises on issues concerning privacy. The committee has given advice on confidentiality and privacy in relation to AIDS, including such issues as testing for antibodies, blood donation, semen donation, and research.

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*Schiff I, Correia B, Ravnikar VA, Schur PH. HTLV-III antibody testing in sperm donors. N Engl J Med 1985; 312:1638.

EFFECT OF COHN FRACTIONATION CONDITIONS ON INFECTIVITY OF THE AIDS VIRUS

To the Editor: Intravenous gamma globulins prepared by means of Cohn fractionation have been reported to transmit non-A,non-B hepatitis viruses,[1-3] suggesting that the alcohol concentration, pH, and temperature used in this process do not completely inactivate these lipid-membrane–coated viruses. Since the virus causing AIDS (human T-cell lymphotropic virus Type III [HTLV-III], lymphadenopathy-associated virus, or AIDS-related virus), hereafter called the AIDS virus, may be present in plasma pools used for manufacturing blood derivatives,[4-6] it is important to determine whether the virus can survive the fractionation procedure.

We therefore performed the following experiment. Plasma from a small number of donors shown to be free of antibody to HTLV-III by enzyme-linked immunosorbent assay was pooled and fractionated according to the Cohn procedure for ethanol fractionation,[7,8] in routine use at the New York Blood Center. Supernatants from Cohn fraction I, containing 8 percent ethanol at pH 7.2, Cohn fraction II+III, containing 25 percent ethanol at pH 7.0, and Cohn fraction III, containing 17 percent ethanol at pH 5.4, were stored at −70°C. To aliquots of the above supernatants, which represent the potentially most inactivating conditions to which viruses are exposed during gamma globulin preparation, 0.1 volume of an AIDS virus stock was added. This stock consisted of RPMI-1640, 20 percent fetal-calf serum, and culture supernatant from H9/HTLV-IIIb producer cells.[9] The virus was added after adjustment of the supernatants to the temperature at which they are normally held during Cohn fractionation: −2°C for fraction I supernatant, −5°C for fraction II+III supernatant, and −6°C for fraction III supernatant. After 2 and 24 hours at these temperatures, samples were transferred to a −8°C crushed-ice–sodium chloride bath. These mixtures and control mixtures of virus diluted in normal plasma were passed through a 20-ml Sephadex G-25 column precoated with human serum albumin and equilibrated with RPMI-1640 medium. Care was taken to pass the samples through these columns as rapidly as possible, in order to maintain low temperatures before the alcohol was removed. The void volumes were recovered, sterile-filtered, and assayed by inoculation of quadruplicate serial microtiter dilutions onto H9 cells.[10] After 14 days the culture supernatants were harvested and assayed for reverse transcriptase.[10] Little or no AIDS virus was inactivated under the conditions used.

Because of the long storage of liquid preparations of intramuscular immune serum globulin (ISG) between formulation and administration, intramuscular ISG may present little or no hazard of virus transmission, as has generally been concluded. However, the increasingly popular intravenous preparations of ISG are lyophilized immediately after formulation, are stored in the dry state, which preserves virus infectivity, and are given in large doses intravenously. This is probably the most sensitive route for infection with hepatitis or lymphotropic viruses. Thus, intravenous preparations of ISG are of particular concern, as shown for transmission of non-A,non-B hepatitis.[3]

Our findings suggest the desirability of applying virus-inactivation procedures to plasma subjected to Cohn ethanol fractionation, or to the resulting plasma derivatives, in order to sterilize them against non-A,non-B hepatitis viruses and also to inactivate the agent of AIDS.

Our results do not necessarily imply that intravenous gamma globulin preparations are unsafe, since some manufacturers have incorporated into their procedures steps that have the potential for inactivating these viruses.

Furthermore, it is possible that virus may fractionate predominantly into fractions other than the gamma globulin fraction, and that any virus in this fraction could be neutralized by antibody; also, it is possible that storage of intermediate fractions in the frozen state could inactivate virus.

Careful surveillance of recipients of intravenous gamma globulin preparations for development of antibodies to the AIDS virus is necessary. To date, no reports of such development have appeared.

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