positive by both tests. This plasma had an OD more than 7× cut-off value. In immunofluorescence it reacted strongly up to a dilution of 1 in 40, with infected H9 cells, but did not react with uninfected HT cells. In western blot analysis, reactivity was detected against all major HTLV-III viral proteins and polypeptide 121 (see figure). By immunoprecipitation, antibody specificity was confirmed by finding reactivity with all the major *gag* and *env* encoded proteins of HTLV-III and the *gag* encoded proteins (p55) of STLV-III$_{AGM}$.

We appreciate that when testing plasmas that were more than 25 years old we would need to confirm any ELISA positive specimen by as many means as possible because of the risk of false-positive reactions. Confirmatory tests were performed on all ratios above 3. By indirect immunofluorescence and western blotting only 1 was positive, and this plasma was also tested in three other laboratories by different techniques. All the assays confirmed that this plasma reacted with HTLV-III in a way similar to that found with sera from individuals with AIDS or lymphadenopathy syndrome. The plasma also cross-reacted with protein p55 of the African green monkey STLV-III, as have most HTLV-III seropositive central African sera in recent years.[6]

We have demonstrated that at least 1 individual from central Africa had been exposed to a virus similar to human HTLV-III more than a quarter of a century ago. The identity of the donor is no longer known. Our results also suggest that the prevalence of HTLV-III was very low in central Africa in 1959. No evidence of the infection was found in sera taken in rural areas of the Belgian Congo or South Africa (1959), Mozambique (1969), the Congo (1982).

P. K. is supported by institutional service award ST32 CA9382; M. E. is supported by grant R35 CA39805. We thank Abbott Laboratories for equipment and reagents and Dr C. Schable at Centers for Disease Control, Atlanta, Georgia, for the first western blot confirmatory assay.

A. J. NAHMIAS
J. WEISS
X. YAO
F. LEE
R. KODSI
M. SCHANFIELD

Department of Pediatrics,
Emory University School of Medicine,
Atlanta, Georgia 30303, USA

T. MATTHEWS
D. BOLOGNESI
D. DURACK

Duke University,
Durham, North Carolina

A. MOTULSKY

University of Washington,
Seattle, Washington

P. KANKI
M. ESSEX

Harvard University School of Public Health,
Boston, Massachusetts

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LYMPHADENOPATHY SYNDROME AND SEROCONVERSION TWO MONTHS AFTER SINGLE USE OF NEEDLE SHARED WITH AN AIDS PATIENT

SIR,—AIDS and other human immunodeficiency virus (HIV) related disorders have been recorded among intravenous drug abusers (IVDA) but little is known about the period of incubation before the development of antibodies and lymphadenopathy. Fincher et al[1] reported a case of lymphadenopathy syndrome (LAS) developing 7 weeks after a transfusion. An observation in one of our patients suggests that the incubation period may be the same for IVDA.

A 27-year-old heterosexual occasional intravenous drug abuser met a 22-year-old woman while she was in hospital with AIDS related to drug addiction. He was warned the she had AIDS. He did not seem to be strongly addicted (less than two "shoots" per week) and he stated that he usually used his own needle and syringe, except 3 days before the physical examination when he used the same needle as she did. His physical examination was normal (no lymphadenopathy, diarrhoea, candidiasis, pruritus, or Kaposi's sarcoma). At that time, he was anti-HIV negative by enzyme-linked immunosorbent assay (ELISA).

2 months later, axillary and occipital lymphadenopathies were noted. He said that he had not experienced fever in the previous weeks. He was by then seropositive for HIV antibody testing both by ELISA and by western blot (p18 and p25). His lymphocyte count was 2100/μl and the T4 cell count was 693/μl (ratio × 0·6). Tuberculin and candidin cutaneous tests were negative. Axillary lymph node biopsy demonstrated follicular and interfollicular hyperplasia. 8 months later his lymphadenopathy syndrome remains the same; no opportunistic infection or Kaposi's sarcoma has developed and the patient has not lost weight. His lymphocyte count is 1900/μl and he is still seropositive.

Though it is always difficult to be sure of the epidemiological picture in drug addicts, this observation suggests that seroconversion for HIV could be the same, regardless of how the virus is introduced, by transfusion or needlestick, although the virus inoculum may be lower. Lymphadenopathy seems to occur as soon as seroconversion is noticed. Drug addicts should be informed of the potential risk of any injection with a non-sterile syringe and needle. This observation confirms that prudence is warranted in health care workers since seroconversion has been observed, although rarely, in those who have been exposed to a needlestick.[2,3]

D. VITTECOQ
B. AUTRAN
E. BOURSTYN

Infectious Disease Department,
Hôpital Saint Louis,
Paris 75010, France

Institute Pasteur,
Paris

J. C. CHERMANN

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EFFECT OF HEAT TREATMENT OF LYOPHILISED BLOOD DERIVATIVES ON INFECTIVITY OF HUMAN IMMUNODEFICIENY

SIR,—Recognition of the transmission of human immunodeficiency virus (HIV) by blood derivatives such as factors VIII and IX has led regulatory agencies to demand sterilisation procedures for these products. In the United States the National Hemophilia Foundation's Medical and Scientific Advisory Council has recommended that lyophilised, heat treated products should be used for the treatment of haemophilia, and the data on which this recommendation was based have been published.[1,2] However, two recent reports of HIV (HTLV-III) seroconversion in recipients who received only heat-treated factor VIII[3,4] and the following laboratory findings suggest caution in reliance on dry heat inactivation.

Commercial preparations of antithrombin III or factor VII concentrates produced at the New York Blood Center, free of non-protein stabilisers, were contaminated by addition of 1/10th volume of HIV culture supernatant (HTLV-III produced in H9/HTLV-III$_B$ cells grown in RPMI 1640 20% fetal calf serum). A sample of each virus contaminated mixture

was rapidly frozen by swirling in alcohol and dry ice. The remainder was shell frozen by swirling in alcohol/dry-ice and lyophilised for 48 h with shelf heating to 27°C (80°F) for the last 24 h. Vials were stoppered under vacuum. The moisture content of samples varied from 0·8 to 1·5%. Vials were heated for different periods of time at 60°C by complete immersion in a water bath.

For assay,[5] vials were rehydrated with sterile distilled water. Frozen samples were rapidly thawed by swirling in a 37°C water bath. Titrations were done in 96-well microtitre plates. To increase the sensitivity of detection of small amounts of residual virus in heated samples macrocultures were set up with 5–10 ml of sample in 50–100 ml cultures. Macrocultures were monitored with weekly tests for reverse transcriptase for 4 weeks.

The virus inactivation resulting from heating alone was surprisingly modest, varying between 0 and 1 $\log_{10}$ at 10 h and between 2 and 4 $\log_{10}$ after 72 h of heating. Lyophilisation alone resulted in an additional 0·5–1 $\log_{10}$ of inactivation. These results are consistent with those reported by Levy et al who found a 2·5 $\log_{10}$ inactivation of their HIV isolate (ARV) with 24 hour heating at 68°C.[6]

Heating in the dry state has only a modest sterilisation effect on hepatitis B virus.[7] Furthermore heated factor VIII products ive transmitted non-A, non-B hepatitis to patients.[8,9]

The finding of only modest sterilisation process efficacy for HIV adds to concern about the efficacy of this procedure. It should, however, be stressed that this finding does not mean that dry-heat treated products are unsafe with respect to transmission of AIDS. Indeed three studies have reported absence of anti-HIV seroconversion in recipients of dry-heat treated FVIII preparations.[10-12] Purification and processing steps before lyophilisation can remove or inactivate virus, and lyophilisation alone under commercial conditions probably inactivates more virus than is observed with shell freezing. Furthermore some products are heated above 60°C. Nevertheless, these findings indicate the need for caution in relying on the efficacy of dry-heat sterilisation. Long-term surveillance of recipients of such products for seroconversion to anti-HIV is still required.

Laboratory of Virology,
Lindsley F. Kimball Research Institute
of New York Blood Center,
New York, NY 10021, USA ALFRED M. PRINCE

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SIR,—Letters by Dr White (March 15, p 611) and Dr van den Berg (April 5, p 803) and their colleagues on seroconversion to human immunodeficiency virus (HIV) antibody positivity after the use of factor VIII concentrate heated in a lyophilised state prompts us to review evidence on the inactivation of HIV when heat treatment is applied to factor VIII or factor IX concentrates in a lyophilised state. McDougal et al[1] have demonstrated that inactivation of HIV is a function of the matrix in which the virus is contained, the temperature used, and the duration for which that temperature is applied. Inactivation in a liquid matrix is more efficient and swift than that achieved in a lyophilised state. Similarly, heating at a lower temperature or for a shorter duration is less efficient than heating at a higher temperature for longer. Anyone recording transmission of active HIV via such products should give details of the duration of heat treatment and the temperature, and they should say if the preparation was in a liquid or lyophilised state during such treatment. After all, heat treatment could be said to have been accomplished if a product is heated to, say, 40°C for 30 min.

Cutter Laboratories,
Berkeley, California 94701, USA RALPH H. ROUSELL

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MEDICAL TREATMENT FOR UNDESCENDED TESTIS

SIR,—Dr de Muinck Keizer-Schrama and colleagues (April 19, p 876) report that only 18% of 271 cryptorchid testes descended completely after 8 weeks of treatment. Having analysed their data we find the success rate to be higher than this. Of the 271 testes treated (fig 1, table II) 15 were "vanishing" testes and should have been excluded from the study. 85 out of the remaining 256 did not require surgery, a descent rate of 33% comparable with that recorded by Illig et al.[1] Furthermore, the conclusion that the lowest success rate was in the youngest patients is incorrect. Using a Fisher's contingency table and the GLIM package with binomial error structure option without standardisation of testicular position to that found in the normal population,[2] we obtained the same statistical inference but a different percentage in group C (6–12 years old). On the other hand, with standardisation of testicular position we arrived at the same percentage but this was not significant. Thus it is not the age of the patient but the position of the testis which is crucial for successful descent. Hormonal evaluation based on LH-RH tests without biopsy correlation is insufficient in recognising the deficiency of the hypothalamo-pituitary-gonadal axis.[3] There is a growing body of evidence that cryptorchidism is due to impaired gonadotropin secretion.[4-6] Because they used inappropriate hormonal and statistical (Student's) tests it is not surprising that the team were unable to detect subtle changes in hypothalamo-pituitary-gonadal axis and so reached incorrect conclusions.

University Children's Hospital,
4005, Basle, Switzerland F. HADZISELIMOVIC

University Computer Centre,
Biozentrum, Basle M. BUSER

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