urge them to speak out on behalf of this colleague or to curtail cooperative activities with the Soviet Union until Dr. Koryagin's safety is ensured.

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INFREQUENCY OF ISOLATION OF HTLV-III VIRUS FROM SALIVA IN AIDS

To the Editor: The acquired immunodeficiency syndrome (AIDS) is a sexually transmitted disease that can also be transmitted through contaminated blood or blood products. This fact is supported in part by the recovery of human T-cell lymphotropic virus Type III (HTLV-III), the etiologic agent of AIDS, from blood and semen.[1,2] However, the report of HTLV-III isolation from the saliva of infected patients[3] has raised concern about the possible casual transmission of this virus, although epidemiologic studies have not supported casual contagion.

In the past 12 months, we have attempted to isolate HTLV-III from 83 saliva samples from 71 homosexual men seropositive for HTLV-III, who were studied at the Massachusetts General Hospital. All saliva specimens were cultured within 60 minutes after collection. In addition, blood was also obtained from 50 of the 71 men for virus isolation. Our results are summarized in Table 1. One of 83 saliva specimens (1 per cent) was positive for HTLV-III, whereas 28 of 50 blood cultures (56 per cent) yielded the virus. The virus-positive saliva (unfiltered) was obtained from a patient with AIDS who had pneumocystis pneumonia, candidal esophagitis, and thrush. His saliva culture demonstrated reverse transcriptase activity only after 21 days in culture, In contrast, his blood culture showed reverse transcriptase activity on day 3. This suggests that the HTLV-III titer of this patient's saliva was substantially less than that of his blood.

Table 1. Isolation of HTLV-III from 83 Saliva and 50 Blood Samples from 71 Seropositive Homosexual Men.*

Patient Group (No.)	Saliva†	Blood‡
	no. positive/no. tested	
Healthy seropositive (20)	0/20	7/17
AIDS-related complex (32)	0/38	14/21
AIDS (19)	1/25	7/12
Total (71)	1/83	28/50

*HTLV-III denotes human T-cell lymphotropic virus Type III, and AIDS acquired immunodeficiency syndrome.

†Fifty of the saliva specimens were cultured as described by Groopman et al.[3]; 24 specimens were similarly cultured except without prior filtering of the saliva through a 0.45-μm filter (Millipore); 9 specimens were cultured with use of H9 cells as targets as previously described.[2]

‡Blood was cultured for HTLV-III as described by Feorino et al.[4]

The infrequent isolation of HTLV-III from saliva reported here is unlikely to be due to improper methods, because our isolation rate from the blood of infected persons is comparable to those reported by other laboratories.[5] In addition, we have had little difficulty in recovering the virus from the cerebrospinal fluid and neural tissues of HTLV-III–infected patients with neurologic dysfunction.[6] Therefore, we conclude that HTLV-III is present infrequently in the saliva of infected persons. When it was detected in the saliva of one patient with intraoral disease, the amount of virus present was small. These findings are consistent with epidemiologic data indicating that casual transmission of HTLV-III does not occur, even among household members exposed to the saliva of infected persons.[7] These results may be useful in allaying public concern regarding the casual spread of AIDS and HTLV-III infection.

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HTLV-III EXPOSURE DURING CARDIOPULMONARY RESUSCITATION

To the Editor: There have been no confirmed occupation-related cases of AIDS in health care workers in the United States.[1] We have been following two nurses who participated in mouth-to-mouth resuscitation of a patient with the AIDS-related complex, who was positive for human T-cell lymphotropic virus Type III/lymphadenopathy-associated virus (HTLV-III/LAV), and we here report their seronegativity nine months after exposure.

A 28-year-old man who had classic hemophilia treated with factor VIII concentrates and was known to abuse oral analgesics intravenously was diagnosed as having AIDS-related complex on the basis of viral isolation, leukopenia, weight loss, and persistent adenopathy. HTLV-III/LAV infection of his peripheral-blood lymphocytes was demonstrated by reverse transcriptase activity, immunofluorescence, and electron microscopy.[2] He had no history of fever, opportunistic infection, or persistent inversion of the T-helper/T-suppressor ratio.

Eighteen months after viral isolation, during a hospitalization for hemophilic arthropathy, the patient was found in cardiopulmonary arrest in his bathroom. Two nurses began mouth-to-mouth resuscitation, each delivering approximately 20 breaths before the patient was intubated. Resuscitation efforts were unsuccessful. Evaluation of the patient's lymph nodes at autopsy revealed a marked depletion of lymphoid elements, and pulmonary pathological studies were suggestive of the recent infusion of solubilized medications. He was positive for HTLV-III/LAV antibody by Western blot analysis[3] (performed by J.S. McDougal and M.S. Kennedy, Centers for Disease Control) at the time of his death.

These two nurses with documented mucous-membrane exposure to potentially infective saliva from a patient with AIDS-related complex have been followed prospectively for nine months. Initial samples as well as eight subsequent samples for each nurse have been negative for HTLV-III/LAV antibody. The nurses' initial physical examinations, lymphocyte counts, and T-helper/T-suppressor ratios were within normal ranges. All clinical and laboratory indexes remain stable at this writing.

Cells producing HTLV-III/LAV and cell-free viral particles have been recovered from the oral secretions of patients with AIDS-related complex,[4] suggesting that saliva may serve as a vehicle for transmission. If this mode of transmission were important, however, one might expect a higher rate of seropositivity among the spouses

of patients with AIDS.[5] Although we cannot confirm that this patient with hemophilia had infectious disease at the time of resuscitation, rates of persistent viremia in persons seropositive for HTLV-III/LAV appear to be high.[6,7] This case provides further evidence that the risk of seroconversion after a point exposure to the oral secretions of an infected person is probably quite low. It should still be recommended, however, that a disposable ventilating bag and oral airway be kept at the bedside of a patient with AIDS or AIDS-related complex, to avoid mucous-membrane exposure in the event of cardiopulmonary arrest.[8]

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PRENATAL DIAGNOSIS OF HEREDITARY PROTEIN C DEFICIENCY

To the Editor: Protein C is a naturally occurring vitamin K–dependent zymogen, which in its activated form is a potent anticoagulant directed against factors V and VIII.[1] Heterozygous protein C deficiency is manifested by recurrent venous thromboembolism at a relatively young age, which is manageable by oral anticoagulant treatment.[2,3] The homozygous state presents in the neonatal period as overwhelming venous thrombosis[4] or purpura fulminans,[5-8] with a high mortality rate. We have successfully carried out second-trimester prenatal diagnosis in a fetus at risk of homozygous protein C deficiency by fetal-blood sampling.

The mother was a 34-year-old woman who had lost two newborn infants because of massive venous thromboembolism due to homozygous protein C deficiency.[4] In preparation for possible prenatal diagnosis, levels of protein C antigen were measured by a sensitive enzyme-linked immunosorbent assay (Stago, Paris) in plasma samples obtained from 21 fetuses who underwent diagnostic fetoscopy and umbilical-vessel puncture for other indications at 18 to 20 weeks of pregnancy.[9] In this assay there is a linear correlation between absorbance and plasma dilutions up to 1:5000, permitting measurement of very low levels of protein C antigen. The levels of protein C in the 21 fetuses ranged from 6.2 to 15.0 per cent of that of normal pooled plasma (mean ±S.D., 9.60±2.50). In 27 healthy adult controls the values ranged from 69 to 164 per cent, and in the homozygous infant previously described,[4] the level was 1.3 per cent of normal. The significant difference in the level of plasma protein C antigen between the deceased infant and the control fetuses encouraged us to counsel our patient about the option of prenatal diagnosis by fetoscopy in a future pregnancy.

Soon after, the patient became pregnant and sought prenatal diagnosis. Fetoscopy and sampling of pure fetal blood were carried out during the 19th week of pregnancy. Assays for protein C antigen in replicate samples showed levels between 4.7 and 5.2 per cent of normal. Factors II, VII, IX, and X were in the normal range for fetuses.[10] We interpreted the results as indicating that the fetus was heterozygous for protein C deficiency.

Since none of the other 14 heterozygous members of this family had had thrombosis,[4] the parents elected to continue the pregnancy. Unfortunately, premature labor threatened during the 28th week, and after 10 days of treatment with ritodrine and betamethasone, uterine contractions became established. Because there had been three previous cesarean sections, a cesarean delivery was performed, and the premature infant, weighing 1850 g, had severe respiratory distress syndrome, which was confirmed radiographically. Notwithstanding mechanical ventilation, plasma infusion, and intravenous bicarbonate for severe acidosis, the neonate died seven hours after delivery. The plasma protein C levels were 6.4 per cent at birth, 13 per cent after the plasma infusion, and 5.3 per cent just before death. Permission for autopsy was not obtained.

Since neonatal respiratory distress syndrome has not been a feature in any of the cases of homozygous protein C deficiency described so far,[4-8] it seems unlikely that the severe syndrome observed in this preterm heterozygous infant was causally related to the moderately diminished plasma level of protein C.

Our results indicate that prenatal diagnosis of homozygous protein C deficiency is practicable and should be considered when families at risk are being counseled. Care should be taken to exclude the rare kindred in which the defect is a functional one with normal levels of protein C antigen.[11]

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