After overnight ventilation the alfentanil infusion was discontinued and the times of resumption of spontaneous ventilation and extubation were recorded. Arterial PCO_2 and respiratory rate were monitored and the endotracheal tube was not removed if the P_aCO_2 was above 6·5 kPa (48·75 mm Hg). The patient's first request for analgesia, after cessation of the alfentanil infusion, was recorded.

The average duration of the infusion was 796 min (range 540–1140) and the mean infusion rate and total dose were 0·4 μg $kg^{-1}min^{-1}$ (SEM±0·5) and 24·11 mg (±3·87) respectively. The clinical end-points are shown in the table.

POST-INFUSION MEASUREMENTS

—	Mean (SEM)	Range
Time (min) from end of infusion to:		
Start of spontaneous ventilation	35 (9·1)	5–75
Extubation	116·3 (21·4)	45–240
Demand for first analgesia (n = 8)	530·6 (77·5)	180–900
Hourly post-infusion respiratory rate (/min)		
1st hour	18·1 (1·1)	14–22
2nd hour	19·4 (1·2)	13–26
3rd hour	20·2 (1·2)	15–27
4th hour	19·4 (1·2)	16–28
5th hour	19·1 (1·2)	14–28
$PaCO_2$ *(kPa)*		
1 h of spontaneous ventilation	5·2 (0·2)	4·1–6·1
5 h of spontaneous ventilation	4·8 (0·1)	4·2–5·7

One patient persisted in fighting the ventilator and he received a further 1 mg bolus of alfentanil, supplemented by 2·5 mg midazolam with good effect. No patient developed tolerance to the effects of alfentanil. Three patients vomited in the immediate post-infusion period. In eight patients the first dose of post-infusion analgesia was given when requested, but two patients were electively given intramuscular papaveretum before removal of the chest drains. Although analgesia and sedation were not measured no patient indicated that he was in pain or had discomfort. On a follow-up interview the patients could not recall the period of ventilation.

The ideal agent for sedation during intermittent positive pressure ventilation would provide analgesia combined with good cardiovascular stability and rapid recovery from any respiratory depression. Currently, mixtures of opioids and benzodiazepines are the most widely used. Of the opioids, morphine and its derivatives are associated with a prolonged duration of action and the possibility of cardiovascular instability due to the release of histamine.[4] Pethidine has a half-life of about 250 min[5] and may cause tachycardia.[6] Fentanyl and its newer derivatives provide good cardiovascular stability, a lack of histamine release,[7] and a high therapeutic ratio. Of this group alfentanil has the shortest half-life (elimination half-life 100 min). Our small study suggests that alfentanil may be useful for the sedation of ventilated patients on the ITU. No evidence of respiratory depression (table) was detected in the post-infusion period. The mean P_aCO_2 was 4·9 (SEM 0·18), which is lower than that in previous studies.[8,9] However, in our hospital there have been two cases of respiratory arrest after alfentanil infusions in larger doses for analgesia (a bolus of 100 μg kg^{-1} followed by 1 μg $kg^{-1}min^{-1}$) during general anaesthesia (Sebel PS, unpublished).

Our impression is that in this category of patient alfentanil at a bolus dose of 15 μg kg^{-1} (1 mg) followed by infusion at 0·4 μg $kg^{-1}min^{-1}$ is a useful single agent for analgesia and sedation. At higher doses there may be a risk of respiratory depression.

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ANTIBODY TO LYMPHADENOPATHY-ASSOCIATED VIRUS IN HAEMOPHILIACS WITH AND WITHOUT AIDS

SIR,—Viral isolation and seroepidemiological studies indicate that the acquired immunodeficiency syndrome (AIDS) is caused by a T-cell lymphotropic retrovirus, known as lymphadenopathy-associated virus (LAV) or human T lymphotropic virus type III (HTLV-III). Patients with AIDS or lymphadenopathy syndrome and other groups at risk of AIDS have a higher incidence of antibody to LAV or HTLV-III than controls;[1–4] and Dr Melbye and colleagues (July 7, p 40) found antibody to this virus in healthy haemophilia patients in Denmark. We looked for antibody to LAV core protein p25 and envelope protein p41[1] in haemophiliacs living in Georgia who had no symptoms associated with AIDS. We also recorded the amount of factor VIII concentrate used and the presence of immune abnormalities. These tests were also done on haemophiliacs with AIDS or lymphadenopathy and on members of haemophiliacs' families.

Serum was collected from 25 patients with haemophilia A in the Hemophilia of Georgia home care treatment programme, 4 patients with haemophilia B, 15 haemophiliacs with AIDS, 2 brothers (aged 12 and 15) with haemophilia A and lymphadenopathy and their parents, the wife and 3 adult children of a haemophiliac with AIDS, and 5 controls. Questionnaires concerning possible risk factors for AIDS and present health status were administered to participants. The first 25 patients with haemophilia A had no other risk factor for AIDS, were healthy, and had no symptoms of AIDS. Sera from the haemophiliacs with AIDS were provided by the patients' private physicians.

Antibody to p25 and p41 antigens was determined by Western blot.[5] LAV was obtained from Dr J. C. Chermann, Pasteur Institut, Paris, and propagated in primary fetal cord lymphocytes.[1]

Antibody to both LAV proteins p25 and p41 was detected in the serum of 18 (72%) of 25 patients with haemophilia A who used factor VIII in 1980–82 but who had no symptoms associated with AIDS. White cell, total lymphocyte, T lymphocyte, and T helper and suppressor cell counts (Ortho Diagnostics), and the T helper to T suppressor ratio of the patients positive for LAV antibodies were not significantly different from those of the patients negative for LAV antibodies (table). The amount of factor VIII concentrate used by the patients positive for LAV antibodies was significantly higher than the amount used by the patients negative for the antibodies (Wilcoxon rank-sum test; $p = 0·008$). All the patients who received more than 150 000 units of factor VIII concentrate over the 3-year period were seropositive.

None of the 4 patients with haemophilia B had antibody to LAV. These patients were all being treated with factor IX concentrates but did not have abnormalities of the immune system. Records of concentrate usage were available for 2 patients; both had taken about 100 000 units over the 3-year period.

Of 15 AIDS patients with haemophilia A 5 had antibody to LAV p25 and p41 proteins. All 15 had severe immunosuppression, with T helper/T suppressor ratio ranging from 0·10 to 0·56. All had been treated with large amounts of factor VIII concentrates. Sera from one seropositive patient collected in 1978, 1982, and 1983 were available. This patient's serum was negative for LAV antibody in 1978, positive in October, 1982, after a 1-year prodrome of malaise and weight loss, and positive in July, 1983. The patient died in August, 1983.

Antibody was not found in the wife and 3 adult offspring of the haemophilia patient with AIDS or in the parents of the two haemophiliac siblings with lymphadenopathy. These 3 haemophiliacs used more than 50 000 units of factor VIII concentrate per year.

RELATION BETWEEN FREQUENCY OF ANTIBODY TO LAV p25 AND p41 PROTEINS, CELLULAR IMMUNE STATUS, AND FACTOR VIII CONCENTRATE USAGE IN 1980–82 IN SYMPTOM-FREE HAEMOPHILIA A PATIENTS: MEDIAN AND RANGE

	Positive for LAV antibody (n = 18)	Negative for LAV antibody (n = 7)	Normal
Cells (/μl)			
White blood cells	5050 (3700–7900)	6700 (3700–9600)	
Absolute lymphocytes	1984 (1000–3300)	1817 (1102–4000)	1050–3118
T	1389 (400–2574)	1163 (857–3040)	679–2061
T helper	505 (220–1083)	690 (353–1880)	408–1583
T suppressor	808 (133–1782)	574 (436–1949)	190–820
Helper:suppressor ratio	0·78 (0·34–2·16)	0·95 (0·46–1·74)	1·0–3·9
Factor VIII (units)	141 928 (30 010–484 170)	33 236 (4496–134 718)	

*Normal laboratory values

In this series 72% of symptom-free haemophilia A patients had antibody to LAV while Melbye et al, who used an enzyme-linked immunosorbent assay (ELISA), found antibody in 64% of patients, all but 1 of whom had haemophilia A. Antibody to LAV has been found in 63% of patients with lymphadenopathy associated syndrome (LAS) and 17% of healthy homosexual men in France[1] and in 72% of LAS patients and 24% of healthy homosexual men in the US.[4] Thus the prevalence of LAV antibody in haemophiliacs is greater than that in homosexuals and essentially the same as that found in LAS.

LAV is a lymphotropic retrovirus and would be expected to affect the cellular immune system. However, we found no association between cellular immune abnormalities and LAV antibody. Several explanations are possible—eg, small sample size, recent exposure to virus, immunity to LAV, or insensitivity of the testing system.

Haemophilia A patients who were seropositive for LAV had used significantly more factor VIII concentrate than had patients seronegative for LAV. This association would be expected if factor VIII concentrates contain LAV or its proteins. In contrast, the haemophilia patients with AIDS had a significantly lower antibody prevalence, perhaps because patients with AIDS have a declining antibody response to antigen despite paradoxically higher levels of circulating immunoglobulins.[6] 4 patients with haemophilia B were negative for LAV antibody and had normal cellular immunity. Patients with haemophilia B, in general, have not been found to have the degree of immune abnormalities seen in haemophilia A.[7,8]

These serological data, indicating a high risk of exposure to LAV for heavy users of factor VIII concentrate, support the contention that LAV may be transmitted by some blood products.

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PROPHYLAXIS OF PNEUMOCYSTIS CARINII INFECTION IN AIDS WITH PYRIMETHAMINE-SULFADOXINE

SIR,—*Pneumocystis carinii* pneumonia (PCP) is the most common opportunistic infection in patients with the acquired immunodeficiency syndrome (AIDS). Treatment with co-trimoxazole or pentamidine may be successful but recrudescence is frequent: of the first 15 patients with pneumocystis and AIDS diagnosed here 5 had a histologically confirmed recurrence and of 10 patients referred after successful treatment for PCP elsewhere 5 had a biopsy-proven recrudescence. In animal studies[1,2] and in AIDS patients[3] co-trimoxazole or pentamidine do not eradicate *P carinii* despite clinical resolution. Oral co-trimoxazole prophylaxis can prevent pneumocystosis in leukaemic children,[4] and prophylaxis has been recommended for patients in whom the estimated risk of disease recurrence is 5–10% per year or more.[5] Patients with AIDS who have had one episode of PCP would seem to be prime candidates for such prophylaxis. Unfortunately, co-trimoxazole in AIDS patients is complicated by hypersensitivity reactions and other serious side-effects.[6–8] As an alternative means of prophylaxis in AIDS patients with a proven first episode of PCP and adverse reactions to co-trimoxazole, we have tried the antimalarial agent 'Fansidar' (pyrimethamine and sulphadoxine in a 1:20 ratio). Pyrimethamine-sulphadoxine was successfully used by Dutz et al to limit endemic infantile pneumocystosis in Shiraz, Iran, in 1965-74.[9,10] For prophylaxis, this drug has the advantage of a long half-life (130 h).

The 12 patients selected for this pilot study had AIDS complicated by histologically confirmed PCP and adverse reactions to co-trimoxazole. In 11 PCP had been the presenting manifestation of AIDS. All patients' T helper/inducer cell counts were below 200/μl. 10 patients had hypersensitivity skin reactions to co-

FANSIDAR PROPHYLAXIS OF PNEUMOCYSTIS PNEUMONIA IN AIDS

Patient (and date of PCP diagnosis)	Duration of fansidar prophylaxis (mo)	Recurrent PCP	Current status
1 (Jan, 1983)	12+	No	Alive; *M avium intracellulare*, cryptosporidiosis, CMV retinitis
2 (April, 1983)	1	No	Dead; KS
3 (Feb, 1983)	12+	No	Dead; KS, CNS toxoplasmosis
4 (Nov, 1983)	3+	No	Dead
5 (Feb, 1983)	0*	No	Dead; disseminated CMV
6 (Nov, 1983)	4·5+	No	Dead
7 (Feb, 1983)	12+	No	Dead; *M avium intracellulare*, CMV retinitis
8 (Nov, 1983)	5+	No	Alive; KS
9 (Nov, 1983)	3·5+	No	Alive; *M avium intracellulare*, cryptosporidiosis
10 (Aug, 1983)	9+	No	Dead; KS
11 (Aug, 1983)	0*	Yes	Alive; stable
12 (Feb, 1984)	3+	No	Alive; stable

*Reacted to first dose of fansidar.