Transmission of tuberculosis in British centre for patients infected with HIV

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Patients infected with HIV are at particular risk of tuberculosis, because of both the reactivation of latent infection and the rapid development of disease after exposure to any new source of infection. Many outbreaks of tuberculosis in patients infected with HIV and in the carers of those patients have occurred in hospitals and other institutions in the United States and Europe.^{1,2} Those with tuberculosis caused by multiple drug resistant strains have been associated with a high mortality.

Study of the epidemiology of tuberculosis has been helped by restriction fragment length polymorphism analysis with the insertion sequence IS6110. This repetitive element is randomly inserted, usually in multiple copies, in the genomic DNA of members of the *Mycobacterium tuberculosis* complex. A standardised methodology for this technique has been proposed.³ We used this methodology to investigate a cluster of cases of tuberculosis in a British care centre for patients infected with HIV.

Method and results

We examined 96 strains of *Mycobacterium tuberculosis* that had been isolated from 69 patients infected with HIV and had been referred to the regional tuberculosis centre at Dulwich Public Health Laboratory between August 1991 and June 1993. We compared the strains with control strains from 84 patients not infected with HIV that had been referred by the same laboratories during the same period. The source laboratories comprised all but one of those that served the care centres for patients infected with HIV in south east England at the time of the study.

DNA was extracted from a fresh subculture of each strain and digested with restriction endonuclease *Pvu* II. DNA fragments were separated by agarose gel electrophoresis and blotted on to nylon membrane. After hybridisation with an IS6110 probe labelled with digoxigenin, fragments containing this sequence were detected by chemiluminescence. The patterns obtained were compared visually.

All the strains contained at least one IS6110

sequence. Except for three pairs and one cluster of four cases, all from the patients infected with HIV, the strains isolated from different patients had different patterns of restriction fragment length polymorphism. We reviewed the case notes of the four patients who had strains with no distinguishable differences (table).

Comment

The first three cases are epidemiologically related: two patients (cases 2 and 3) were in a ward with a patient (case 1) whose sputum smear test yielded a positive result and in whom bronchoscopy was performed in the ward. The two patients both had low CD4 lymphocyte counts and developed disseminated tuberculosis within several weeks of exposure to the other patient. The relationship between these three patients and a fourth (case 4) is not known. The latter was a man who had never been married, had no known contact with hospital 1, and resisted attempts at contact tracing. An intermediate patient whose strain was not referred to us was perhaps involved.

This small cluster of cases shows the rapid progression and dissemination of mycobacterial infection in patients with advanced HIV disease. The outbreak would not have been recognised without restriction fragment length polymorphism analysis. Recognition and investigation of future outbreaks might be helped if all strains of tuberculosis are routinely stored and typed at reference laboratories.

Tuberculosis that is acquired in a hospital might be prevented by attention to infection control precautions designed to limit the spread of airborne pathogens. Guidelines have been published by the Centers for Disease Control, Atlanta,⁴ and the British Thoracic Society.⁵ Probably the most important factors are the early recognition of tuberculosis and the adequate isolation of cases. Also, procedures likely to generate aerosols, such as bronchoscopy, should be performed in a suitable environment. Units that care for patients infected with HIV should review their procedures and policies for preventing and managing tuberculosis. Conversion of such units to the standards recom-

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BMJ 1994;309:639-40

Details of four patients* positive for HIV antibodies from whom strains of *Mycobacterium tuberculosis* with no distinguishable differences were isolated†

Case No	Age (years)	CD4 count (cells × 10 ⁹ /l)	Date of admission(s)	Location	Reason for admission	Tuberculosis diagnosed	Outcome
1	23	100	Jun to Aug 1992	Wards A and B, hospital 1	Pulmonary tuberculosis	<i>M tuberculosis</i> isolated from bronchoalveolar lavage fluid and sputum, Jun 1992	Recovered with standard treatment for tuberculosis
2	27	30	Jun to Jul 1992	Ward B, hospital 1	Retinal branch vein occlusion	<i>M tuberculosis</i> isolated from bronchoalveolar lavage fluid and liver biopsy specimen, Sep 1992	Responded to treatment for tuberculosis Died Apr 1993 from other disease related to HIV infection
			Aug to Oct 1992	Ward B, hospital 1	Disseminated tuberculosis		
3	42	30	Jun 1992 Jul 1992 Aug 1992	Ward B, hospital 1 Ward B, hospital 1 Wards B and C, hospital 1	Cytomegalovirus retinitis Hickman line infection Sepsis syndrome	<i>M tuberculosis</i> isolated from blood and urine, Aug 1992; acid fast bacilli seen in mediastinal lymph node at postmortem examination	Died Aug 1992
4	41		Feb 1993	Hospital 2	Pulmonary tuberculosis	<i>M tuberculosis</i> isolated from bronchoalveolar lavage fluid, sputum, and urine, Feb 1993	Recovered with treatment for tuberculosis

*All patients were men except case 2.

†On basis of pattern of restriction fragment length polymorphism and antimicrobial sensitivity.

mended by the Centers for Disease Control might be expensive but should be considered carefully.

The equipment used in this study was bought with a grant to ALP from King's College School of Medicine and Dentistry. NGS was funded partly by the Overseas Development Administration.

- 1 Uttley AHC, Pozniak A. Resurgence of tuberculosis. *J Hosp Infect* 1993;23: 249-53.
- 2 Di Perri G, Danzi MC, De Checchi G, Pizzighella S, Solbiati M, Cruciani M,

- et al.* Nosocomial epidemic of active tuberculosis among HIV-infected patients. *Lancet* 1989;ii:1502-4.
- 3 Van Embden JDA, Cave MD, Crawford JT, Dale JW, Eisenach KD, Gicquel B, *et al.* Strain identification of *Mycobacterium tuberculosis* by DNA fingerprinting: recommendations for a standardized methodology. *J Clin Microbiol* 1993;31:406-9.
- 4 Centers for Disease Control. Guidelines for preventing the transmission of tuberculosis in health-care settings, with special focus on HIV-related issues. *Morbidity and Mortality Weekly Report* 1990;39 (RR17):1-29.
- 5 Subcommittee of the Joint Tuberculosis Committee of the British Thoracic Society. Control and prevention of tuberculosis in Britain: an updated code of practice. *BMJ* 1990;300:995-9.

(Accepted 27 April 1994)

Relation between alcohol and nose bleeds

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BMJ 1994;309:640

Nose bleeds in adults are the commonest reason for emergency admission to an otolaryngology ward, but the cause of the condition remains unknown. Case reports and clinical experience suggest an association between nose bleeds and regular, high alcohol consumption.¹

The possibility that alcohol is a causal factor in nose bleeds is supported by evidence of profound cardiovascular and haemostatic effects produced by even moderate alcohol consumption. We conducted a prospective case-control study to compare the alcohol habits of adults with nose bleeds with those of controls being treated for other otorhinolaryngological conditions.

Subjects, methods, and results

The alcohol habits of 140 consecutive patients admitted with nose bleeds (79 men; mean age 54.5 years, range 23-93) were compared with those of 113 age and sex matched controls selected from patients being treated for otorhinolaryngological conditions other than nose bleeds (65 men; 56.4, 21-92). Patients whose nose bleeds were secondary to a known cause such as trauma, anticoagulant treatment, or blood dyscrasia were excluded.

All patients were interviewed by an admitting doctor within 24 hours of admission, and a questionnaire was used to record a history of alcohol consumption for each patient.

We defined them as non-drinkers if they never drank alcohol; occasional drinkers if they drank alcohol less than once a week; and regular drinkers if they drank alcohol more than once a week. We estimated units of alcohol drunk each week for occasional and regular drinkers by using their self reports of an average week in which they drank alcohol; one unit was regarded as one measure of spirits, one glass of wine, or one half pint (284 ml) of beer.² Also we recorded whether the patients had drunk alcohol within 24 hours of admission.

The table shows results of the questionnaire. The proportion of non-drinkers in the patients with nose bleeds was similar to that in the controls (34% (47/140) v 35% (39/113)), but the proportion of regular drinkers was significantly higher (45% (63/140) v 30 (34/113); $P < 0.025$, χ^2 test of proportions). The patients with nose bleeds drank more alcohol than the controls (33 (mean) units a week v 7).

Because of the skewed distribution of alcohol consumption, we compared the patients and controls with the Mann-Whitney U test, which showed a significant

difference ($P < 0.01$). This difference remained when the non-drinkers were excluded and was apparent also both for men and for women, although men drank more units of alcohol than women both in the patients with nose bleeds and in the controls. These differences in frequency and amount of alcohol consumption were supported by the finding that the patients with nose bleeds were significantly more likely than the controls to have drunk alcohol within 24 hours of admission ($P < 0.01$, χ^2 test of proportions).

Comparison of 140 patients with nose bleeds and 113 controls by amount and frequency of alcohol consumption. Values are numbers (percentages) of patients and controls unless stated otherwise

Alcohol consumption	Patients (n=140)	Controls (n=113)	Significance
Non-drinkers	47 (34)	39 (35)	
Occasional drinkers	30 (21)	40 (35)	
Regular drinkers	63 (45)	34 (30)	$P < 0.025$
Alcohol drunk within 24 hours of admission	63 (45)	31 (27)	$P < 0.01$
No of units of alcohol per week:			
Median	10.0	2.0	$P < 0.01$
Interquartile range	0-50	0-10	

Comment

This study confirms an association in adults between regular, high alcohol consumption and nose bleeds. The method for recording alcohol history was similar to that used in a survey of Scottish drinking habits.² Although self report of drinking habits may under-report alcohol consumption, any inaccuracy is likely to be found both in the patients with nose bleeds and in the controls.

Arterial nose bleeds in adults are serious and potentially life threatening whose cause is undetermined in 85% of cases.³ Our finding that alcohol is an important causal factor in nose bleeds is supported by the growing evidence of the cardiovascular and cardio-respiratory effects of alcohol. Regular alcohol consumption reduces platelet aggregation and prolongs the bleeding time; these effects, coupled with haemodynamic changes such as vasodilatation and changes in blood pressure, may be important in causing some cases of arterial nose bleeds in adults.^{4,5} While the cause of nose bleeds in adults is likely to be multifactorial, the importance of high alcohol consumption should not be overlooked, and a detailed alcohol history should always be obtained.

- 1 Jackson KR, Jackson RT. Factors associated with active, refractory epistaxis. *Arch Otolaryngol Head Neck Surg* 1988;114:862-5.
- 2 Dight SE for the Office of Population Censuses and Surveys. *Scottish drinking habits*. London: HMSO, 1976.
- 3 Stell PM. Epistaxis. *Clin Otolaryngol* 1977;2:263-73.
- 4 Hart MJ, Cowan DH. The effect of ethanol on hemostatic properties of human blood platelets. *Am J Med* 1974;56:22-33.
- 5 Klatsky AL, Friedman GD, Sieglaub AB, Gerard MJ. Alcohol consumption and blood pressure: Kaiser-Permanente multiphasic health examination data. *N Engl J Med* 1977;296:1194-2000.

(Accepted 18 May 1994)