

large cities in industrialised nations.⁵ This might be because tuberculosis may be suspected and investigated more readily among men or black or Asian people.

Our study was limited by the amount of missing surveillance data. It was also impossible to determine the relative contribution of patient and healthcare provider to the total delay. Potential confounders—for example, coinfection with HIV or the accuracy of the data among patients whose first language was not English—were not taken account of.

Recent campaigns have tried to raise awareness of tuberculosis, particularly among ethnic minority groups. Our data suggest that campaigns also need to be targeted at white people, who comprise a third of cases.

We thank John Watson for access to the anonymised data from the national tuberculosis survey 1998.

Contributors: AR, SJ, SP, and AH conceived and designed the study. AR and SJ conducted the analysis. JC manages the

database. AR drafted the paper and all authors revised drafts and approved the final version. AR is guarantor.

Funding: Shabbar Jaffar is supported by a Medical Research Council strategic grant in epidemiology.

Competing interests: None declared.

- 1 Wright A, Atkinson P, Maguire H. *Communicable Disease Surveillance in London 2000*. London: Communicable Disease Surveillance Centre, 2001.
- 2 Zahar JR, Azoulay E, Klement E, De Lasseuse A, Lucet JC, Regnier B, et al. Delayed treatment contributes to mortality in ICU patients with severe active pulmonary tuberculosis and acute respiratory failure. *Intensive Care Med* 2001;27:513-20.
- 3 Chin DP, Crane CM, Diul MY, Sun SJ, Agraz R, Taylor S, et al. Spread of Mycobacterium tuberculosis in a community implementing recommended elements of tuberculosis control. *JAMA* 2000;283:2968-74.
- 4 Wares D. Delay in diagnosis of tuberculosis: of remaining concern in England and Wales. *J Public Health Med* 1999;21:355-6.
- 5 Rodrigo T, Cayla JA, Galdos Tanguis H, Garcia de Olalla P, Brugal MT, Jansa JM. Proposing indicators for evaluation of tuberculosis control programmes in large cities based on the experience of Barcelona. *Int J Tuberc Lung Dis* 2001;5:432-40.

(Accepted 4 December 2002)

Drug points

Erythromelalgia induced by possible calcium channel blockade by ciclosporin

Gurvinder P Thami, Mala Bhalla

Erythromelalgia, a symptom complex of painful inflammatory vasodilatation of extremities, is usually idiopathic or due to thrombocythaemia. It has often been regarded as inverse Raynaud's phenomenon, rarely induced by calcium channel blockers.¹ We report a case of erythromelalgia induced by ciclosporin.

A 37 year old man had been taking ciclosporin 75 mg twice daily for psoriasis vulgaris for four weeks when he developed marked erythema, oedema, and tenderness over fingers and toes. Symptoms increased with warmth and were relieved partially with cold compresses. His full blood count, serum biochemistry, urine analysis, and collagen profile were normal. Erythromelalgia induced by ciclosporin was considered, and the drug was withdrawn. Lesions regressed within a week but recurred when ciclosporin was restarted. No recurrence was observed at one year follow up.

Erythromelalgia is a multifactorial peripheral vascular phenomenon akin to sympathectomy, with attenuation of vasomotor tone probably mediated through vasoactive substances and drugs such as nifedipine, nicardipine, verapamil, and bromocriptine.¹

Ciclosporin, a calcineurin antagonist, acts by inhibiting calcium-calmodulin signalling systems of target cells in a way similar to calcium channel blockers.² It binds to calmodulin, with a consequent inhibition of dephosphorylation of calmodulin induced kinases and other calmodulin dependent intracellular activities.³ Ciclosporin also affects the calmodulin regulated activity of the actomyosin complex of smooth muscle of peripheral vessels, which leads to vasodilatation. In this way, ciclosporin has also been observed to potentiate the peripheral vasodilatory effects of calcium channel blockers.⁴

The erythromelalgia in this patient may have been the result of ciclosporin acting in a similar way to calcium channel blockers. Though burning sensation of the hands and feet has been mentioned as an adverse effect in the product leaflet of ciclosporin (Panimun Bioral, Panacea Biotec) and a leg pain syndrome has been described, an erythromelalgia-like effect has not been reported.⁵ This possible vasoactive effect of ciclosporin needs further

evaluation given that vasoactive peptides may be present in psoriasis.

Funding: None.

Competing interests: None declared.

- 1 Levesque H, Moore N, Wolfe CM, Courtois M. Erythromelalgia induced by nicardipine. *BMJ* 1989;298:1252-3.
- 2 Kanitakis J, Thivolet J. Cyclosporine. An immunosuppressant affecting epithelial cell proliferation. *Arch Dermatol* 1990;126:369-75.
- 3 Colombani P, Robb A, Hess A. Cyclosporin A binding to calmodulin: a possible site of action on T-lymphocytes. *Science* 1985;228:337-9.
- 4 Von Vigier RO, Fossali E, Edefonti A, Vogt B, Bianchetti MG. Cyclosporin enhances the tendency towards oedema and flushing noted on dihydropyridine calcium channel blockers. *Br J Clin Pharmacol* 2002;54:333-6.
- 5 Naredo Sanchez E, Balsa Criado A, Sanz Guajardo A, Pantoja Zarza L, Martin Mola E, Gijn Banos J. Leg bone pain syndrome due to cyclosporine in a renal transplant patient. *Clin Exp Rheumatol* 1994;12:653-6.

Corrections and clarifications

Mark Twain on evidence based practice

This Endpiece attributed the quotation "It ain't what people don't know that hurts them it's what they know that ain't so" to Mark Twain (25 January, p 211). However, a reader has corrected us, confirming that this quotation is attributable not to Mark Twain but to Josh Billings (and in support has cited various sources, including the *Penguin Dictionary of Modern Humorous Quotations*, Penguin, 1987). A trawl of the web, however, has revealed that people often get it wrong, attributing the quotation in question not to Josh Billings but to Mark Twain—or to Will Rogers or Herbert Stein (or possibly others). The quotation always appears in slightly different forms; indeed, the one cited in the Penguin dictionary is not exactly the same as the one we published.

Filler: He died "peacefully" at home

Although editors are aware of the dangers of confusing words that differ in spelling by only one letter, there is always a danger that the wrong word will slip through. Unfortunately, this is what happened in this account by David Veale of the death of his father—we used the word prostrate, rather than prostate (12 April, p 792).

Department of Dermatology and Venereology, Government Medical College and Hospital, Sector 32 B, Chandigarh, 160047, India
Gurvinder P Thami
reader
Mala Bhalla
senior resident
Correspondence: G P Thami
thamigp@yahoo.com

BMJ 2003;326:910