period in which pyrazinamide was not prescribed and served as controls; they were treated by the same method.

The table shows the mean concentrations of pyrazinamide in the serum and cerebrospinal fluid two, five, and eight hours after dosage. Two hours after dosage the concentrations in the cerebrospinal fluid were about 75% of those in serum, but at five and eight hours cerebrospinal fluid concentrations were about 10% higher than the corresponding serum values. Penetration of pyrazinamide into the cerebrospinal fluid was not influenced by the clinical stage of disease at presentation, the presence or absence of active disease, the concomitant use of steroids, the duration of antituberculosis treatment before the sample of cerebrospinal fluid was obtained, the administration of either ethambutol or streptomycin, or the age or sex of the patient. The extent to which pyrazinamide penetrated into the cerebrospinal fluid was remarkably similar among all the patients, and most of the variability in the calculated ratios of cerebrospinal fluid to serum pyrazinamide concentrations was estimated to be due to errors inherent in the analytical procedure.

Mean (SD) concentrations of pyrazinamide in serum and cerebrospinal fluid

Hours after dosage	No of samples	Pyrazinamide dosage (mg/kg)	Concentration (mg/l)		Ratio of cerebrospinal fluid to serum concentration
			Serum	Cerebrospinal fluid	
2	64	41 (8)	52·0 (14·7)	38·6 (11·1)	0·74 (0·14)
5	14	36 (9)	39·5 (13·1)	44·5 (13·8)	1·15 (0·22)
8	14	34 (6)	28·4 (5·1)	31·0 (6·7)	1·09 (0·11)

Comment

The excellent penetration of pyrazinamide across the blood-brain barrier was to be expected in view of its physicochemical properties: it is moderately lipophilic, uncharged at body pH, and not bound to serum proteins. In view of its unique bactericidal activity against tubercle bacilli in an acid environment resulting from local inflammation,[5] its important contribution in short course treatment of pulmonary tuberculosis,[1] and its excellent penetration into the cerebrospinal fluid we recommend that pyrazinamide should be included in treatment regimens for tuberculous meningitis.

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(Accepted 16 October 1986)

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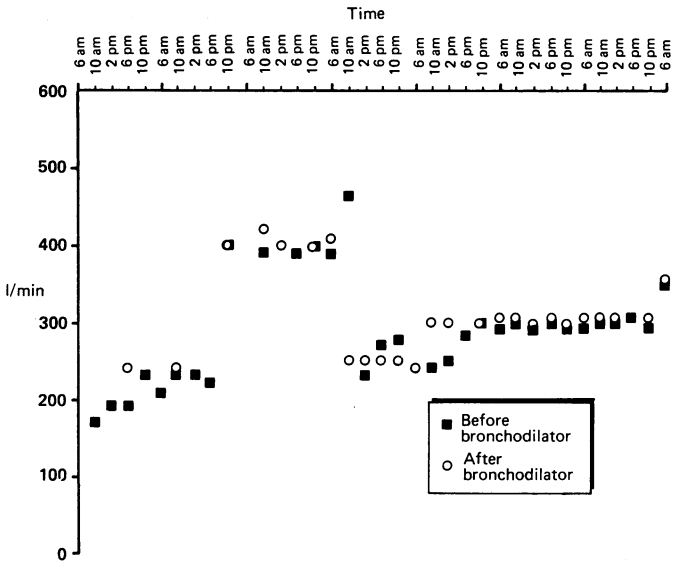
Falsely high peak expiratory flow readings due to acceleration in the mouth

Asthma is a major cause of morbidity and mortality, which might be reduced by a more aggressive approach to diagnosis and management.[1] Peak flow rate is often used particularly in continuous monitoring, to diagnose and assess the response to treatment of asthma and other forms of airway obstruction[2] and may be the most satisfactory method of assessing the response in chronic partially reversible airway obstruction.[3] Though the normal range is wide (about a third of the normal mean measurement) repeated measurements usually give consistent results in normal subjects and many patients with persistent obstruction. Some subjects, however, cannot produce consistent results, while others produce falsely high figures by accelerating the air flow from the mouth with a spitting action.

I report such a case.

Case report

A man aged 64 with a long history of increasing breathlessness and wheeze and previous doubtful response to bronchodilators was admitted for a formal assessment of his response to maximal doses of bronchodilators and corticosteroids. The peak expiratory flow rate was recorded every four hours. He was treated with nebulised salbutamol, and after three days the peak flow rate suddenly increased without apparent immediate response to a bronchodilator (figure). When asked to show how he used the peak flow meter, the patient performed a spitting action, using the tongue and buccal musculature to accelerate the air through the mouth. When he used the simple maximal blow the peak flow rate fell to previous levels. Further recordings showed a slow rise, compatible with gradual clinical improvement.



Four hourly peak flow chart showing the different measurements achieved by the patient with the correct technique and the trick manoeuvre.

Comment

The ability to accelerate the peak flow rate has been seen in several patients. In this case a mini peak flow meter with a mouthpiece circular in cross section was used. The patient put the mouthpiece just inside his lips, but when asked to put it further back into the mouth so that it overlay the anterior part of the tongue, he could not perform the trick manoeuvre. The peak flow rate could not be accelerated beyond that obtained with the mouthpiece forward in the mouth using a simple blow. Though this patient was using the mini meter, the phenomenon has also been seen in patients using a standard instrument. This may, however, be slightly more difficult to manipulate—for example, another patient with peak flow rates of about 250 l/min produced readings of 295, 375, and 305 l/min with a standard instrument and 390, 410, and 420 l/min with the mini meter. This patient could also produce falsely high readings only with a mouthpiece of eliptical rather than circular cross section. Six attempts in random order produced readings of 250, 250, 270 l/min with a circular mouthpiece and 400, 420, and 420 l/min with the mouthpiece of eliptical section. The patient stated that he could not manipulate his tongue into the orifice of the circular mouthpiece.

This phenomenon has not been seen in patients during standard spirometry, presumably because of the emphasis on full expiration. The problem can usually be avoided if the mouthpiece is well inside the mouth, overlying the tongue, and is less likely to occur if a mouthpiece of circular rather than eliptical cross section is used. The standard peak flow meter may be slightly less susceptible to this manipulation than the mini meter.

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(Accepted 3 October 1986)

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