avoided by heating the spirometer or using a heated pneumotachograph. The problem of truncation of the spirogram has previously been argued in the literature and limits the usefulness of MTT (3). Other time domain indices have been shown to be of value in that they more readily identify subjects whose results deviate from expected normal values (4). I agree with the authors view that MTT is unlikely to play a major part in the clinical evaluation of lung function in children. However, the reasons behind this finding should have been more adequately presented and it is possible that other time domain indices, such as a truncated first moment, could be extremely useful in a paediatric population.

M. R. MILLER
4 November 1992

References

Reply to the letter from Dr Miller

We accept that volume measurements may be overestimated by assuming instantaneous cooling to room temperature of air in a wedge spirometer, and that mean transit time may therefore be underestimated by as much as 15%.

However, because children reach the plateau of the forced expirogram much earlier than adults (which is why many paediatricians use FEV<sub>0.75</sub> rather than FEV<sub>1.0</sub> in many children having completed the manoeuvre within 1 s), the prolonged terminal phase of the expirogram, which bedevils studies on adults, is seldom seen in children, even in asthmatics, and the effects of truncation at 95% FVC would therefore be much less than in adults. In our study, readings which failed to stabilize were discarded; such tracings usually lasted for less than 3 s before the child inspired. As our analyses were performed manually, we are not in a position to reanalyse the tracings following truncation, although we agree that this, and the examination of other time domain indices, would be an interesting exercise.

Nevertheless, the effects of delayed cooling cannot be ignored and we are grateful to Dr Miller for drawing our attention to this problem.

M. HUDSON, T. K. NINAN AND G. RUSSEL
3 December 1992

Dear Editor

The phenomenon of rifampicin-induced discolouration of body fluids is well recognized, and urine discolouration is widely used as a simple method of monitoring treatment compliance. We report a case in which the red discolouration disappeared temporarily in spite of continued and verified patient compliance.

A 70-year-old non-insulin-dependent man was admitted with smear positive pulmonary tuberculosis. Sputum culture subsequently grew Mycobacterium tuberculosis, sensitive to the standard drugs. He was treated as an in-patient with rifampicin 10 mg kg<sup>−1</sup> d<sup>−1</sup>, isoniazid 300 mg daily, and pyrazinamide 25 mg kg<sup>−1</sup> d<sup>−1</sup>. His only other medication was pyridoxine and gliclazide. Initially, as expected, his urine turned reddish-orange in colour, but after 3 weeks it was noticed that his urine colour had returned to normal, even though supervised treatment in hospital had continued throughout.

The N-butanol extraction test was employed in further investigation of this phenomenon. Urinary rifampicin concentrations of greater than 50 μg ml<sup>−1</sup> are usually visible to the naked eye, but the assay detects unmetabolized rifampicin in urine and can conveniently be used to identify urinary concentrations down to 2.5 μg ml<sup>−1</sup> (1). In this patient the level of rifampicin detected in the urine by N-butanol extraction was unrecordable. Nevertheless, a sample of his urine showed considerable bactericidal activity against a precultured Staphylococcus colony, indicating, in the absence of any other active antibiotic, the presence of a specific antistaphylococcal agent(s).

After 2 months treatment, the pyrazinamide was discontinued. At this point, the reddish-orange discolouration of his urine returned. A repeat N-butanol extraction assay for rifampicin revealed significant amounts of the unchanged drug in the urine.

It is well known that rifampicin and its metabolites are chromogens and impart an orange colouration to body secretions, including urine (2). The main metabolite, desacetylrifampicin, is microbiologically active, with bile as the main route of elimination (3). Desacetylation of rifampicin most probably takes place in the hepatocyte and results in a more polar compound, which facilitates its excretion in bile.

The ability of rifampicin, pyrazinamide and other drugs to induce such reactions reliant on cytochrome