health: those needing to abstain may unwittingly drink if they believe low alcohol drinks to be effectively alcohol free. Others wanting to limit their drinking by counting units may drink far more than their chosen amounts if they fail to make adjustments for extra strong drinks.

There are two possible strategies for minimising these errors. Firstly, all drinks could have their alcohol content clearly labelled in units as well as in percentage alcohol by volume. This suggestion was endorsed by nearly all our subjects. Secondly, posters and leaflets providing current data on the strengths of commonly

available drinks, similar to those provided by the Health Education Council for the tar and nicotine contents of cigarettes, could be widely distributed.

- 1 Royal College of Psychiatrists. *Alcohol—our favourite drug*. London: Tavistock, 1986.
- 2 Royal College of General Practitioners. *Alcohol—a balanced view*. London: RCGP, 1986.
- 3 Royal College of Physicians. *Alcohol—a great and growing evil*. London: Tavistock, 1987.
- 4 Robertson I, Heather N. *Let's drink to your health! A self-help guide to sensible drinking*. Leicester: British Psychological Society, 1986.

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Digoxin toxicity due to interaction of digoxin with erythromycin

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Both erythromycin and digoxin cause gastrointestinal side effects. Erythromycin, however, may double digoxin concentrations in a minority of patients, and gastrointestinal side effects may mistakenly be attributed to it. We describe a patient in whom a course of erythromycin was associated with cardiac and gastrointestinal complications of digoxin toxicity.

Case report

A 59 year old woman (weight 50.1 kg) presented with bradycardia and a two day history of nausea and vomiting four days after starting erythromycin 500 mg three times a day for an upper respiratory tract infection. She had received maintenance treatment with digoxin (0.25 mg/day) and warfarin since 1972 after a mitral valve replacement. For three years she had received bumetanide (1 mg/day) and potassium chloride (Slow K; 16 mmol/day). Eighteen months previously her serum digoxin concentration had been 2.3 nmol/l (therapeutic range 1.0-2.8 nmol/l). On examination she had an irregular heart rate (40-50 beats/min) and cardiomegaly. An electrocardiogram confirmed slow atrial fibrillation (rate 40 beats/min), right bundle branch block with left anterior hemiblock, and ventricular bigeminy (figure (top)). Biochemical investigation showed normal plasma urea, sodium, and calcium concentrations and liver enzyme activities. Plasma potassium concentration was 3.6 mmol/l, serum digoxin concentration 4.7 nmol/l, and the international normalised ratio of the prothrombin time 2.4.

Twenty four hours after digoxin and erythromycin were stopped her symptoms and the arrhythmia resolved. Electrocardiography showed atrial fibrillation (rate 60 beats/min) without evidence of a

ventricular conduction defect (figure (bottom)). Two weeks after she was discharged taking her usual treatment her serum digoxin concentration was 2.7 nmol/l. She recalled that one year earlier she had experienced similar symptoms during a course of erythromycin.

Comment

For many years digoxin was generally considered to be excreted unchanged in the urine, but it is now clear that in about 10% of patients ("excretors") 30-40% of the drug is excreted in the urine as reduced metabolites.¹ Compared with digoxin, its principal metabolites are taken up less well by cardiac muscle and have less cardiac activity, and some are more rapidly excreted in the urine.² Some patients may therefore require daily doses as high as 1-2 mg.^{1,3}

Urinary concentrations of these metabolites fall considerably and the serum digoxin concentration rises by as much as twofold after a change to a formulation of digoxin with greater bioavailability or during treatment with erythromycin or tetracycline.⁴ These effects are due to reduction of digoxin by *Eubacterium lentum*, a common constituent of the normal gut flora. Other unknown factors, however, must also play a part as stool cultures from a fifth of "non-excretors" also grow this organism.⁵ Whether other commonly used antibiotics cause a similar interaction is not known, but a preliminary report suggests that the β lactam antibiotics have little effect and that in vitro sensitivity of *E. lentum* to an antibiotic does not mean that the formation of digoxin metabolites will be reduced.²

Suspicion of an interaction may be aroused by the need for high oral doses of digoxin. This was not, however, the case with our patient. Nevertheless, her gastrointestinal symptoms one year previously might have been due to digoxin toxicity and might have warned of future problems. Preparations of digoxin with greater bioavailability, such as encapsulated liquid digoxin or paediatric elixir, may reduce the risks of such interactions.⁴ Alternatively, a temporary reduction in the dose of digoxin should be considered when erythromycin or tetracycline is required.

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Electrocardiographic recordings obtained from lead II on day of admission (top) and next day (bottom)

- 1 Peters U, Falk LC, Kalman SM. Digoxin metabolism in patients. *Arch Intern Med* 1978;138:1074-6.
- 2 Lindenbaum J. The dihydrogenation of digoxin. In: Erdman E, Greef K, Skou JC, eds. *Cardiac glycosides 1785-1985*. New York: Springer-Verlag, 1985: 263-8.
- 3 Luchi RJ, Gruber JW. Unusually large digitalis requirements: a study of altered digoxin metabolism. *Am J Med* 1968;45:322-8.
- 4 Lindenbaum J, Rund DG, Butler VP, Tse-Tung D, Saha JR. Inactivation of digoxin by the gut flora: reversal by antibiotic therapy. *N Engl J Med* 1981;305:789-93.
- 5 Dobkin JF, Saha JR, Butler VP, Neu HC, Lindenbaum J. Digoxin-inactivating bacteria: identification in human gut flora. *Science* 1983;220:325-7.

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