altitude,[8 9] and neurotransmitter depletion[10] and membrane depolarisation[11] may occur. Fluid shifts[12 13] and endocrine changes[14] are described, but whether they are cause or effect is not clearly established.

Acute mountain sickness usually occurs during the first few days at altitude, before respiratory acclimatisation is complete.[15] During this time renal and perhaps other mechanisms partly correct the respiratory alkalosis that initially limits the ventilatory response to hypoxia.[16] Herein lies the rationale for prophylaxis with acetazolamide, a sulphonamide that inhibits renal carbonic anhydrase causing bicarbonate diuresis and extracellular acidosis. Though it was possible to acidify the blood with ammonium chloride and produce in the alveoli a higher partial pressure of oxygen and lower partial pressure of carbon dioxide,[17] there was no symptomatic benefit.[18] Acetazolamide has, however, been shown repeatedly to lower blood pH, improve blood gases, and improve symptom scores for acute mountain sickness.[1 19-24] It produces striking improvements in sleep hypoxaemia and quality of sleep,[25 26] reduces proteinuria,[27] improves exercise performance, and reduces loss of muscle mass,[28] probably by improving oxygen supply to the tissues. It is not useful in treating established acute mountain sickness.

Doses used have varied from 250 mg to 1 g daily, and probably 500 mg daily as a sustained release preparation begun in the 24 hours before ascent is adequate. Methazolamide appears equally effective.[29] Side effects from acetazolamide are irritating rather than serious: paraesthesia is common but tolerable; fizzy drinks taste flat; and "beer tastes awful."[2] Sensitivity to sulphonamides is a contraindication. There are advocates of dexamethasone[30] and those who prefer spironolactone in prophylaxis.[31 32]

Should we recommend general acetazolamide prophylaxis for acute mountain sickness as recently proposed?[33] Minor symptoms are reduced and performance is improved, but there are many recorded cases of severe acute mountain sickness in those taking acetazolamide.[22 34 35] We lack proof, but freedom from minor symptoms probably encourages people to go "too high too fast" and so be attacked by severe disease without warning. The mainstay of prevention should be sensible rates of ascent that are modified further if symptoms occur. Those who make emergency ascents on rescue missions and those who have previously suffered acute mountain sickness at reasonable ascent rates are candidates for drug prophylaxis. Many, however, are unwilling to pay the "price of acrophilia,"[35 36] and the demand for drug prophylaxis is likely to remain high.

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Overexposure to radiology

Three factors contribute to the excessive use of ionising radiation in radiology: inappropriate examinations, an excessive number of films per examination, and repeat exposures during an examination. A working party of the Royal College of Radiologists as well as the World Health Organisation have taken leading roles in publishing guidelines on the first of these.[1-3] Recently a Cardiff group closely aligned to the working party has reported on the frequency with which radiographers at different hospitals repeat films.[4] The overall repeat rate was 10%, though nearly half the departments exceeded this. One department repeated almost one in five of all films.

What are the reasons for the high repeat rate, which (together with rejected films) may cost £3-4m a year? Poor exposure due to errors by the radiographer or the machine accounts for most of them. Student radiographers have overall repeat rates twice as high as that of trained ones, whereas expensive devices for automatic exposure control can halve them.[4] Nevertheless, even where these devices are installed they seem to be little used,[4] and much simpler measures such as exposure charts in each room and calipers to measure the size of the patient may be just as effective.[5]

More importantly, however, the question of repeat rates should be considered in the context of the overall use of ionising radiation in diagnostic radiology. Indeed, the Cardiff

study inadvertently provides an example illustrating the importance of fundamental reassessments. The authors claimed that no fewer than a fifth of all repeat films were to obtain a lateral view of the lumbar spine. But should all these views have been obtained? Waddell described guidelines for the use of radiography in backache suggesting that patients with no suspicious features and backache that had lasted less than three weeks (or had settled) do not require radiography.[6] Furthermore, patients aged 20-55 with persisting backache but without any of several well defined clinical criteria require only a single long lateral radiograph—but three films (occasionally five) are often routine. Hence in many patients the radiographer can concentrate on producing a single well positioned, properly exposed film. Applying these guidelines to the problem of backache alone would reduce repeat films for the simple reason that fewer examinations and films would be obtained in the first place—but this is rarely done at present.

I hope that the exciting but demanding changes in diagnostic imaging during the past 10 years will not divert the interest and time of radiologists and clinicians from the need to continue rigorously to assess the important effects, both ionising and economic, of what we do to patients. Surely simple measures to reduce repeat rates—say, to less than 5%—are not difficult to suggest or to implement. But the greatest reduction will be achieved if we take time to ask not only why we are repeating a film, but whether we need all the customary exposures. Most importantly, does the patient need any exposure at all?

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How best to use nitrates

Although nitrates have been used to treat angina for over a century, we still do not know how to use them most effectively. Because the drug is metabolised fast in the liver and because of wide variations between individuals in absorption and metabolism when the drug is used orally it must be given many times a day. One response to this has been to produce transdermal patches that deliver nitroglycerine at a constant rate over 24 hours: they release glyceryltrinitrate at a rate of about 0·5 mg/cm² of disc area.[1] The patches have been widely accepted[2] but have provoked controversy over whether they maintain steady plasma concentrations over 24 hours, whether they are clinically effective throughout that time, and whether they encourage the development of tolerance.

Some trials have suggested that the average conventional dose of the patches (9·3 mg/24 h) leads to plasma concentrations of nitroglycerine of only 0·5 μg/l—that is, below the 1 μg/l that is generally accepted as the lowest concentration that is therapeutically effective.[3,4] Dickenstein and Knutsen confirmed these results in a double blind multiple crossover trial using patches of 10-60 cm² (designed to deliver 5-30 mg of nitroglycerine over 24 hours): only those larger than 20 cm² were clinically effective.[5] Parker and others studied patches delivering 5, 10, 15, 30, and 45 mg nitroglycerine over 24 hours and showed that most prolonged treadmill exercise duration after four hours.[6] Only the 45 mg dose, however, prolonged exercise duration at 24 hours—and then only by 6%, which was statistically significant but probably not clinically important. Hollenberg and others studied 2·5, 5, and 10 mg patches at four and seven hours and showed a 30% improvement over placebo.[7] Cerri and others found significant improvements of 28% and 30% with 5 and 10 mg patches respectively after three hours but no statistically significant improvements after 24 hours.[8] Finally, Pucci and others compared transdermal patches of nitroglycerine 10 mg/24 h with isosorbide dinitrate 20 mg three times a day in a non-randomised non-blinded study.[9] They showed that the patch produced a 63% increase compared with placebo in total work performed on a bicycle after three hours and 45% increase after 24 hours. Isosorbide dinitrate was equally effective.

These short term trials thus tend to show benefit after four hours for both high and low dose patches, but there is often no benefit after 24 hours. Benefits from long term treatment are even harder to show.

Parker and Fung found no improvement in exercise time in patients given 15 mg patches for two weeks,[6] and Crean and others found no significant difference after 5 mg patches were given for two weeks.[10] Martines, in contrast, gave 5 and 10 mg patches for 21 days and found significant 33% increases in exercise time (measured three hours after the last application) for the smaller dose and 59% for the larger dose.[11] Andreoli (quoted in ref 1) gave 5 and 10 mg patches to 28 patients for three weeks in a double blind crossover trial, and 24 hours after the last patch was applied those treated with the 5 mg patch had a significant 38% increase in exercise time and those treated with the 10 mg dose a significant 65% increase. Thus in patients treated long term with nitroglycerine patches exercise time tends to be statistically increased two to four hours after the last patch is applied but results are uncertain after 24 hours. The variations in the designs of the study mean, however, that we have no clear answer on whether the patches work long term.

An important worry with long term treatment with nitrates is that it may lead to tolerance—that is, that larger and larger doses are needed to achieve the same haemodynamic and clinical effects. Tolerance has been reported after long term treatment with oral and transdermal isosorbide dinitrate and with transdermal nitroglycerine.[6,12,13] This evidence combined with the poor evidence on the long term efficacy of transdermal isosorbide dinitrate and nitroglycerine suggests that the concept that steady plasma concentrations of nitrates may provide continuous protection against angina may be wrong.

It is not clear how long tolerance takes to develop, but Parker showed reduced haemodynamic responsiveness after just 24 hours of sublingual isosorbide dinitrate; 24 hours after stopping the drug the responsiveness returned to normal.[12] He then compared the antianginal effects of oral isosorbide dinitrate given four times a day with transmucosal