But the trainee year is supernumerary, and nationally the scheme costs more than £30 million a year. Is the public getting value for money? Some lay commentators find it strange that accreditation in general practice is assessed only on the basis of time spent in the discipline and not by any other formal criteria.[16] Devising appropriate assessment is long overdue.[17] Negotiation for an extension of time spent in the general practice phase is unlikely to be successful unless the question of assessment is addressed. Extending learning into the early life of a principal is a good idea but should happen anyway: we should be learning until we retire.

Future plans for vocational training need both to ensure basic standards and to encourage excellence. Those planning the curriculum face the traditional paradox of having to create a system in which the pupils will be better practitioners than the teachers themselves. Medical education, however, is expensive, and cost containment is likely to affect teaching even more than service. Any improvements or innovations in training are unlikely to be cheaper or directly wealth creating, so we must be clear about the values we wish to espouse.

Few incentives seem to exist for trusts or budget holding practices to focus on training. Any review of vocational training might well find more to be concerned about than to applaud in such testing circumstances. But general practice has a key place in the health service, which the recent reforms have enhanced. Education for trainees has been pushed to the back of the debate recently. This must now change—for the sake of young learners and their future patients.

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Omeprazole

For resistant peptic ulcers and severe oesophageal reflux disease

For 15 years histamine H_2 antagonists have been the first line treatment for acid peptic disease. Now a more powerful group of acid suppressants is challenging this hegemony.

Omeprazole, the first of its class, is a proton pump inhibitor which binds with the potassium hydrogen ATPase of the parietal cell, though not of the renal tubule. Its action is irreversible until new enzyme is synthesised, and therefore inhibition takes several days to pass off. (This is similar to what happens with aspirin, which irreversibly inhibits cyclo-oxygenase.) By contrast, the histamine H_2 antagonists are competitive antagonists of the histamine H_2 receptor. Though they are capable of almost completely inhibiting basal nocturnal acid output, their effects are short lived and secretory inhibition is less obvious at times when normal physiological stimulation of acid output occurs, as with meals.

Treatment with H_2 antagonists has revolutionised the management of peptic ulceration. Four weeks of a once daily nocturnal regimen (to take advantage of when the stimulus to secretion is lowest) will heal two thirds to three quarters of gastric and duodenal ulcers, and a further four weeks' treatment will heal most of the rest.

If omeprazole is given once daily (timing is not critical) ulcers usually heal faster than they would with H_2 antagonists, although this rarely confers much advantage as symptoms usually respond quickly to H_2 antagonism and virtually all ulcers heal in those who comply with treatment.[1-7] Omeprazole should be used for the 5-10% of ulcers that fail to respond to H_2 antagonism. One group of patients whose ulcers respond poorly to treatment with H_2 antagonists are those taking non-steroidal anti-inflammatory drugs. For them omeprazole may have advantages over H_2 antagonists, although the evidence is limited.[6]

The conventional range of ulcer healing drugs extends beyond the H_2 antagonists and omeprazole to include the synthetic prostaglandin misoprostol, the selective anti-atropinic drug pirenzepine, sucralfate, and chelated bismuth. Measured solely in terms of their ability to induce healing these differ little from the H_2 antagonists.

Relapse is the norm when treatment with acid suppressants stops, which is predictable as the drugs do not permanently reverse the causes of ulceration. The same happens with omeprazole. More logical measures directed at eradicating *Helicobacter pylori* (a consistent associate and possible cause of ulcers) are in prospect as combinations of chelated bismuth and antibiotics show promise of providing cure, although problems of antibiotic resistance and antibiotic induced diarrhoea have yet to be solved.

In practice the first line treatment to suppress acid should be H_2 antagonists, which usually work and have an impressive safety record. Omeprazole should be reserved for poor responders. Once a course of antisecretory treatment is finished H_2 antagonists should be used for prevention. Omeprazole is not yet licensed for prolonged use as doubts remain over the consequence of its long term, virtually complete, suppression of acid. (For the old and frail who have severe disease, however, continuing with omeprazole may be sensible.)

Omeprazole is the best treatment for patients with disease caused by oesophageal reflux who have responded poorly to H_2 antagonists, alginates, antacids, or cisapride.[8-10] (Predictors of poor response include severe disease with confluent ulceration and the formation of strictures.) Difficulty arises when treatment is stopped because symptoms promptly return, and the doctor must choose among continuing

treatment outside the licensed indication, substituting a treatment that the patient finds unsatisfactory, or recommending surgery. Many gastroenterologists believe that continued omeprazole may be the best option.

Omeprazole is effective and probably the drug of choice in treating the gross hypersecretion of acid of the Zollinger-Ellison syndrome.[11] Omeprazole will also prevent breakdown in the stomach of oral pancreatic supplements (as do the H_2 antagonists) and will reduce the volume of stool in some patients with disabling diarrhoea after massive intestinal resections.[12] Disappointingly, a large trial has failed to show that patients with haematemesis and melaena benefit from omeprazole,[13] but this is no different from what has been found with H_2 antagonists.[14]

The pattern of short term adverse effects is generally reassuring. Headache, rash, and diarrhoea have been reported often enough to make coincidence unlikely.[15] Headache is also a recognised adverse effect of H_2 antagonism, and whether it is more common with omeprazole is unknown. A rash develops as a variable maculopapular eruption, although the cause is unknown. The cause of the diarrhoea is also unknown. Gastric acid is a barrier to intestinal infection, and treatment with omeprazole could impair this. It is odd, however, that an effective treatment for diarrhoea after resection of the small bowel should cause the same complaint.

Inhibiting the production of gastric acid may affect the metabolism of certain drugs. Cohen and colleagues have described how in the relatively anacid conditions produced by omeprazole digoxin is metabolised to lower concentrations of active metabolites, which have shorter durations of action than their parent compound.[16] This suggests that patients with unstable arrhythmias receiving digoxin may not be ideal candidates for treatment with omeprazole. Omeprazole also inhibits a specific subset of the cytochrome oxidase system in the liver responsible for the metabolism of certain drugs (such as phenytoin),[17 18] but this seems clinically unimportant.

The main concern about omeprazole has been that long term potent suppression of acid might predispose to cancer of the stomach. This matches the plausible fears in the late 1970s, which later proved groundless, that H_2 antagonists might predispose to cancer. In rats treatment with large doses of omeprazole expands the population of gastric carcinoid cells, with the occasional development of tumour-like nodules.[19] This has led to suggestions that omeprazole is a mutagen.

The bulk of evidence suggests that this is not so. Firstly, carcinoid nodules seem particularly likely to develop in rats. Secondly, they do not occur if the gastric antrum (which synthesises gastrin, a stimulant of mucosal growth) is resected. Thirdly, a range of other compounds which also stimulate release of gastrin, tend to do the same thing.[20-23] Lastly, if the gastric fundus is resected in rats carcinoids develop as the acid brake on release of gastrin from the antrum is removed.[24] Examination of the animal toxicology of omeprazole seems therefore to have shown an unsuspected, and as yet ill understood, effect of the natural hormone gastrin. Gastrin concentration increases with omeprazole because suppression of intragastric acidity stimulates gastrin output.

In humans omeprazole raises serum gastrin concentrations, sometimes quite considerably, but by a logarithmic measure of magnitude less than occurs in pernicious anaemia,[25-27] in which carcinoids rarely occur. Patients with pernicious anaemia develop gastric cancer about two to four times more commonly than expected. The likelihood is, however, that this increase derives from an unstable inflamed mucosa just as it does in atrophic gastritis without complete atrophy.

One set of experimental data awaits full explanation. Burlinson and colleagues at Glaxo, using a technique designed to separate proliferating (crypt cells) from non-proliferating (superficial) gastric epithelial cells, reported that pretreatment with omeprazole initiated proliferation in the superficial zone.[28] Astra's scientists and others have retorted that the technique is flawed because the separation is incomplete and they cannot find evidence that the drug is potentially carcinogenic.[29 30] Do the results of Burlinson and colleagues reflect a true effect, a flawed technique with chance divergence between results obtained with omeprazole and control results, or strain based differences between rat varieties which may be irrelevant to humans?

These questions need answers.[31] While we wait for them omeprazole should be considered for patients with peptic ulcers resistant to conventional treatment and those with severe oesophageal reflux disease.

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