Britain the equipment costs over £50 000, whereas urological resectoscopes cost less than a 10th of that figure and all urological departments are equipped with them. Only in hospitals where the Nd-YAG laser is employed in vascular and oesophageal surgery may it seem sensible for colorectal surgeons to perform palliative procedures with it.

With the increased availability of computed tomography in district general hospitals and the advent of prospective Medical Research Council trials in the management of colorectal cancer, tomography is becoming accepted as a routine preoperative investigation in patients with cancer once the diagnosis has been established historically. Often patients with a short history who seem to be in good general health will be found on scanning to have extensive liver metastases or advanced spread to the local lymph. Such patients may commonly become symptom free after local removal of the tumour by transanal diathermy loop excision performed under fluid distension of the rectum or by Nd-YAG laser ablation through an endoscope.

Surgeons who have to care for patients with colorectal cancer should select those patients for whom radical excision will not be curative and treat them with procedures that are cost effective and have a low morbidity. This approach will spare the humiliation and misery of spending the last few months of their lives adjusting to a colostomy or recovering incompletely from major operations. One of the reasons why the idea of a colostomy strikes fear into the hearts of patients is that there have been too many anecdotal accounts of patients who have had a colostomy for rectal cancer, have never recovered completely, and have gone relentlessly downhill. Our aim should make these stories a thing of the past.

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Vigabatrin

Rational treatment for chronic epilepsy

The neurochemical mechanisms underlying seizure disorders are largely unknown, but a logical pharmacological approach to treatment is to develop antiepileptic drugs which either enhance synaptic inhibition or reduce excitatory neurotransmission.[1] Most experimental work has focused on synaptic inhibition mediated by γ-aminobutyric acid (GABA),[2] and this has reached clinical fruition in the licensing of vigabatrin in Britain in 1989.

Vigabatrin (γ-vinyl-γ-aminobutyric acid; 4-aminohex-5-enoic acid) is a synthetic derivative of GABA and a specific, irreversible inhibitor of GABA transaminase—the enzyme responsible for the catabolism of GABA.[3,4] The drug seems to exert its antiepileptic action by inhibiting the breakdown of GABA and so increasing the concentrations at the synapse of this inhibitory neurotransmitter. It increases, in a dose dependent manner, concentrations of GABA in the brains of mice[5] and rats[6] and in the cerebrospinal fluid of patients with epilepsy.[7] In models of epilepsy in animals vigabatrin shows variable but generally broad spectrum anticonvulsant activity.[3,4] The time course of seizure protection relates more closely to the increase in synaptosomal GABA concentrations than to concentrations in the whole brain.[8]

In man vigabatrin is rapidly absorbed—peak plasma concentrations occur within one to two hours, the bioavailability is 60-80%, and the half life is five to seven hours. Most (80%) of the drug is detected unmetabolised in the urine, and its renal excretion correlates with the creatinine clearance. A preliminary single blind clinical trial suggested a dose related antiepileptic effect in patients whose epilepsy was resistant to treatment.[9]

Since 1984 seven European double blind placebo controlled trials (six crossover [10-15] and one parallel[16]) lasting up to 12 weeks have confirmed the antiepileptic efficacy of the drug in adults with chronic epilepsy. About 50% of patients showed a reduction in the frequency of seizures of more than a half, including roughly 15% with a reduction of more than three quarters, but complete control of seizures was uncommon. In a few patients the frequency of seizures may have increased, as may occur with any multiple treatment.[17] Patients with partial seizures with or without secondary generalisation (the commonest form of chronic epilepsy) showed the best response. Acute and reversible side effects were remarkably similar to those with the standard antiepileptic drugs, the most common being drowsiness, fatigue, dizziness, and behavioural changes. Slight weight gain was also noted in a few patients. There may be a slightly increased risk of depression, but most patients show an improved mood associated with better control of seizures (K A Birkbeck *et al*, 18th epilepsy international congress, New Delhi, 1989). The total daily dose of vigabatrin in these studies varied from 1·5 g to 3 g, usually given twice daily, though a once daily regimen was also reported to be effective.[18]

No clear relation between the concentration in the blood and the clinical effect of the drug has been shown, presumably because the antiepileptic action of the drug is related to the pharmacokinetics of GABA transaminase inhibition.[9] As the drug is not bound by protein, is excreted unchanged in the urine, and is not influenced by enzyme inducing drugs, interactions with other antiepileptic drugs are not expected and have not been reported, apart from a slight unexplained fall in serum phenytoin concentrations.[19]

As with all antiepileptic drugs the acute exacerbation of seizures may occur after the sudden withdrawal of vigabatrin.[16] Experience of its use has been limited in the various epileptic syndromes in childhood that are resistant to treatment, but again partial seizures seem to respond best and myoclonic syndromes do less well[20]; excitement and agitation are prominent side effects in children.

Long term follow up studies for one to four years have not shown any tolerance to the efficacy of the drug or any long term side effects (E H Reynolds *et al*, 18th epilepsy international congress, New Delhi, 1989).[21-23] Vigilance for possible long term toxicity should continue because early studies of toxicity in rats and dogs showed that microvacuoles suggestive of intramyelinic oedema were reversibly formed in the white matter in a dose related manner.[24 25] In dogs microvacuolation was accompanied by changes in the transmission time through the central nervous system of somatosensory evoked potentials, but such changes have not been observed in patients receiving long term treatment.[26 27] No evidence of intramyelinic oedema has been seen in six necropsies and 23 biopsy specimens taken from patients treated with vigabatrin for a mean of 25 months (D Scholey *et al*, Merrell Dow files, personal communication).

The clinical evaluation of vigabatrin has proceeded cautiously, and the drug will be available only for treating epilepsy that is not satisfactorily controlled by other anti-epileptic drugs. Nevertheless, it may prove to be a milestone in the treatment of epilepsy not only because it is the first new antiepileptic drug since the licensing of sodium valproate in 1973 but also because it is the first successful rational approach to the treatment of chronic epilepsy.

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Regular Review

Non-steroidal anti-inflammatory drugs and peptic ulcers

Facts and figures multiply, but do they add up?

Evidence of an association between non-steroidal anti-inflammatory drugs and peptic ulceration in the elderly has prompted a search for effective prophylaxis.[1 2] The flood of publications giving guidance has, however, washed up some important new questions and inconsistencies.

The story so far

Ever since aspirin was shown to injure the human gastric mucosa aspirin and non-aspirin non-steroidal anti-inflammatory drugs have been suggested as causes of peptic ulcers.[3] Changes in the rates of perforation and bleeding in parallel with changing patterns of prescribing have reinforced this suspicion.[4-8] Case-control and cohort studies from both Britain and the United States of patients with symptoms of gastric ulceration,[9-15] haematemesis and melaena,[10 13 16-25] perforations,[18 23-28] or death related to ulcers[18 23 24] have shown increased risks in patients taking these drugs. Endoscopic surveys have also reported a high prevalence[29-33] and incidence[1 2 34] of gastric and duodenal ulceration in patients taking non-steroidal anti-inflammatory drugs. Some have suggested that the type of arthritis has an influence, with gastric ulceration being especially common in patients with rheumatoid arthritis,[30 31 33] but others have rejected this suggestion.[12 29]

How big is the risk?

CASE-CONTROL STUDIES

In general five end points have been used—presentation with gastric ulcer, presentation with duodenal ulcer (whether complicated or uncomplicated), presentation with upper gastrointestinal bleeding (sometimes restricted to presentation with bleeding peptic ulcer), perforation of an ulcer, and death attributable to peptic ulceration. The results of case-control studies have been consistent in associating both aspirin and non-aspirin non-steroidal anti-inflammatory drugs with the development of gastric ulceration (fig 1).

Because most studies have provided raw data an average relative risk can be derived from a simple meta-analysis by the Mantel-Haenszel technique with individual studies as separate strata.[30] When the risks for different periods of ingestion have been quoted in individual studies those for regular ingestion in the past one to four weeks have been used. In studies using both hospital and community controls data relating to community controls have been used. When 95%