when the drug is stopped. The combination of captopril with large doses of loop diuretics in patients with impaired renal function can further raise serum concentrations of urea and creatinine. Hyperkalaemia is unusual but has been seen occasionally. One small double blind study found no evidence of a euphoriant effect of captopril¹⁹; such trials might usefully be extended and refined.

Some problems that had been expected with treatment with captopril have not materialised. For example, patients on long term dosage may attain very high circulating concentrations of angiotensin I and renin. Indeed, because renin substrate levels fall with captopril, measurements of plasma renin activity will underestimate the rise of renin concentration,²⁰ and increases in circulating renin may be a good deal higher than appeared from some of the early reports. So far, however, no adverse effects attributable to angiotensin I or renin have been identified. Furthermore—at least with captopril 150 mg three times daily—despite the very high resulting concentrations of renin and angiotensin I, no evidence has been found of any breakthrough of converting enzyme inhibition and consequent generation of angiotensin II or angiotensin III in the circulation.²¹

We believe that the introduction of orally active converting enzyme inhibitors has been a major advance in cardiovascular treatment. The past five years have seen a widening of their therapeutic range, but this has yet to be fully delineated. Problems associated with the use of these agents have been identified and substantially resolved. The next five years should see their potential exploited.

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Irritable bowel syndrome: still in search of its identity

The irritable bowel syndrome accounts for a third to a half of referrals to gastroenterologists,¹ yet remarkably little is understood of its pathogenesis. Anyone who looks after patients with the syndrome knows that they vary greatly, both in their symptoms and in their response to treatment. Indeed, experts are trying hard to identify subgroups with more constant symptom patterns and—they hope—a more predictable response to treatment.

This urge to subdivide and classify the irritable bowel syndrome dominated an international workshop on the disease held at Chateau Impney in June this year. One important step, made in 1962, was when Chaudhary and Truelove separated a group with painless diarrhoea from the majority who had pain and a variable bowel habit, the spastic colon group.² Since then we have learned that pain may arise in the small intestine as well as the colon and that patients often have symptoms arising from the oesophagus and gastroduodenum.^{3 4} Hence most gastroenterologists now speak of the irritable bowel or even the irritable gut⁵ rather than of the irritable colon.

One of the problems in defining varieties of the irritable bowel syndrome is the lack of objective evidence of gut dysfunction in this condition. Patients with the irritable bowel syndrome who attend hospital have a high prevalence of neurotic traits and some regard them as merely oversensitive and overanxious people who notice and complain about normal abdominal sensations and about normal variations in bowel habit. This is unfair, since obvious spasm may sometimes be seen on barium radiographs (as well as on manometry), and the excess excretion of mucus is clear evidence of colonic malfunction, if not irritation. Nevertheless, patients with the irritable bowel syndrome are oversensitive to distension of the bowel,⁶ and they tend to make more of a fuss about minor ailments than other people.⁷

Classically the patient with the irritable bowel syndrome complains of alternating constipation and diarrhoea. This should be easy to document. What could be simpler than weighing the stools for several weeks and repeatedly measuring the passage time of radio-opaque pellets in a series of patients and then relating the findings to their symptoms? That would at least indicate how far the patients' bowel function varies from normal and whether it does indeed swing from constipation to diarrhoea and back again. Such a study has never been reported, and even in normal people the scanty data show that the function of the colon varies wildly, not only among individuals but even in the same normal person at

different times.⁸⁻¹⁰ For example, when the transit time through the whole gut was measured five times in as many weeks in healthy women it fluctuated in some of them from under two days to over five days. There was even more variation in the size of individual stools—in one person from a mere 7 g on one day to 330 g on another.⁸ It would be difficult to show that patients with the irritable bowel syndrome fluctuated more than that.

Some patients with spastic colon complain predominantly of diarrhoea, some predominantly of constipation. It should at least be possible to show that these patients differ from each other. Surprisingly, one group of workers has reported no difference in mean stool weight or transit time, but they did not give their data and they collected stools for only 48 hours.¹⁰ A recent study in Sheffield was more thorough and tells a different story.¹¹ In women whose predominant bowel complaint was diarrhoea the average weight of stool passed in 24 hours was 128 g, whereas in those with predominant constipation it was only 61 g, and there was an appropriate difference in whole gut transit time (35 versus 87 hours). Nevertheless, the women with "diarrhoea" passed no more stool than did a control group of normal women, in whom it averaged 112 g a day. So why did they complain? Possibly they were bothered by urgency (due perhaps to the soft consistency of their stools) but urgency has been little studied and is poorly understood. In the Sheffield study the men with predominant diarrhoea had bulkier stools than their healthy controls (230 versus 166 g a day), but even this does not prove that their stools were abnormal. British vegetarians normally pass stools weighing 225 g a day and in India and Africa healthy people regularly pass stools of 300 g to 500 g a day.¹² In Sheffield, like the women, the men claimed that most of their stools were unformed and perhaps this is what bothered them. But were the stools of the patients with the irritable bowel syndrome pathologically loose or were the patients pathologically intolerant of normal variation in stool consistency?

A novel finding in this study was that transit through the small bowel was fast in the patients with spastic colon and predominant diarrhoea and slow in the constipated group. The average time taken for the head of a test meal to reach the caecum (as judged by a sudden rise in breath content of hydrogen) was 4.2 hours in healthy controls, 3.3 hours in the group with diarrhoea, and 5.4 hours in the group with constipation. This was interpreted as evidence that the irritable bowel syndrome affected the small bowel—a reasonable conclusion, but one that does not necessarily imply that the small bowel was functioning abnormally. Indeed, the asymptomatic controls had very variable small bowel transit times (1.5-7.4 hours) and all the patients with the irritable bowel syndrome fell within this range. So it remains true that physiological measurements have not yet shown a definite abnormality of bowel function in patients with the irritable bowel syndrome except perhaps in those with constipation.

The pain of the irritable bowel syndrome seems to be due either to abnormally strong contraction (spasm) of the intestinal smooth muscle or to undue sensitivity of the intestine to distension. Until recently this oversensitivity had been shown only in the rectum and sigmoid,^{6,13} but now the Sheffield group has evidence that the caecum or ascending colon may be oversensitive too. Two thirds of their patients had pain after a test meal, and in three quarters of these the onset of pain coincided with the arrival of the meal residues in the caecum. Why should the caecum hurt when it is given its normal job of work to do? That is just one among many

questions about the irritable bowel syndrome which are waiting for an answer.

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Postviral neurological syndromes

Many different neurological and psychiatric syndromes follow viral infections, but their clinical picture and pathogenesis are poorly understood. They form a heterogeneous group including well known entities such as acute disseminated encephalomyelitis and the Guillain-Barré syndrome; disorders in which the virus probably causes enzyme abnormalities—for example, Reye's syndrome and epidemic myalgic encephalomyelitis; and diseases which are not primarily caused by viruses but are occasionally precipitated or made worse by a viral infection—for example, the genetic disorder Refsum's disease (polyneuropathy, ichthyosis, retinitis pigmentosa, and deafness)¹ or multiple sclerosis.² Some idea of incidence is given by the fact that Reye's syndrome is the second most common cause of death in childhood due to diseases associated with viral infection affecting the central nervous system,³ and that acute disseminated encephalomyelitis accounts for one third of all the encephalitides.⁴

Acute disseminated encephalomyelitis is, indeed, the most common demyelinating disease in the world because of the frequency with which it follows measles and other viral infections. Its clinical presentations range from seizures and coma to isolated neurological defects. The neurological findings may, however, be minimal in patients with florid psychiatric manifestations. The Guillain-Barré syndrome is precipitated by similar viruses and its clinical course is analogous to that of acute disseminated encephalomyelitis. Both disorders are likely to be vasculopathies mediated by immune complexes with the lesions occurring in central nervous tissue myelin in acute disseminated encephalomyelitis