slight dysplasia. More recently Skarstein and his colleagues carried out a similar cohort study of patients 12 years after surgery and found a high incidence of chronic superficial gastritis—though (perhaps because of shorter follow-up) the changes were for the most part mild and dysplasia was found in only 15% of biopsy specimens.

This study also examined late deaths and the clinical state of the survivors. The death rate for patients treated surgically for peptic ulcer is 40%, greater than that of the general population. Whether this is the consequence of the diathesis, of surgery, or of risk factors such as tobacco and alcohol consumption remains uncertain. The health of the survivors is consistent in long-term follow-up studies: around 80% of patients are symptom free—though some may have subclinical deficiency of iron or vitamin B12 and have some degree of anemia—and 9% will have mild gastrointestinal symptoms, 7% moderate symptoms, and 4% severe problems. Since similar results are found at earlier follow-up assessments the functional results seem to be stable.

How much might have been done to reduce this moderate and perhaps reasonably acceptable morbidity? Some of the patients will have been ill selected and merely persist in their preoperative state; but selection is difficult, as every surgical gastroenterologist knows. Careful studies of dietary intake have shown that some of the poor results in terms of weight loss and anaemia are due to dietary factors and can be reversed. Armed with such knowledge surgeons might now hope to achieve better results with partial gastrectomy; in practice the decline in incidence of ulcer, the use of H2-antagonists such as cimetidine, and—above all—the development of vagotomy have made the question largely hypothetical.

The crucial problem now is whether malignant change in the stomach is really going to affect 5%, or more of the survivors of the gastrectomy bonanza of the 1950s and 1960s. Assuredly there is no ground for complacency. The only hope of curing this lesion lies in detecting it at an early phase of mucosal infiltration. The poor correlation of gastritis with symptoms makes routine endoscopy essential for patients who have survived 20 years; and that requires stable populations, good records, and a determination to maintain follow-up. Can we meet such requirements, and if so can we afford to take the necessary next step of attempting to carry out endoscopy on what will shortly be many thousands of patients?

Surgeons, like cooks, know they cannot make omelettes without breaking eggs. Most of their time they are worried about early catastrophe—death and immediate serious complications. The low mortality and morbidity associated with much modern surgery should now be changing attitudes: firstly, surgeons should reset their time scales to think forward to much longer-term effects; and, secondly, they will need to devise avoiding actions, either by developing operations that should be less harmful in the long run or by making sure that long-term surveillance is adequate. The history of partial gastrectomy for duodenal ulcer is rapidly emerging as a model for good surgical behaviour on both counts.

6 Scharmpf E, Stadaas J, Myren J, Serck-Hanssen A, Aune S, Omses M.

Adult polycystic disease of the kidneys

Inherited autosomal dominant adult polycystic disease of the kidneys is characterised by the development of multiple renal cysts. It frequently leads to end-stage kidney failure in the fourth decade and is the most common inherited kidney disease. Dalgaard1 estimated the morbidity risk up to the age of 80 as amounting to 80 to 90 cases per 100 000 population; the condition accounts for 7% of patients with end-stage renal failure.2 Whereas adult polycystic disease of the kidneys may remain symptomless, its presentations are many and varied. They include high blood pressure, recurrent urinary tract infections, pain and a mass in one or both loins, renal colic due to the passage of clots or stones, symptoms of kidney failure, and subarachnoid haemorrhage from a ruptured berry aneurysm—an abnormality commonly associated with adult polycystic disease of the kidneys.

Identification of the disease depends on excretion urography and ultrasound examination. Neither of these are sensitive, and cysts measuring less than 1-5 cm diameter may not be detected. Even with the use of computed tomography cysts measuring less than 0-5 cm diameter may be missed.3 A clean bill of health should not, therefore, be given to relatives of affected persons much before the age of 30—which is, unfortunately, well into the reproductive period. This makes for difficulties with genetic counselling and in choosing suitable live kidney donors from among the relatives of patients with kidney failure due to adult polycystic disease of the kidneys. More sensitive methods for early diagnosis are urgently required.

Milutinovic and his colleagues4 in Seattle recently performed renal biopsies on 16 asymptomatic relatives of patients with adult polycystic disease of the kidneys who belonged to five different families. Fourteen of the 16 had normal excretion urograms at the time of the biopsy, and in four adult polycystic disease of the kidneys had "developed" three years later. In three of these four people the initial biopsy specimen had shown dilatation of the distal and collecting tubules and splitting of glomerular and tubular basement membranes; these histological features may prove to be the earliest markers of the disease in carriers of adult polycystic disease of the kidneys. The Seattle group did not suggest renal biopsy as a routine method for the early detection of carriers because the histological changes are not uniformly distributed. Their observations may, however, throw some new light on the pathogenesis of the disease.

Past theories have included intrarenal renal infection accompanied by tubular obstruction5 and non-union of the branches of the urteric bud with the nephrogenic blastema,6 neither of which has been verified. Microdissection7 has shown that cysts communicate with the drainage system and no
evidence to suggest intrauterine renal infection has ever been produced. Obstruction due to polypoid and papillary hyperplasia of tubular epithelium may play a part in the initiation of cyst formation both in experimental models of the disease, such as the diphenylamine-induced polycystic disease of rats, and in the human disease. Acquired obstruction of this kind may possibly lead to cystic dilatation of the tubules because of a change in the composition of the tubular basement membrane that causes it to split and renders it less resistant to distention. Adult polycystic disease of the kidneys may, indeed, be due to an abnormality of the genetic locus that determines the structure of the collagen of the glomerular and tubular basement membranes, and the defect in these membranes may be related to a single enzyme deficiency. If that were so identification of the enzyme deficiency might lead to prenatal diagnosis becoming possible.

Meanwhile, the management of adult polycystic disease of the kidneys remains conservative with control of blood pressure and urinary tract infections. Patients should be advised to avoid sports and occupations with a risk of trauma to the kidneys. Drainage of cysts or their decapitation probably has no place; most studies have shown that such surgical interference accelerates the deterioration of the kidney function. A recent report from China claimed that symptomatic improvement was obtained by deroofing the cysts in patients who presented with aching in loins. The Chinese also found that hypertension was more readily controlled after the procedure, but these observations were uncontrolled. Patients with end-stage kidney failure due to adult polycystic disease of the kidneys fare no better or worse than patients with other forms of end-stage kidney disease when treated by dialysis or transplantation. The cysts shrink after such treatment; might this possibly be the result of belated removal of an unidentified cystogenic substance?


Another look at zinc

A few rare clinical syndromes are associated with low concentrations of zinc in the blood; symptoms disappear when the patient is given zinc. They include a particular type of dwarfism and a specific skin disorder, acrodermatitis enteropathica.

Some biochemical physicians now assert, however, that subclinical zinc depletion may be much more common than clinically obvious depletion. Unfortunately, the plasma concentration of zinc is only about 1%, of the total body zinc, and is not a reliable guide. Another reason, and probably a more important one, for the unreliability of estimations of plasma concentrations of zinc as a clinical pointer is that zinc in plasma is almost entirely bound, largely to plasma proteins, including albumin (50%), α2-macroglobulin (40%), and transferrin, and to amino-acids (5%). A low plasma concentration of zinc is almost certainly much more commonly due to a change in the concentration of one of these zinc binders than to a true depletion with a fall in the cell content of zinc.

A relation has been shown between the change in plasma concentrations of albumin and of zinc in some disease—but correction of the zinc for the albumin value would be justified only if albumin was known to be the only zinc binder affected. The presence of several binders probably also explains why there is no predictable relation between plasma concentrations of zinc and protein as they each increase during venous occlusion.

Though large (20%), the fall in plasma zinc after meals is unexplained. It might be due to changes in the concentration of one of the non-albumin zinc binders, though the changes in α2-macroglobulin are too small to be the explanation. Because of the binding to plasma protein and the effect of meals, plasma concentrations of zinc need to be measured at a standard time and without venous occlusion.

A reduction in concentration of one or more of the zinc binders is the most likely explanation of the fall in plasma zinc by as much as 30%, currently being described in so many diseases. These include acute traumatic episodes such as myocardial infarction, chronic "inflammations" such as rheumatoid arthritis, and conditions such as liver disease where there is a change in the plasma concentration of albumin. Indeed, the fall in the plasma zinc concentration after myocardial infarction is so consistent that it has been described as diagnostically useful. This fall has been attributed to an increased uptake of amino-acids (with the zinc bound to them) into the liver under the influence of a leucocyte endogenous mediator—but only 5% of plasma zinc is bound to amino-acids.

The plasma concentration of zinc is reduced by about 20% in patients with rheumatoid arthritis, a change related to the sedimentation rate and to the plasma content of albumin. The fall in albumin could account for the fall in zinc, or possibly some other factor such as the leucocyte endogenous mediator may be at work. Whatever the explanation, the effect on zinc in these various conditions seems to be non-specific and part of the metabolic response to trauma and inflammation.

With zinc (and other trace metals) the general view is that cellular rather than plasma depletion is the important factor that explains symptoms. But what does a low cell content of zinc mean? Most of the zinc in cells is bound to protein or incorporated into enzymes, and any change might be due to a diminished cell content of these zinc binders or enzymes. For example, the low zinc content of erythrocytes in patients with hyperthyroidism is attributed to a diminished cellular content of carbonic anhydrase. Keeling and his colleagues have recently confirmed that in patients with chronic liver disease a low plasma concentration of zinc is associated with, and related to, a low albumin concentration. They showed further, however, that their patients also had a low zinc content in the leucocytes but not in the erythrocytes; some of their patients...