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IN this year's annual review of general surgery, the author has once again picked out a number of topics which appear to be particularly highlighted in current interest. These can be assessed by the bulk of publications dealing with them, their being featured as subjects for symposia and meetings, and the simple fact that they crop up in discussions when two or three surgeons are gathered together. Once again, however, we must confess that the topics here chosen also represent the narrow vistas and limited reading of the reviewer. This year we have elected to consider surgical diseases of the pancreas, abdominal pain in children, the complications of peptic ulcers, carcinoma of the breast and of the of the thyroid, wound healing and microvascular surgery. All but one or two of the references quoted were published in 1976.

The pancreas

The pancreas is deeply placed, surrounded by vital structures and is difficult to investigate even by the most sophisticated modern techniques. Not surprisingly, therefore, pancreatic trauma, pancreatitis and pancreatic tumours persist as difficult diagnostic and therapeutic problems.

Trauma

The pancreas may be injured either by blunt trauma, usually a road traffic accident, or by penetrating injuries. Because of its deeply placed position, there are often other associated injuries to liver, spleen or major vessels (Warren & Hoffman, 1976). Injury is often followed by traumatic pancreatitis, abscess formation, external fistulas and the formation of a pseudopancreatic cyst. Balasegaram (1976) reviews ninety-one patients with pancreatic injuries treated in Kuala Lumpur. Forty-four of these resulted from blunt injuries and forty-seven were penetrating wounds. No less than nineteen died (20.8%) and eighty-one of the patients had associated and concomitant injuries to head, chest, spleen, liver, intestine, skeleton, etc.

From Louisville, Kentucky, Heitsch and his colleagues (1976) report on 100 patients with pancreatic trauma; seventy-seven were penetrating and

twenty-three were blunt injuries. Sixteen died within the first 24 hr, fourteen of whom had major hepatic and/or retroperitoneal venous injury. Seventeen patients died subsequently and fourteen of these deaths were secondary to Gram-negative sepsis. The prognosis was much better if the pancreatic duct was not injured and in these cases drainage alone was found to be adequate treatment. Drainage was inadequate if the major ducts were damaged and here more radical surgery, including partial pancreatic resection, must be carried out.

Fortunately, pancreatic trauma is comparatively rare in the U.K.; Heyse-Moore (1976), for example, could collect only four cases, all of blunt trauma, over a 10-year period in the Bristol hospital group.

Acute pancreatitis

The aetiology and management of acute pancreatitis, as well as problems of diagnosis, continue to be the subject of numerous investigations. Storck, Pettersson & Edlund (1976) review autopsies upon 116 patients with acute pancreatitis in Goteborg, Sweden, between 1957 and 1970; 43% were associated with gall-stones, 25% with alcohol abuse, 18% were idiopathic and 14% were post-operative. They note an increasing incidence due to alcohol and a decreasing incidence due to gall-stones over this period of time. There have been several reports of acute pancreatitis following cardiac surgery and it has been shown that the serum amylase may rise after heart operations using extracorporeal circulation. Feiner (1976) reviewed 182 post-mortems in adults dying within 10 weeks of cardiac surgery (mostly pump cases) and no less than thirty-four had pancreatitis; five of these were probably or possibly related to other events but of the remaining twenty-nine cases no other aetiological factor could be determined. Of these, seventeen were mild, eight were moderate and four were severe examples of pancreatitis. Feiner postulates an ischaemic origin of this complication, which might either be functional, due to hypo-perfusion, or mechanical due to thromboembolism and this latter finding was identified in nine of the twenty-nine patients in a fairly superficial examination of only

one or two sections through the organ. Postoperative pancreatitis most frequently follows upper gastrointestinal surgical procedures such as gastrectomy or common bile-duct exploration in which local trauma to the pancreas is likely to occur. The incidence of pancreatitis after operations not in the direct location of the pancreas is very low, in the region of 0.1%, but in Feiner's series of cardiac surgical patients it was 16% and she suggests that estimation of serum levels of pancreatic enzymes might aid in the early recognition and management of this complication in patients undergoing cardiac surgery.

There is a rare and not completely explained association between acute pancreatitis and hyperparathyroidism. Rosin (1976) reports three such cases, two of whom also formed pancreatic cysts, and gives a detailed review of this subject.

The association between gall-stones and pancreatitis has always been difficult to explain since ampullary calculi are found in only 5–8% of patients with gall-stone pancreatitis, the stones much more commonly being confined to the gall-bladder itself. Kelly (1976) brings forward some interesting evidence suggesting that migrating gall-stones frequently cause the disease. The stools of forty-five patients with proved gall-stone pancreatitis were screened for stones and an equal number of patients with gall-stones but without pancreatitis served as the control group. Gall-stones were found in the stools of thirty-eight of the forty-five patients (84%) with gall-stone pancreatitis and in only five (11%) of the control group. The patients with gall-stone pancreatitis experienced relief of symptoms and a decrease in the serum amylase and serum bilirubin before the rectal passage of the stones. Operative cholangiography revealed reflux of contrast material into the pancreatic duct of 67% of the patients with gall-stone pancreatitis compared with only 18% of the controls. Kelly postulates in his 'migratory stone' concept that gall-stone pancreatitis develops when a stone migrates from the gall-bladder, impacts temporarily at the ampulla of Vater, causes reflux pancreatitis then passes through the ampulla and continues its journey into the gastrointestinal tract.

Acute pancreatitis due to alcohol is a common problem in the U.S.A. and is being seen more frequently in the U.K. Patients with acute alcoholic pancreatitis usually respond well to medical therapy and surgical treatment is not often indicated. However, surgical correction of biliary tract disease in patients with acute gall-stone pancreatitis is curative and recurrence of pancreatitis is rare. The differentiation between the two groups is not usually difficult and is based on history of alcohol abuse and on subsequent cholecystography. Paloyan & Simonowitz (1976), in a study of sixty-four patients

with gall-stone pancreatitis and forty-six with acute or recurrent attacks of alcoholic pancreatitis, found that the mean serum amylase value in the former group was 1855 i.u. compared with a mean value of 800 i.u. in the alcoholic group. Similarly, the mean serum alkaline phosphatase and bilirubin levels were significantly higher in the gall-stone group. They commend these laboratory tests on admission as a useful aid in differentiating between the two entities.

It is important to remember that although conventional radiology of the gall-bladder (oral cholecystogram and intravenous cholangiogram) have a high degree of accuracy, gall-stones may be present even when these tests are completely normal. Smith, Williams & Cotton (1976) report three patients, each with acute relapsing pancreatitis and with normal routine biliary radiology. Endoscopy and retrograde cholangiopancreatography (ERCP) showed gall-bladder stones together with a stone in the common bile duct in two patients. In the third, the gall-bladder and duct system appeared normal at ERCP although at operation the gall-bladder contained many small cholesterol stones and there was a pin-hole lumen to the papilla of Vater. These authors conclude that when faced with a patient, particularly a woman with recurrent attacks of pancreatitis and normal biliary radiology, it is necessary to maintain a high index of suspicion that gall-stones may be present. This is particularly so when there are no other obvious factors such as alcoholism or hypercalcaemia. ERCP may help in such cases but in others a diagnostic laparotomy may be appropriate.

Fernandez & Rosenberg (1976) discuss pancreatitis as a complication of renal transplantation; they estimate that this occurs in 3% of these patients and carries a 70% mortality. Possible predisposing factors are immunosuppressive therapy, secondary hyperparathyroidism and increased susceptibility to infection.

Acute pancreatitis varies in its clinical manifestations from a mild transient affair to a catastrophic and fulminating attack with poor prognosis. Ranson, Rifkind & Turner (1976), reviewing 300 cases of acute pancreatitis with twenty-two deaths, point out that poor prognosis is associated with an age of 55 years or more, a white cell count above 16 000, blood glucose above 200 mg, a serum calcium below 8 mg and an arterial oxygen below 60 mmHg. It is interesting that in this series from the Bellevue Hospital, New York, no less than 207 cases were due to alcoholism and only fifty-one to biliary disease.

If the diagnosis of acute pancreatitis is made, the initial treatment is conservative. Operation is advised if the diagnosis cannot be made with certainty, for example, if a strangulated intestinal

obstruction cannot be excluded. The other indication for surgery is rapid deterioration under medical treatment and this applies to probably less than 10% of the cases. If operation is required there are three schools of thought, the first advocates immediate resection of the necrotic pancreas to prevent subsequent haemorrhage and sepsis (Warren & Hoffman, 1976); the second advises peritoneal dialysis to remove toxic vasoactive substances (Ranson *et al.*, 1976); and the third, represented by White & Heimbach (1976), advocates gastrostomy, a feeding jejunostomy, drainage of the gall-bladder or common bile duct if stones are present, drainage to the pancreatic bed and parenteral hyperalimentation. Sequestrectomy is later performed if there is any remaining necrotic pancreatic tissue. In thirty cases thus treated 50% required subsequent sequestrectomy. There were six deaths in the series and sixteen patients were completely rehabilitated with minimal exocrine or endocrine disturbance. Between 1 and 5% of cases of haemorrhagic pancreatitis proceed to abscess formation and Grace & State (1976) advise drainage and antibiotic therapy in the management of this complication. Occasionally fistula formation may occur and Henderson & Macdonald (1976) describe such a case in which a fistula developed into both the small intestine and the colon.

Because of the widely varying clinical profile of acute pancreatitis and its relatively low overall mortality, it is difficult to be certain of the efficacy or otherwise of the many suggested forms of conservative treatment in this condition. At present a Medical Research Council double-blind trial is being carried out at several centres on the use of glucagon and aprotinin (trasylol) or a placebo (Williamson, 1976) and obviously the results of this investigation will be of considerable interest. A recent randomized trial of the use of ampicillin in acute pancreatitis by Finch, Sawyers & Schenker (1976) showed no advantage in those patients receiving the antibiotic. It should be noted, however, that of the fifty-eight patients admitted to the trial, thirty-eight were alcoholic, sixteen had pancreatitis of undetermined origin and only four had associated gall stones, so that obviously further trials will be necessary to determine the role of antibiotics in pancreatitis related to biliary calculi as well as in the haemorrhagic and acute necrotizing forms of the disease.

Carcinoma of the pancreas

The incidence of cancer of the pancreas is increasing so that now it surpasses that of cancer of the stomach in the U.S.A., where it was estimated that there were 20 000 deaths from this cause in 1975. Brooks & Culebras (1976), in giving these

figures, also underline the very serious prognosis of this condition. In a review of 101 patients admitted to the Peter Bent Brigham Hospital in Boston, twenty-two were too ill for any form of surgery, twenty-five had a laparotomy and biopsy only, thirty-five underwent a palliative bypass, and only nineteen were submitted to attempted curative surgery. The average survival of those patients undergoing laparotomy only was 3 months and those undergoing palliative surgery 5.8 months. If nodes were involved there was no difference between the survival rate of total pancreatectomy and bypass surgery but if the nodes were not involved then the prognosis following radical surgery was improved compared with the palliative group. Thus, even in the very best centres, only a small percentage of patients can be offered any hope of cure and this only by an operation which carries with it a very considerable mortality and morbidity.

The difficulty of diagnosing early pancreatic cancer remains a serious barrier to any improvement in the 90% mortality rate which occurs during the first year after diagnosis. Recent years have seen the introduction of numerous most sophisticated investigative techniques, including air contrast duodenography, duodenal drainage and cytology, hormone assays and detection of tumour-associated antigens. Wood and his colleagues (1976) compared their experiences with ultrasonography, pancreatic scanning, selective arteriography and endoscopic retrograde cholangiopancreatography. Eighty-nine patients suspected of pancreatic cancer were studied by one to four of these tests. Fifty-eight of the patients underwent laparotomy; thirty-three were found to have a pancreatic cancer, one a cancer of the duodenum and two cancer of the ampulla of Vater. Seven had other malignant tumours within the abdomen and nine had pancreatitis on biopsy. Five had other benign disease and there was one negative laparotomy. The remaining thirty-one patients who did not undergo laparotomy were followed-up and were free of symptoms for over 1 year; none demonstrated subsequent evidence of pancreatic cancer. The ERCP gave an accuracy of 88% in the fifty-eight patients examined and is the only one capable of making a histological diagnosis. However it is a difficult and expensive technique. Pancreatic scan and arteriography each gave a 64% accuracy and ultrasound a 72%. This last is the least unpleasant technique for the patient to undergo. Computerized axial tomography using the EMI body scanner may be an important addition to our armamentarium. Cotton, Denyer & Kreel (1976) report on its use in thirty-two patients being investigated for suspected or known pancreatic lesions with encouraging results. The techniques and interpretative skills with this instrument continue

to develop but its precise application alongside other investigations, particularly ultrasonography, remains to be defined.

In a disease which is so often incurable at the time of diagnosis, it is important to assess the role of palliative measures. Mallinson and his colleagues (1976) report a prospective randomized controlled study of cytotoxic therapy in forty-one patients with pancreatic cancer diagnosed at laparotomy. Twenty-one controls were given no placebo but were merely followed-up. Twenty patients of comparable age, sex and tumour load were given an initial course of cyclophosphamide, methotrexate, vincristine and 5-fluorouracil. Maintenance treatment of 5-fluorouracil and mitomycin C was then given at 6-week intervals. The median survival of twenty-one untreated patients was 2 months and of treated patients 11 months, demonstrating clearly that this regime has significant benefit in some patients with pancreatic cancer. It is important that the treatment proved acceptable, caused only occasional reversible toxicity and no patient-refusal.

A bizarre case of carcinoma of the ampulla of Vater in a haemophilic patient aged 42 is reported from Westminster Hospital (Catford *et al.*, 1976). The presentation was obstructive jaundice complicated by repeated gastrointestinal haemorrhages. Diathermy excision of the tumour was carried out and the patient remains well 2.5 years later.

Acute abdominal pain in childhood

Any experienced clinician will agree that the diagnosis of acute abdominal pain is particularly difficult in the very young, the very old and in the postoperative patient. The child with an 'acute abdomen' presents a whole series of problems; the difficulty of obtaining an accurate history, the problems presented by the wide range of differential diagnoses which may present with this symptom, the difficulty in getting a small child in pain to co-operate in clinical examination and all this in the presence of anxious parents. Appendicitis is rare below the age of 1 year and thereafter increases in prevalence. The morbidity and mortality are higher in pre-school children than in those over the age of 5, partly because of the difficulty in obtaining a clear history and performing a reliable examination on an ill, frightened young child. There are also differences in presentation. In children the classical early central abdominal colic is not always followed by continuous deep pain in the right iliac fossa. Vomiting is usual but not inevitable. There may be diarrhoea, constipation or no bowel upset whatsoever. A number of other conditions may closely mimic appendicitis in children. Some, such as intussusception, require laparotomy in their own right; others such as mesenteric adenitis may require laparotomy to

achieve a definite diagnosis. Others should be diagnosed without laparotomy and here, indeed, surgery may be distinctly harmful. Among these are included diabetes mellitus, infectious hepatitis, urinary tract infection, pneumonia and sickle cell disease. Gastroenteritis creates much confusion and constipation may also cause dramatic pain and tenderness in children, although a rectal examination allows the correct diagnosis (Leading Article, 1976).

Valerio (1976) reports three cases of acute abdominal pain in children with undiagnosed diabetes and stresses three important clinical features: (i) a history of polyuria, polydipsia and anorexia preceding the abdominal pain; (ii) deep sighing and rapid respirations; (iii) severe dehydration. The abdominal tenderness is usually generalized. Because of the dehydration it may be difficult to get a urine specimen for testing and the most important step in confirming the suspected diagnosis is an immediate blood-sugar estimation, while 'Dextrostix' and 'Ketostix' tests may be performed in the ward. In the diabetic presenting as an acute surgical emergency without an abdominal lesion, the abdomen will become pain free and soft within a few hours of treatment of the ketoacidosis.

Jona & Belin (1976) review 250 children presenting with an acute abdomen; twelve had a basal pneumonia as the sole cause. Eight of the children had mild respiratory symptoms, four had none at all and only two of the children had abnormal physical findings in the chest, so that the pneumonia was not diagnosed until after X-ray examination. The abdominal pain was severe and sustained and associated with abdominal tenderness and sometimes absent bowel sounds. This report certainly suggests that a chest X-ray is worth ordering in children presenting with an acute abdomen when there is any question at all about the diagnosis. This examination should include a good lateral film to demonstrate consolidation which may be hidden by the diaphragm in the usual postero-anterior film. However, it should also be noted that acute appendicitis may occur in children who actually have respiratory tract infection or even pneumonia!

Some recent surveys give us a useful idea of the likelihood of the various diagnoses to be encountered. Lari, Kirk & Howden (1976) review 110 emergency appendicectomies performed at the Sheffield Children's Hospital. In seventy-six the appendix was acutely inflamed and twenty-five of these were actually gangrenous. In the remaining thirty-four patients, the appendix was normal and the diagnosis here was mesenteric adenitis in twenty, twisted ovarian cyst in two, primary peritonitis in two, septicaemia due to *Escherichia coli* in one patient and in nine patients no definite diagnosis was made. Jones (1976) reviews 363 children

admitted to the Children's Hospital, Aberdeen, with acute abdominal pain. Thirty-five per cent (126 patients) came to operation and of these 102 had acute appendicitis, eight had mesenteric adenitis, four had a normal appendix removed with no other pathology and two had Meckel's diverticulitis. There were three examples of intussusception, two of abdominal trauma, two strangulated inguinal hernias, one torsion of the testicle, one adhesive band and one caecal volvulus. The remaining 237 patients did not require surgery. Of these, forty were found to be constipated, twenty-nine had an upper respiratory infection and eight pneumonia, there were twenty-five cases of urinary tract infection and thirteen examples of gastroenteritis. No less than 108 of these children were labelled as 'non-specific abdominal pain', amounting to 30% of the total admissions. Jones stresses the importance of repeated careful examinations in doubtful cases and close observation of the patient. A particularly valuable sign in differentiating non-specific abdominal pain from acute appendicitis in children was found to be the presence of abdominal guarding. This was found to be present in 94% of the children with acute appendicitis compared with only 9% in the children with non-specific abdominal pain.

Andrássy and his colleagues (1976) comment that gall-bladder disease in children and adolescents appears to be increasing. They review seventy-nine patients, 20 years of age or younger, in a group of 1803 cholecystectomies performed for biliary disease in Texas. There were sixty-nine females and ten males. Sixty were Mexican-Americans, five were black and fourteen were white. The average age of the males was 12.5 years and the age of the females averaged 17.8 years. The youngest was 3 months. Twenty-one of the patients were 17 years of age or younger and the average age in this group was 11.6 years; sixteen of these were found to have stones. All five of the black patients had haemoglobinopathies. The incidence in children and adolescents in this series was 4.3% over the past 5 years. This quite substantial figure may be due to increased recognition of the disease with the increasing availability of diagnostic aids, the influence of diet and obesity on the general population and the specific prevalence of this disease in the racial population reviewed. The high incidence in Mexican-Americans contrasted with the fact that they composed only 47% of the local population. It is possible that diet or other factors contribute to the lithogenic qualities of the bile in these patients. It is interesting that the 3-month-old patient in this series was found to have a perforation of the common duct at the junction with the cystic duct. Two similar cases are reported by Howard, Johnston & Mowat (1976), both of whom were 5 weeks of age, and this constant site

of perforation may represent a developmental weakness.

Cholecystitis should obviously be considered early in the child or adolescent with unexplained abdominal pain and an oral cholecystogram is a safe and reliable method of diagnosis. In the Texas series, oral cholecystography was performed in sixty-nine patients. Stones were found in forty-one, non-function on double dosage occurred in twenty-six and the results were normal in only two instances.

Complications of duodenal ulcer

Although the incidence of duodenal ulcer appears to be falling and in spite of ever-improving medical therapy and earlier recourse to elective surgery in patients who fail to respond to the physician, the complications of duodenal ulcer (perforation, haemorrhage and stenosis) are still frequently seen.

Perforation

This complication of duodenal ulcer reached its highest peak at the end of World War II. Although it is now on a decline in the U.K., it is still a common surgical emergency. Mackay & Mackay (1976), in a review of the Glasgow area, found a 4.4 : 1 male to female ratio and nearly nine times as many duodenal perforations occurred compared with perforations of gastric ulcer. In Glasgow there is a peak incidence at New Year and men tend to perforate on Fridays and Saturdays after the factories have closed and the public houses have opened. The overall mortality in this study remains at 11% and, as in all publications on this subject, increases with the age of the patient and the delay in surgical intervention. Provided that the patient is otherwise fit, that the diagnosis is made promptly and surgery instituted at once, the immediate outlook for survival is now reasonably good. There is much interest, however, in the ultimate prognosis of the patient who has had his perforation repaired and in the choice of the emergency operation which should be carried out. Until recent years, simple closure of the perforation was almost universally employed and gastrectomy resorted to in those relatively rare cases where there was recurrence of perforation, associated stenosis or concomitant haemorrhage. Subsequent prognosis following simple repair depends to a great extent on whether the perforation is an acute episode involving a previously healthy duodenum, when the outlook is relatively good, or whether it is merely part of the progressive natural history of a chronic peptic ulcer, when recurrent symptoms are very likely to occur. As a rough guide, many surgeons state that 20% of patients having suture of an acute perforation with a short or absent previous history will require subsequent elective surgery but something like 80%

of chronic ulcers which have perforated are going to relapse after simple suture and are going to require a vagotomy or gastrectomy.

Griffin & Organ (1976), in a review of 174 perforated duodenal ulcers treated over a 25-year period, have been able to give some interesting features of the natural history of this condition. Of 122 patients undergoing suture repair, twenty were lost to follow-up, twenty-six died of unrelated causes, leaving seventy-six for follow-up. Five of these died from later complications of the ulcer (four of haemorrhage and one of a further perforated ulcer); thirty-nine (32%) required re-operation of which thirty-four were elective and five were for further perforation, two of whom later required definitive surgery. Recurrence of symptoms, re-operation and higher mortality were characteristic of the 80% of cases who had a long previous history of duodenal ulceration. There were thirteen deaths from perforation (7.4%) and seven of these thirteen deaths occurred in patients over 70 years of age. The mortality was 6.5% in patients undergoing simple suture and 9.6% in the fifty-two patients undergoing an immediate definitive operation. These authors conclude that suture of the perforation is an excellent life-saving procedure but it is of limited value in terms of definitive cure. Skarstein and Høisaeter (1976) from Bergen, Norway, report a long-term follow-up on 126 patients with perforated peptic ulcer of whom fifty-three underwent gastrectomy and seventy-three simple closure. None of the former required subsequent surgery but 27% of the latter needed further operation between 3 months and 10 years after perforation. The good results of gastrectomy were found particularly to occur in the 50 to 59-year age group and those with a long history of peptic ulcer pain and perforations under 6 hr in duration.

Because of the poor long-term prognosis of simple repair, more and more surgeons have been turning to more radical surgery at the time of the emergency procedure and in recent years vagotomy and drainage has come into favour, excising the perforated ulcer in fashioning the pyloroplasty. The original fears of the dangers of a mediastinitis as a result of opening the oesophageal hiatus in the presence of peritoneal contamination has not proved to be a problem in practice. However, there do not appear to be any randomized prospective trials comparing the two techniques, nor indeed would these be justified, since even those surgeons who advise radical surgery avoid so doing in most poor risk late cases with established peritonitis. Thus Jordan & Korompai (1976), who carried out a randomized prospective survey comparing vagotomy and drainage with vagotomy and hemigastrectomy in perforation, rejected forty out of

157 patients for the trial because of poor risk and performed a simple closure in such a situation. Not surprisingly, there were no less than eight early deaths in these seriously ill patients (20%). This compared with only one postoperative death in the 117 patients undergoing definitive surgery. There was little to choose between the two types of curative operation and the long-term results were about the same as those that might be anticipated from other published series performed on elective patients. These authors then performed thirteen simple closures combined with a highly selective vagotomy, confined to denervation of the parietal cell mass in patients who were candidates for definitive treatment because of the chronicity of their ulcers. There were no deaths, no significant morbidity apart from one intestinal obstruction due to adhesions and the results are satisfactory in a short follow-up period of only 21 months. In a later report Jordan and his colleagues (1976) reported on twelve patients operated upon by colleagues in Sweden and thirteen patients in Houston who underwent selective vagotomy for the treatment of perforated duodenal ulcer. A drainage procedure was added in four of the cases. There were no operative complications and no deaths. Twenty-two of the patients were followed up from 6 months to 4 years and none had recurrent ulcer, dumping, diarrhoea or other significant gastric symptoms. At the time of their last follow-up, the results were considered excellent or good in all twenty-two patients. If the long-term results are maintained, this may indeed provide the operation of choice for the uncomplicated but chronic perforated duodenal ulcer.

What, then, is the wisest course of treatment? In the U.K. much emergency surgery is carried out by junior staff in less than ideal conditions and we must anticipate that this situation will deteriorate sharply in the immediate future. For these circumstances, the simplest possible life-saving procedure should be carried out which is repair of the perforation using an omental patch (Leading Article, 1976a). This remains the wisest move in the desperately ill or elderly patient or when the perforation has been established for 24 hr or more. Once life has been saved, the patient can then be reviewed and subsequent surgery advised if he has undoubted chronic duodenal ulcer or if, in the previously asymptomatic case, symptoms subsequently appear. In expert hands and under good conditions further hospital admission can, however, be obviated by performing definitive surgery at the time of perforation in the otherwise fit patient with a chronic duodenal ulcer.

Haemorrhage

Bleeding from a duodenal ulcer which continues

or recurs while the patient is under medical care is an established indication for surgical intervention. Unfortunately, it is not uncommon for these patients to be in an extremely poor condition, frequently as a result of co-existing disease, for example chronic bronchitis or congestive cardiac failure. The radiologists are becoming more and more skilled at selective catheterization of blood vessels and there is considerable interest in their ability to use this technique in haemorrhage control. Eisenberg & Steer (1976), of the Harvard Medical School, describe the use of a balloon catheter for the injection of retracted autologous clot injected into the bleeding vessel which is located angiographically. In six poor risk cases, bleeding was controlled in five although two later bled from other sites. The excellent collateral blood supply in the pyloroduodenal area makes infarction unlikely. In passing, we can note that a similar technique may be used in the treatment of bleeding oesophageal varices. Scott and his colleagues (1976a,b) report from the Royal Free Hospital on their technique of passing a catheter via the liver into the portal vein and then selectively catheterizing the left or the short gastric veins. They employ a mixture of hypertonic glucose and human thrombin, although others are using cyanocrylate, which is a quick-setting acrylic monomer.

A rare cause of duodenal ulcer complicated by haemorrhage is discussed by Muir & Jones (1976). This is the Curling's ulceration of the duodenum, which may complicate severe burns. This was first described in 1842 by T. B. Curling who, when assistant surgeon to the London Hospital, reported three severely burnt children who bled from posterior penetrating duodenal ulcers 10–18 days after burning. Muir & Jones report a case in a 30-month-old child with 50% burns complicated by a penetrating posterior duodenal ulcer who suffered fatal haemorrhage. Enquiry among the surgical units treating burns in Great Britain showed that only eighteen cases of gastrointestinal bleeding had been seen in the course of treating some 32,500 patients.

Undoubtedly the most exciting news in the treatment of peptic ulcer is the introduction of potent histamine H_2 -antagonists which dramatically suppress gastric acid secretion to a level which permits peptic ulcers to heal and yet are without the other antihistamine effects. The first drug of this group to be produced, metiamide, was found to have a bone marrow depressing effect and has now been replaced by cimetidine, which differs from it in having a cyano-guanidine group in place of the thiourea group in the side chain (Pounder *et al.*, 1976). Macdonald, Steele & Bottomley (1976) report the use of metiamide in fourteen episodes of bleeding from stomach or duodenum in eleven severely ill patients (including five with renal transplants). In

eleven instances bleeding was due to erosive gastritis or duodenitis and bleeding promptly ceased after one or two doses of 300 mg orally at 6-hourly intervals and did not recur as long as the drug was continued. Bleeding from one chronic duodenal ulcer ceased but two other patients with chronic ulcers eroding major vessels continued to bleed and in this state of affairs it would obviously be necessary to carry out emergency surgery. Cimetidine appears equally effective in arresting bleeding from gastric erosions (Leading Article, 1976b). Obviously the long-term results of cimetidine treatment will be awaited with interest.

Stenosis

Duodenal ulcer remains the commonest cause of gastric outlet obstruction in the adult in the U.K. Thus, in a consecutive series of 204 patients with pyloric stenosis at Westminster Hospital, 123 had duodenal ulcer, sixty-five gastric carcinoma, six benign gastric ulcer, three had pyloric hypertrophy, there were two examples of carcinoma of the pancreas and one example each of lymphosarcoma, Hodgkin's disease, congenital web, idiopathic narrowing and an ectopic pancreatic nodule (Ellis, 1976). Once organic stenosis has occurred, surgical intervention is inevitable and most surgeons would now advise vagotomy combined with some sort of gastric drainage, either pyloroplasty, gastro-jejunotomy or antrectomy. However, McMahon and his colleagues (1976) report on twenty-three patients with stenosis treated with highly selective vagotomy combined with digital dilatation of the stenosis through a small gastrotomy incision and they compare this with twenty-three other patients treated by their colleagues with conventional truncal vagotomy and drainage. In a follow-up of from 4 months to 5 years there were no recurrences. Two patients in each group required further surgery for gastric stasis. In the highly selective vagotomy group twenty-two out of twenty-three eventually obtained excellent functional results (Visick grades I or II) compared with only seventeen in the drainage group. In four patients the dilatations actually perforated the duodenum and this was repaired with catgut. Certainly these results of extremely conservative surgery are interesting and, once again, one awaits the results of a larger series followed-up for a longer period with considerable interest.

Thyroid cancer

Primary malignant tumours of the thyroid gland are fortunately uncommon in this country. Thus, at the London Hospital in the 27 years between 1945 and 1972 there were 179 patients with primary malignant thyroid neoplasm. The histological classification of these cases has been well reviewed

by Beaugie and his colleagues (1976). They are best classified according to their cells of origin. From the follicular cells derive the differentiated papillary and follicular tumours and the undifferentiated anaplastic carcinoma. From the parafollicular cells (or C cells) develops the medullary carcinoma and from the lymphoreticular cell originates the malignant lymphoma.

The papillary carcinomas can be further subdivided into the occult (less than 1.5 cm in diameter), the intra-thyroid and the extra-thyroid, which has breached the thyroid capsule. The follicular carcinomas are sub-divided into microangio-invasive (whose spread is restricted to capsular venous sinuses) and angio-invasive (where spread has extended into extra capsular veins).

Of a total of 179 patients, there were eighty-one papillary, thirty-two follicular, thirty-one undifferentiated, and fourteen medullary carcinomas. There were twenty-one examples of malignant lymphoma. It is interesting that none of the patients was thought to have been exposed to known goitrogens or had undergone previous thyroid irradiation, a topic which we shall refer to again below.

The importance of the histological classification of these relatively rare tumours is because it is a valuable aid to both treatment and prognosis. Staunton & Greening (1976) have reviewed the 293 patients with thyroid cancer treated at the Royal Marsden Hospital between 1931 and 1963. Of the tumours 36% were papillary, with a 36% 20-year survival. Twenty-one percent were follicular tumours with a 20% survival and 42% were anaplastic with only 4% 20-year survival. There was a 1% incidence of medullary tumours. As a result of their review of these patients they advocate subtotal resection of the thyroid for papillary tumours unless there is gross bilateral spread, where total thyroidectomy is indicated. The rather poorer experience with follicular tumours leads them to advocate total thyroidectomy for a trial period. Radiotherapy is usually all that is available for the anaplastic cases and there are occasional long-term survivals in this group. Radioactive iodine is beneficial in many cases of follicular and papillary tumour but confers no check on anaplastic growths.

It should be pointed out that there is still no uniformity of advice about the treatment of the various types of well differentiated thyroid cancer, simply because numbers are small, prognosis in many early cases excellent and the individual experience of any one surgeon, or even centre, limited.

Malignant lymphoma of the thyroid is a rare tumour which at one time was confused with anaplastic small cell carcinoma. Adjacent lymph nodes are nearly always involved and their histological examination may be the only way of establishing a

firm diagnosis. Taylor (1976) reviews eight such cases from Sheffield, collected over a 10-year period. The disease has a strong female preponderance, especially in the elderly, and is more likely to occur in a gland affected by Hashimoto's disease. This relationship was found in four of Taylor's eight patients.

In the U.S.A., radiation-induced carcinoma of the thyroid has become a relatively common clinical problem. Some 20–30 years ago a large number of infants had irradiation of the thymus with the mistaken idea that this would prevent 'cot deaths' from tracheal obstruction. Others between the ages of 3 and 8 years had X-ray treatment to the tonsils and adenoids, again with the mistaken idea that this would eliminate the need for tonsillectomy. By the late 1950s, a relationship between irradiation in childhood and the subsequent development of thyroid cancer came to be recognized. Kaplan & Taylor (1976) suggest that 7% of patients who have received 180–1500 rad are likely to develop carcinoma of the thyroid, although other series give an incidence of only 1–1.5%. The latent period in this study was about 25 years. Cancer did not appear to develop in patients who had received high X-ray dosage for malignant disease. The tumours which develop are papillary, follicular or mixed types. They are frequently multicentric and often bilateral, so that these authors advise total thyroidectomy with identification and preservation of the recurrent laryngeal nerves and of the parathyroid glands. Because irradiation-induced tumours are slow growing, prognosis is good if correct treatment is given. Paloyan and his colleagues (1976) estimate that in Chicago some 71,000 individuals were exposed to head and neck irradiation as children. They studied seventy patients with nodular goitre who gave a history of previous irradiation. These were treated by total thyroidectomy and thirty-eight of the patients (54%) were found to have cancer of the thyroid; twenty of these had lymph node deposits and four had distant metastases, seventeen (45%) had tumour involving both lobes of the gland and four had a tumour in the contralateral lobe to the one containing the clinically obvious nodule. Unlike the non-irradiation cancer, with its female sex preponderance, the irradiation-induced cancers have an equal sex distribution. These authors also advocate total removal of the thyroid with parathyroid preservation. If these glands are inadvertently removed, the parathyroid tissue should be minced up and re-implanted into adjacent muscle.

The presence of a single thyroid nodule always raises the possibility of malignant disease and this is especially so if the nodule on scanning concentrates less radio-iodine than the surrounding parenchyma and hence appears 'cold' on the scintiscan.

The incidence of malignancy in 'cold' thyroid nodules reported from different countries varies from 4.8 to 58%. At one time it was thought that carcinoma was almost unknown in the presence of hyperthyroidism, but this is by no means true. Livadas, Psarras & Koutras (1976) report on sixty-five patients with hyperthyroidism in whom a thyroid nodule showed as a 'cold' area on scanning. No less than fourteen (21.5%) were malignant. Interestingly enough, this compared with a 12% incidence of malignancy in their series of 859 euthyroid patients with 'cold' nodules. In their fourteen malignant neoplasms associated with hyperthyroidism, seven were follicular, six papillary and one an anaplastic carcinoma. These authors point out that a hyperfunction of the thyroid gland is by no means a guarantee against malignant disease.

Haff and his colleagues (1976), at a U.S. Air Force hospital in Texas, review 348 thyroid masses explored over a 10-year period; fifty-seven of these (16.4%) were malignant. The risk of malignancy was 25% in males and 13% in females, a statistically significant difference. The presence of enlarged cervical nodes was also a highly significant clinical feature and malignancy was found in twenty-five of thirty-eight patients with this physical sign (65.8%). However, the physical characteristics of the gland itself were not found to be significantly important. The presence of multiple 'cold' nodules or of functional nodules on scanning decreased the probability of malignancy, but three of thirty-eight functional nodules (8%) proved to be malignant. Katz & Zager (1976) have studied 910 patients with solitary 'cold' nodules in Los Angeles. Of these, 78% were female with a 21% incidence of malignant disease compared with a 27% incidence in their male patients. Cancer was less common in their black compared to their white thyroid population.

It may be that these interesting racial and geographical variations in this disease may provide valuable clues to aetiology and management.

Cancer of the breast

It is unusual to open a medical journal today without finding an article dealing with breast cancer. The intense interest in this subject is easy enough to understand when we realize that in spite of all the efforts of surgeons, radiotherapists, oncologists and basic scientists, the introduction of screening clinics and mammography, and the expenditure of millions of pounds on research, breast cancer remains the commonest cause of death from malignant disease in the Western world. In 1973 some 11,500 women in England and Wales died from this condition and indeed the mortality from the disease is actually on the increase, especially among those aged 45-64 years (Armstrong, 1976).

Among topics of particular interest are the value of screening programmes for breast cancer, the role of more conservative surgery than the standard mastectomy and the place of cytotoxic therapy as adjuvant treatment for early cases.

Screening

The most elaborate and largest screening programme is the Health Insurance Plan trial in New York, which is now able to publish 7-year follow-up figures (Strax, 1976). This enormous scheme incorporates about 30 000 women in the studied group compared with 30 000 controls and comprises an annual mammography and clinical examination. Of the tumours detected, some 33% are picked up on mammography only, 44% on clinical examination only and 22% are detected by both, whereas in ordinary practice 80% are detected by both methods. Certainly mammography alone without clinical examination appears not to be justified (Lewis *et al.*, 1976). Mammography is especially useful in the large, fatty, post-menopausal breast and is of less use in the small dense pre-menopausal organ. The results reported by Strax are showing a 35% reduction in the number of deaths from breast cancer in the group offered annual screening examinations when compared with the control group which received only normal medical care, but this benefit was confined entirely to the 50-year-plus age group.

Assuming that the New York figures would be applicable to the patient groups in other countries, a number of problems still remain. How often should screening be carried out? Should mammography be restricted as far as possible to the over 40 age group? and is there a risk of radiation-induced breast malignancy in younger women exposed to repeated small doses of X-rays? Can health services afford the costs of these programmes? George and his colleagues (1976) from Manchester represent one of the three centres (the others being in Edinburgh and Ealing) set up by the DHSS to investigate the feasibility of establishing a nation-wide service. The Manchester group set itself to investigate whether screening could be done by non-medical staff, to assess the safety of repeated mammography, to study the acceptability of screening to women at risk and to assess how great an additional surgical work load this programme would provide. Patients were examined independently by trained nurses and surgeons. Similarly each mammogram was read and recorded separately by a radiographer and by a consultant radiologist. It was found that when acting together as a team nurses and radiographers could detect significant abnormalities as effectively as medical staff and could therefore act satisfactorily as primary screeners if adequate facilities for subsequent referral and treatment were available. It

has been estimated that unless the dose level per mammography examination is reduced to at most 2 rad then the risk of breast cancer induction might have to be taken into account in population screening examinations. The Manchester group found that doses below 2 rad per total examination cannot be achieved with traditional industrial quality film, which should not be used for screening. Low dose systems can be used with the loss of some fine detail and the best compromise between dose of radiation and high quality films is still being investigated. The screening programme was offered to all women over the age of 50 attending two large group practices in South Manchester. Those who failed to respond received a second invitation; 54% of the women invited actually attended for screening. The biopsy rate for invited women was 1.9% but this might apply only to the first year of a screening service and would probably decrease in subsequent years. It would not appear that the work load presented by this group of patients would overwhelm the surgical services of the Manchester hospitals.

With an already over-stretched National Health Service, the cost of any screening programme must obviously be taken into consideration (Leading Article, 1976a). It has been estimated that a screening programme in the U.S.A. for women over the age of 40 would cost \$622 million annually. A similar scheme in England and Wales was estimated at £12 million annually at 1975 prices. Further mathematics indicated a 12% reduction in mortality from breast cancer and a cost of £8000 per 'life saved'.

If we could define more accurately those women at high risk of developing breast cancer and concentrate our screening efforts on this group (such as X-raying the chests of heavy cigarette smokers) then obviously there would be a great saving in both time and money. Stark (1976) reports on the screening programme at Gateshead which combines clinical examination, mammography and thermography. Women between 35 and 75 years of age are included and are self-selected. The pick up of cancer is 7.6/1000 women screened. Stark considers that those at high risk are women with a previous abnormal thermogram or equivocal mammogram, a previous family history of breast cancer, women who are childless or of low parity or have a first child born after the age of 35, have had a previous benign breast lump removed or who have a late menopause. In this group the pick up is 24.5/1000 and the annual pick-up in the high risk group after a negative preliminary screening is 8.3/1000 over a 6-year period. Stark does not re-screen the low risk group unless the patient asks for a re-appointment since the yield is low and, with low financial and personnel resources, it is considered wiser to concentrate entirely on the high-risk women.

The search for markers of high-risk patients is obviously of importance. Lynch and his colleagues (1976) note that approximately one patient in twelve with breast cancer is familial, i.e. with two or more first degree relatives suffering this disease. In fifty-two breast cancer-prone families, six had at least one patient with cancer manifest before the age of 30 and one had two. Kessler and his colleagues (1976) found that 26% of patients with bilateral breast cancer had a family history of this disease and were on average younger than patients with unilateral breast cancer. In 967 cases, thirty-five had a second primary tumour (3.6%) of which seventeen (1.8%) occurred synchronously. Kapadi & Wolfe (1976) have investigated the relationship of breast cancer to thyroid supplements for hypothyroidism. In a review of 5505 mammographies, 635 patients were found to be on thyroid supplements. In the control group, breast cancer was found in 6.2% whereas in the supplement group the incidence rose to 12.1% and in those receiving thyroid for 15 years or more it reached 19.5% (thirty cancers in 154 patients). In the nulliparous women on 15 years of thyroid supplements the incidence was a surprising 33%. Wolfe (1976), in an important retrospective study of 7214 mammograms, was able to define a high-risk group with prominent duct pattern and/or mammary dysplasia and argues whether such patients might, in selected instances, warrant bilateral simple mastectomy as a prophylactic measure.

Most investigators are disenchanted with the value of thermography in breast screening. Moskowitz and his colleagues (1976) found 'no ability of thermography to select patients harbouring early carcinoma detectable by other means from a general population of patients'. Johnson and his colleagues (1976) studied fifty thermograms on women subsequently shown to have histologically proved carcinoma of the breast. Only thirty-two showed increased heat production on the affected side. In six the affected side was cooler, in eleven there was no asymmetry between the breasts and one had equivocal findings. There was poor correlation also between thermography and the size and depth of the tumour. If economies are to be made, one appears to be in the purchase of further thermographic equipment for breast screening programmes!

The relationship between previous benign breast disease and the development of carcinoma remains the subject of controversy. Monson and his colleagues (1976), from Boston, report a study of 733 women who had undergone a breast biopsy which had led to the diagnosis of chronic mastitis and who were then followed-up for an average of 30 years. Forty-nine died from breast cancer compared with an expected number of 18.8. However, Devitt (1976), in a review of 1059 patients presenting with breast

disorders, found that only 11% of patients with breast cancer had had a previous benign breast biopsy specimen. He points out that the incidence of clinical benign breast disease in the population is unknown, but he calculates that at least 30% of the female population have clinical benign breast disorders. This almost certainly underestimates the incidence and indeed it is quite rare to examine the breast of any woman over the age of about 35 without finding at least some granularity of the breast tissue which could be labelled 'chronic mastitis'. Devitt points out the relative rarity of previous biopsies or aspirations for benign disease in women with breast cancer and considers that preventative measures should be no different in this group of patients than in those without previous benign breast lesions.

Leis & Raciti (1976), after reviewing known facts and possible theories concerning women at high risk, sum up by stating 'the search for the patient with the highest risk of developing breast cancer would culminate in the finding of a 51-year-old, fat, hypothyroid, Caucasian nun, living in a cold climate in the Western hemisphere, with a wet type of cerumen and a prolonged menstrual history, whose mother and sister had pre-menopausal bilateral breast cancer, who was nursed by a mother who had B viral particles in her milk, who has had endometrial cancer and a cancer in one breast, whose random biopsy of the other breast showed a pre-cancerous mastopathy, who has a low oestriol fraction and an abnormal Bulbrook discriminant, who is immunodeficient, who received heavy radiation exposure during treatment for tuberculosis by repeated fluoroscopies and who has a high dietary fat intake'!

The management of the 'early' case

One might think that the management of small cancer confined to the breast without evidence of dissemination would be a simple problem. Yet opinions concerning the correct treatment of this lesion vary widely from the most radical to the most conservative surgery. Moreover, views range from the most optimistic to the most pessimistic about prognosis; from those who claim that early diagnosis must be correlated with a high chance of cure to those who consider with Bond (1968) that 'breast carcinoma should be regarded as a disseminated disease, the metastases remaining dormant, or growing at a very slow rate until they present clinically. Although the condition is not necessarily lethal, cure in the sense of its total elimination is impossible by present methods'. Duncan & Kerr (1976), in a study of 982 women treated for localized breast cancer, showed that even 15-19 years after treatment the death rate from breast cancer in the treated groups still exceeded

that in the control population. Baum (1976) points out that some 20-30% of women with early breast cancers have a normal life expectation after local treatment and that 25% of these have involved axillary nodes. He criticizes our complacent attitude in continuing current practice of subjecting at least 70% of women with primary disease to a futile mutilating procedure without further questioning; if we were able to define more accurately those patients who have dissemination before this can be detected either radiographically or clinically, results might be improved, he argues, by adjuvant systemic therapy.

Certainly, the controlled trials which are now in progress and which are being reported show that the particular type of local treatment given to early cases, provided that this is adequate, is not likely to affect prognosis with regard to expectation of life. Hamilton, Langlands & Prescott (1976), for example, report that at 10 years they have a 47% disease-free survival in patients submitted to radical mastectomy compared with 45% for simple mastectomy combined with radiotherapy. Prognosis has thus not been affected *quae* survival by treatment but depends far more on other factors; for example, in the radical mastectomy group the node-negative patients enjoyed a 66% disease-free survival compared with only 27% when the nodes were involved. The International Multicentre trial (1976) of 2268 patients compares simple mastectomy and radiotherapy with simple mastectomy alone. With a 5-year follow-up there was no evidence that routine postoperative radiotherapy was harmful or that it conferred further benefit as regards survival or distant recurrence. Radiotherapy did, however, reduce the incidence of local recurrence.

As screening programmes and greater awareness of the population are producing more and more 'early' tumours, surgeons are experimenting with more conservative surgery in such cases. Poisson and his colleagues (1976), in Montreal, for example, are carrying out wide local excision of tumours measuring 1 cm or less and clearing the axillary lymph nodes either through the same or separate incision. Their mean follow-up is only 30 months and obviously a longer period of follow-up is essential in the assessment of such a technique. Watts (1976) has been carrying out simple mastectomies with immediate or delayed replacement of the breast using a plastic prosthesis. In 200 patients spread over a 7-year period there have been seven local recurrences which have been irradiated without loss of the prosthesis and five others have had surgical removal of local recurrences, two on several occasions. Once again this is a technique which will require very careful long term assessment and evaluation.

Adjuvant cytotoxic therapy

Many women with apparently early, operable, breast cancer will develop metastases and die within 5 years of mastectomy. This means that these metastases must have been present, but occult, at the time of initial treatment. The development of sophisticated bone scanning techniques has shown that up to 30% of such patients have evidence of bony metastases at this early stage, and this is particularly likely to be so when the primary tumour is more than 4 cm in diameter and when the axillary lymph nodes are involved (Campbell, Banks & Oates, 1976; Citrin *et al.*, 1976; El-Domeiri & Shroff, 1976). Indeed, the presence of extensive metastatic involvement of the axillary lymph nodes (four or more) is about the best marker we have today of the likelihood of tumour dissemination having occurred. In this context it is interesting that Schwartz & Zeok (1976), in a review of women aged 30 years or under with carcinoma of the breast, found that if the nodes were clear the prognosis was equivalent to breast cancer in other age groups but if the nodes were involved only 16.3% survived 10 years from the time of surgery.

The threat to the patient's life lies in the micro-metastases that have already seeded to distant sites by the time she reports for treatment of the primary tumour and so there is immense interest in important recent trials of adjuvant cytotoxic therapy in patients following mastectomy who have involved axillary lymph nodes. Fisher and his colleagues (1975) reported a widely publicized trial using L-phenylalanine mustard (L-PAM). Evaluation of 108 patients on placebo and 103 on L-PAM was reported over a 2-year period. Recurrences had occurred in 22% of the placebo group and 9.7% of the treated group, which was statistically significant. This significance, however, was confined to the pre-menopausal women and although a similar trend was observed in post-menopausal patients, the difference was not statistically significant. Fisher and his colleagues point out that it is not known whether the differences will be sustained or will be found to be only transient and it is not known whether a difference in survival rate will be demonstrated. It is also possible that undesirable sequelae, such as lympho-proliferative neoplasms, might possibly become apparent after prolonged follow-up so they stress that additional observations over an extended time are required. Bonadonna and others from Milan (Bonadonna *et al.*, 1976; Bonadonna & Rossi, 1976) have tested the effects of a triple drug regime of cyclophosphamide, methotrexate and 5-fluorouracil. There are now 386 evaluable patients randomized after surgery in 1973. Relapses occurred in forty-three of 179 control patients (24%) and ten of these have died, whereas there have been eleven relapses in 207 treated patients (5.3%) with one death.

These are interesting results but it must once again be stressed that they are early. There is no evidence yet that life has been prolonged (Leading Article, 1976b). The fact that the results are particularly encouraging in pre-menopausal women may suggest that at least a major part of the cytotoxic action may be due to depressed ovarian activity especially as amenorrhoea is reported in the majority of treated pre-menopausal patients. Stoll (1976) has therefore suggested that it would be logical and practical to select treatment for high-risk patients after mastectomy by means of an oestrogen receptor assay of their tumours. Those with a positive assay would be considered for trial of anti-oestrogen therapy but those with negative assay would be considered for trial of cytotoxic therapy. The British Breast Group (1976) advise that until firm answers are obtained from controlled randomized studies chemotherapy should not be used electively in primary operable breast disease.

Wound healing

It has been said that surgeons are physicians who are condemned to operate. As such, they are naturally intensely interested in the techniques of how to inflict surgical wounds with the minimum of blood loss and tissue injury, and how to repair them with the maximum of safety to the patient. One of the greatest contributions of the U.S.A. to surgery was the introduction of the electrocautery for both cutting and haemostasis. Yet many surgeons, especially the Americans themselves, are hesitant to use this apparatus because they fear impairment of wound healing. We have studied the healing of diathermy incisions made in the rat stomach compared with a standard scalpel-inflicted wound. Healing was assessed by bursting strength measurements, angiography and histology. All incisions were soundly healed by the tenth day and the only significant difference discovered was that histologically there was a definite lag in healing up to the fifth day in the diathermy incisions. This seemed to be due to the mucosa having been dragged into the wound edges by adherence to the diathermy knife in the thin-walled rat stomach, a situation that may well not apply to the human organ (Rosin, Exarchakos & Ellis, 1976). There is great interest in the introduction of the Laser beam in surgery and much developmental work has been carried out with this apparatus in Israel (Kaplan, 1976). Kott and his colleagues (1976) have compared scalpel incision, diathermy and the Laser beam in the healing of intestinal anastomoses in cats. There were no instances of macroscopic leakage. Complete healing had taken place by the eleventh day using the scalpel and by the thirteenth day with both the Laser and the diathermy. Histo-

logically there was more necrosis seen with the diathermy than with the Laser beam. The Laser may well prove of value in surgery on highly vascular structures, for example liver tumours, but further careful clinical studies are obviously necessary.

The technique of closure of the laparotomy wound remains the subject of much debate and a great deal, indeed, remains to be learnt. Regretfully wound failure, by which we mean both burst abdomen or the subsequent development of an incisional hernia, remains an important and all too common problem. Most surgeons believe that suture of the peritoneum is an essential step in laparotomy wound closure, yet we have shown that peritoneal defects heal smoothly and with remarkable speed in the experimental animal (Ellis, 1962). Karipineni, Wilk & Danese (1976) have demonstrated no difference in the bursting strength of laparotomy wounds in dogs whether or not the peritoneum was sutured. In his Arnott demonstration (Ellis, 1977) the author reported a series of patients undergoing laparotomy randomized between a double layer closure of catgut to peritoneum and nylon to the fascia and a second single layer group in which the peritoneal layer was omitted. Up to October 1976, 137 patients had been closed by the two-layer and 137 by the one-layer technique. There were three examples of complete dehiscence of the abdominal wall in each group. In the 202 patients who to date have been followed-up from 3 months to 1 year from the time of operation, the incidence of incisional hernia was 5% in both groups. Surgeons still debate the best technique to employ in closing the abdominal wall and much remains to be learned from carefully constructed prospective trials. Leaper and his colleagues (1976) have confirmed that catgut gives an unacceptably high rate of burst abdomen and in their series there was a 6% incidence of this complication. Using mass closure with interrupted steel sutures in ninety-eight patients there was not a single case of burst abdomen and only one incisional hernia. It is extraordinary that in the face of this and other reports that some surgeons still continue to close the abdominal incision with catgut. Martyak & Curtis (1976) confirm the excellent results of mass closure, but employ a continuous nylon suture. Irvin, Koffman & Duthie (1976) have compared the new synthetic absorbable polyglactin and polyglycolic acid sutures with the non-absorbable polypropylene suture in the closure of 161 laparotomy wounds using a layered closure technique. The total incidence of wound dehiscence and herniation was 8% and there was no significant difference between the three suture materials (similar findings are reported by Kjaergaard *et al.*, 1976).

Interestingly enough wound failure was significantly more common in wounds closed by surgeons in training. None of these suture materials is therefore entirely free from wound complication and further studies of techniques of closure are still required.

The fact is that most wounds heal up satisfactorily in healthy patients who run a complication-free post-operative course and the prevention of abdominal and wound dehiscence is largely the prevention of pulmonary complications, abdominal distension and infection (Peacock & Van Winkle, 1976). Future progress may depend a good deal on our being able to define those patients at particular risk of wound failure, either from local or systemic factors, and to devise the most effective way of combating the risks presented by these factors. Pitkin (1976), for example, found a much higher incidence of wound complication in obese women undergoing abdominal hysterectomy compared with their thinner sisters. There was a significant increase in the rate of wound infection and of superficial and deep separation of the wounds in the obese. There were 300 patients in each group; three of the obese patients underwent evisceration and there was not a single example in the control group, an interesting observation even though this did not reach statistical significance.

However, the clinical study of wound healing is complicated by the fact that it is uncommon for any one factor to exist in isolation. Consider, for example, the patient who undergoes laparotomy for a carcinoma of the pancreas. He may be elderly, intensely jaundiced, anaemic, protein depleted and of course, he is suffering from an advanced malignant disease. Postoperatively he may develop uraemia, and put additional stress on his wound by going into ileus as well as developing a pulmonary collapse and perhaps he may by now have been placed on cytotoxic drugs. Which factor or factors do we blame if his abdominal wound bursts? Add to this, what part does the choice of incision, the suture material, the technique of closure or the seniority of the surgeon play in this disaster? This is why we often have to go to the laboratory in order to dissect out each of these multiple factors and to try to determine their significance, if any, on wound healing. Thus we have shown (Bayer & Ellis, 1976) that jaundiced rats, prepared by ligation and division of the common bile duct, demonstrate a significant loss of tensile strength in their abdominal wounds with impaired fibroblast proliferation and delayed angiogenesis. Yet during this period other factors such as the plasma protein, serum electrolytes, urea and haemoglobin remain the same as controls. Sandblom, Mirkovitch and Gardiol (1976) have demonstrated in dogs that liver wounds heal at the same rate as those of muscle or kidney. Yet when

such a wound is placed in contact with bile (via a polythene catheter threaded into the liver from the gall-bladder) serious delay in healing takes place. Interestingly enough, in our clinical study of laparotomy wound healing, we noted two complete ruptures of the laparotomy wound in eleven patients jaundiced at the time of surgery (18%) compared with four examples in 263 patients free from jaundice (1.6%). Although the jaundiced group was small, these preliminary results are interesting and reach statistical significance. It has often been suggested that jaundice impairs wound healing (Schilling, 1976) yet, surprisingly, we have not been able to trace other prospective trials comparing the wound healing of jaundiced and non-jaundiced patients treated under identical conditions.

Colin (1976) has demonstrated that a reliable and reproducible uraemic model can be prepared in the rat by unilateral nephrectomy combined with resection of the upper and lower poles of the opposite kidney. With this preparation, he has demonstrated a significant diminution in the bursting strength of laparotomy wounds and a standard small bowel anastomosis compared with controls. He has also demonstrated in tissue culture marked inhibition of fibroblast growth when either urea or uraemic rat serum was added to the culture medium. To date, regrettably, surprisingly little prospective clinical information has been collected on wound healing in uraemic patients, a subject that merits much greater attention on the part of the surgeon.

Fong and his colleagues (1976) found that chronic anaemia failed to affect the tensile strength of a skin incision in rabbits. The anaemia was produced either by iron deficiency (repeated bleeding together with diet) or a haemolytic anaemia induced by water or phenylhydrazine. In contrast, McGinn (1976a) studied the effects of acute haemorrhage on the bursting strength of skin and laparotomy wounds in the rat. After a 13% blood volume loss, the blood was returned to the animal either at 4 or 60 min. After 4 min there was no effect but at 60 min the bursting strength of the wounds was significantly lowered compared with control animals. McGinn (1976b) also compared wound healing in patients undergoing emergency surgery for acute upper gastro-intestinal haemorrhage with those undergoing elective peptic ulcer surgery. The incidence of wound dehiscence was 12.6% in the ninety-five patients operated on for haemorrhage compared with only 1.8% in the 380 elective patients. Mortality and morbidity after haemorrhage were correlated directly with the amount of blood transfused before surgery. It is known that patients with peptic ulceration have low ascorbic acid levels and McGinn & Hamilton (1976) have recently shown that ascorbic acid levels in stored blood fall rapidly

over the first 7 days so that blood replacement using stored blood would be relatively deficient in this vitamin. It may be, therefore, that the increase in wound complications in the haemorrhage group might be due to low ascorbic acid levels. This explanation would not explain the rat findings mentioned above and it is possible that a wound healing hormone or some similar substance could in some way be compromised by removal from the circulation of a portion of the circulating blood volume and its storage for periods longer than 30 min. However, in man, administration of adequate amounts of ascorbic acid to patients receiving substantial amounts of stored blood before or during surgery would appear to be a wise precaution.

The study of the physical and histological criteria of healing wounds in man is difficult since the opportunities of measuring tensile or bursting strength or of obtaining biopsy material are obviously limited. Viljanto (1976) has devised an ingenious and simple technique in which he employs a piece of cellulose sponge placed within a silastic silicone tube which is used as a wound drain. This can be left in place for up to 5 days and then studied histologically for the degree of fibroblast infiltration (usually commencing 3–4 days after implantation). It may also be possible to study other cytological and biochemical responses in human wounds by this method.

Microvascular surgery

If this author were asked which aspect of surgical technique is likely to produce the most dramatic advances in the next few years, undoubtedly his answer would be the field of microvascular reconstructive surgery. Already clinical applications are in current use and there are further exciting possibilities coming off the drawing boards of the experimental laboratories. Ostrup & Fredrickson (1976), in a useful review, list replantation of digits, the free transfer of intestine (for example to replace the cervical oesophagus), and the replacement of large skin and subcutaneous tissue defects, including their neural supply, as applications which are already in clinical use. Experimental studies are being carried out on transplantation of the entire mammary gland in dogs (with later successful pregnancy and lactation), transplantation of complete muscle with its nerve supply, transplantation of the entire joint with its vascular supply, and of bone with its nutrient vascular system.

One of the pioneers of microvascular surgery, O'Brien (1976a), has now carried out digital replantation in eighty-six patients at St Vincent's Hospital, Melbourne, with survival rates of 58% for complete and 82% for incomplete amputation. Careful selection is vital. Digits are discarded in

patients with serious general injuries or where the digits have a warm ischaemia time exceeding 10 hr, where there is gross crushing, extensive tissue loss and vessel damage or multiple fractures. The thumb is replanted wherever possible and other digits where there are multiple losses. Single digits are re-attached in children but only in special circumstances in adults. The severed parts have been used 1-7 hr after injury, even after retrieving them from waste-paper baskets, factory floors, machines and fields. The digits should be cooled pre-operatively by insertion into a plastic bag which is then packed in ice. Skeletal fixation is achieved using Kirschner pins and then seriatim tendons, veins, nerves, arteries and skin are repaired. In fourteen cases major replantation of limbs proximal to the metacarpophalangeal joints have been carried out with survival in ten, although all three above elbow replantations failed.

O'Brien (1976b) has also reviewed other aspects of microvascular replantation and reconstructive surgery. Wide areas of skin removed as part of radical surgery for cancer can now be replaced in one stage by free graft of skin together with its arterial and venous supply. The amputated thumb can be replaced with the patient's great toe, with excellent functional and cosmetic results, and there are exciting preliminary clinical results following anastomosis of lymphatics to vein in secondary obstructive lymphoedema.

Freidberg & Walsh (1976) point out that the most significant development in neurosurgery since the time of Harvey Cushing is the use of microsurgical techniques which have allowed many surgical procedures, not previously possible, to become feasible, as well as allowing other pre-existing operations to be considerably refined. The operating binocular microscope gives not only magnification of some six to forty times but also stereoscopic vision and brilliant illumination. The microscope enables more accurate removal of tumours of the cerebellopontine angle (particularly the acoustic neuroma) with preservation of underlying cranial nerves and less risk of brain stem damage. It is valuable in transphenoidal hypophysectomy in, for example, advanced breast cancer. Microsurgery has become of great value in the management of intra-cranial aneurysms, allowing accurate dissection of the structures at the circle of Willis at considerable depth. Of great interest is the possibility now of carrying out reconstructive intra-cranial vascular surgery by bypass anastomosis between the superficial temporal artery and the middle cerebral artery for patients with symptomatic middle cerebral artery stenosis or occlusion or a stenotic lesion of the internal carotid artery. More recently, bypass grafts have been described between the common carotid

artery and the intracranial portion of the internal carotid artery. The initial reports on long-term patency and clinical improvement are encouraging but obviously more experience will be required in this exciting field before indications and results can be fully evaluated. New techniques are still under development in the laboratory; for example, Feely (1976) has described experimental carotid-basilar artery bypass in the dog using the saphenous vein with patency in two out of four dogs at 3 months after operation. This type of approach may in future enable augmentation of blood flow in the vertebro-basilar system.

Subarachnoid haemorrhage due to rupture of an intra-cranial aneurysm has an immediate mortality of 43%. Conservative management of surviving patients will be followed by death of 33% of the survivors within a year and 50% within 5 years. Before the introduction of microsurgery, direct operative management of the aneurysm did not significantly improve overall mortality and morbidity. Adams, Loach & O'Laoire (1976) analysed 100 patients with intracranial aneurysm treated by microneurosurgical methods in which the aneurysm was obliterated by application of a clip or, if technically not feasible, had its wall reinforced with cotton wool and cyanoacrylate glue. At 6 months, fifteen of the patients had died, sixty-four had achieved good, twelve fair and nine poor results. Modern surgical techniques halved the total mortality but the morbidity was unaltered. The authors suggest that results can be improved by delaying surgery for 7 days and by treating any hypertension before surgery is undertaken; thirteen of the fifteen deaths occurred in patients operated on within the first week of surgery and six of the deaths as well as five of the poor results were in untreated hypertensive patients.

Each special field of surgery has good reason for considering the application of microsurgical techniques to its own particular field. Merkel and his colleagues (1976) described thirty-two patients in whom kidney transplantation surgery was carried out and in whom polar vessels of between 1.2 and 2.5 mm in diameter were anastomosed to the inferior epigastric, the main renal or the external iliac artery using microvascular surgery and employing 7/0 or 8/0 Tevdek sutures. The long-term patency in this series was 95%. Hutchinson and his colleagues (1976) have carried out no less than 1200 internal mammary artery to coronary artery anastomoses over a 3-year period using microvascular techniques with high intensity lighting and report late patency of 96% as demonstrated by postoperative angiography. Suruga and his colleagues (1976) in Tokyo report forty-six repairs in cases of congenital biliary atresia using the operating microscope with long-term patency

of the bile duct to jejunum anastomosis in 50% of their patients.

Microsurgical suturing is tedious and requires considerable practice in the laboratory before the surgeon can carry out successful anastomoses in the clinical situation. It is a young man's game. Obviously simpler techniques are under consideration and Ostrup (1976) describes the use of Nakayama's stapling apparatus (which places a ring with four to six staples of vitallium to join the divided vessel) in a laboratory study of the anastomosis of the posterior facial vein in rabbits. These vessels are between 1.5 and 2 mm in diameter. Comparison was made between the use of this apparatus and conventional suturing with atraumatic 10/0 nylon. Compared with the insertion of conventional sutures, Nakayama's apparatus gave a lower incidence of early thrombosis, no incidence of late thrombosis and took one-third of the time. Obviously considerable advances await the application of engineering to microsurgery.

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