studies suggest that platelet aggregation is increased in polycythaemia rubra vera. Despite reservations about the applicability of these ex vivo tests of platelet function, it may be that even when the platelet count has returned to normal—for example, with hydroxyurea—the functional platelet abnormality may persist, giving continued risks of thrombotic complications. I think that in such patients there is a case for using aspirin, which is probably the best antiplatelet drug available.

HJFH: Would you advocate continuing her treatment with warfarin?

LL: That is a difficult question. I think the answer must be yes, at least initially, because while large thrombi are still present they could form a focus for recurrence or extension. I think that it would be reasonable to consider withdrawing warfarin after six months, but in this decision you would need to be guided by the ultrasonic appearances of the splanchnic venous system and the calculated flows within it.

JMBH: Why should her portal vein be thrombosed? Is there any evidence for hepatic disease here?

HJFH: We have seen that the liver function tests and ultrasonography of the upper abdomen gave normal results and that there was no indication for a biopsy. The portal vein carries blood at a low flow rate between two venous circulations, making it particularly susceptible when there is a hypercoagulable state. Interestingly, studies are now showing a much higher incidence of haematological disease in patients presenting with splanchnic vein thrombosis. Given these observations, I think that good clinical management of such problems must now include careful haematological investigation at presentation and longer follow up.

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New Drugs

Gall stones

Ian A D Bouchier

In the 100 years after the first operation on the gall bladder by John Stough Bobbs cholecystectomy became the accepted method of treating patients with cholelithiasis. The recent introduction of agents that can safely dissolve gall stones and the advent of lithotripsy have added new dimensions to managing this common and economically important disorder. Gall bladder stones can be removed at operation, systemically dissolved with bile acids, crushed by extracorporeal shock wave, or locally dissolved with methyl *tert*-butyl ether; endoscopic sphincterotomy has been successful in managing common bile duct stones. Doctors can now offer several therapeutic options to patients with gall stones; and though this has enhanced the scope for manoeuvre, it has created new difficulties in making decisions.

Diagnosis

Gall stones may present in various ways. The most common and characteristic are either acute cholecystitis or obstruction of the common bile duct. Only 5% of patients with acute cholecystitis do not have coexistent gall stones. Thus stones may commonly rupture into the bowel, obstruct the terminal ileum, or cause pancreatitis. Gall stones and cancer of the gall bladder may coexist. A few patients with cholecystitis may have jaundice but not choledocholithiasis, but most patients with gall stones who are jaundiced have stones obstructing the common bile duct. Cholangitis is diagnosed when, in addition to cholestasis, there are chills, fever, and pain and tenderness in the right upper quadrant. Flatulence, intolerance of fatty food, and vague right upper quadrant and epigastric pains are often ascribed to gall stones and chronic cholecystitis. Such complaints, however, are equally often related to other common gastrointestinal disorders, and one of the main difficulties for doctors is to decide what treatment to offer patients with gall stones who present with these symptoms alone. Because only 15% of gall stones are radio-opaque a plain abdominal radiograph is often unhelpful. Ultrasonography or oral cholecystography, or both, are the basic diagnostic tools. When choledo-

cholitis is suspected endoscopic retrograde cholangiopancreatography or percutaneous transhepatic cholangiography can be performed in addition to ultrasonic scanning and computed tomography.

Gall stones in the gall bladder

Gall stones and acute cholecystitis are an indication for cholecystectomy, which is the major abdominal operation most often performed in Britain. The gall bladder is removed via a vertical paramedial incision or a subcostal incision, which is favoured in obese patients with a wide costal angle. Because choledocholithiasis occurs in 10-15% of patients, often with no overt symptoms, the common bile duct should also be investigated for gall stones. Until recently, operative cholangiography was considered to be essential in any patient undergoing cholecystectomy. The routine use of operative cholangiography has the advantage of reducing unnecessary bile duct exploration; of diagnosing gall stones that would otherwise have been overlooked by palpation, thereby reducing the number of residual gall stones in the common bile duct; and of showing unsuspected disease. Other techniques exist, however, for evaluating bile ducts, such as preoperative ultrasonography and peroperative choledocscopy, which have the advantage of avoiding an operative cholangiogram.

The consensus has moved towards early operation for patients with acute cholecystitis. On admission to hospital they receive appropriate medical support. Analgesics recommended include morphine, pethidine, and pentazocine, the last having the theoretical advantage of not raising biliary pressure. Intravenous fluids are given if the patient is vomiting and an adequate urinary flow is maintained; it is seldom necessary to use a nasogastric tube. Appropriate treatment is provided for associated cardiac or pulmonary disease. There is no evidence that anticholinergic agents are of value.

The rational use of antibiotics in acute cholecystitis remains controversial. Only half the patients coming to operation have infected bile, from which various

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aerobic and anaerobic organisms may be cultured. The yield of bacteria increases if there is obstruction of the cystic duct or cholangitis. A correlation exists between the incidence of positive bile cultures and the incidence of wound infection, intra-abdominal sepsis, and death. The choice of antibiotic may be governed by either the degree to which the antibiotic is concentrated in the bile or the probable bacterial sensitivity. Liver dysfunction or obstruction of the cystic or common bile duct, however, make therapeutic concentrations of antibiotics in the bile unlikely. Recommended antibiotics include a cephalosporin given intravenously or orally—for example, parenteral cefuroxime (750 mg to 1.5 g intravenously every eight hours or 500 mg orally twice a day), gentamycin (2-4 mg/kg/day), ampicillin (4 g a day), or tetracycline (2-4 g/day). Some authorities recommend Gram staining uncentrifuged bile obtained at cholecystectomy to help make the choice of antibiotic, thereby avoiding unnecessary prophylactic treatment. Each patient must be considered individually, but generally the following recommendations can be made: no antibiotics are required for most patients with acute gall bladder inflammation; antibiotics are given if the illness is of more than four days duration, if the clinical condition is deteriorating, in the elderly, or if there is any evidence of perforation, general peritonitis, cholangitis, or jaundice.

It is general surgical practice to perform a cholecystectomy as soon as the patient is fit for operation, usually within 12-72 hours after admission. Thus though emergency operations are occasionally indicated, urgent cholecystectomy is the procedure performed most often. After 14 days organisation and fibrosis become more prominent, which makes a cholecystectomy more difficult and necessitates a wait of 2-3 months before an elective operation is possible.

An emergency operation on the biliary tract is seldom needed because the average patient is not critically ill. For patients who have toxæmia, a perforation, spreading infection, or severe cholangitis, however, immediate intervention is necessary. In such circumstances a cholecystectomy may not be possible and the wiser decision is to undertake a cholecystostomy. In this way gall bladder stones may be removed, but they will recur unless the gall bladder is excised later. The management of choledocholithiasis and ascending cholangitis has been revolutionised by the widespread use of oral endoscopic sphincterotomy. This may be performed before an abdominal operation to remove the gall stones and drain an infected biliary system, thereby reducing the degree of toxæmia and infection and making the subsequent cholecystectomy much safer.

Gall bladder disease in the elderly

The risk of operation is not greatly increased in elderly patients who are otherwise medically fit, but general ill health or the need for an emergency operation increases the death rate considerably. The death rate of patients aged under 50 undergoing cholecystectomy is about 0.1%, but it rises to nearly 3% in patients who are elderly and may approach 8% if elderly patients are operated on for complications associated with gall stones. Elderly patients tolerate emergency operations on the biliary tract poorly, and most perforated or gangrenous gall bladders are found in this age group. A cholecystostomy may often be the most advantageous operation in the elderly because it can be performed rapidly through a small incision and under local anaesthesia if necessary. On recovery the biliary tree is evaluated by ultrasonography. If the biliary tree is normal no further operation is necessary, and the wisest course may be not to undertake any additional operations. If stones are shown in the

gall bladder or the bile duct system, however, a cholecystectomy may be warranted or an endoscopic sphincterotomy and removal of bile duct stones may be necessary. The decision will depend largely on the patient's age and state of health.

Cholelitholytic drugs

Oral drugs may be used to dissolve cholesterol rich gall stones as an alternative to elective cholecystectomy. In Western communities about 75-80% of gall stones are composed mainly of cholesterol and are theoretically amenable to dissolution using drugs that increase cholesterol solubility in bile. The outstanding biochemical abnormality in patients forming cholesterol gall stones is the secretion of hepatic bile that is saturated or supersaturated with cholesterol. At least two factors are responsible either singly or in combination: increased secretion of biliary cholesterol and reduced secretion of bile acids in bile, which is associated with a smaller than normal bile acid pool.

The two main oral drugs used are chenodeoxycholic acid and ursodeoxycholic acid. Both are naturally occurring bile acids. Ursodeoxycholic acid is the 7- β -hydroxy epimer of chenodeoxycholic acid. They are absorbed to some extent by passive non-ionic diffusion in the jejunum, but most absorption occurs in the distal ileum, where an active transport system ensures the conservation of free and conjugated bile acids. After returning to the liver the bile acids are excreted in the bile having been conjugated to glycine and taurine.

DOSES OF DRUGS AND SELECTION OF PATIENTS

Chenodeoxycholic acid is effective at doses of 10-15 mg/kg/day. The dose of ursodeoxycholic acid is 8-10 mg/kg/day. Ursodeoxycholic acid is more expensive than chenodeoxycholic acid, and to provide more cost effective treatment the two drugs may be combined in doses of 7.5 mg/kg/day chenodeoxycholic acid and 6.5 mg/kg/day ursodeoxycholic acid. There are also theoretical reasons why the combination of drugs may be more effective than single drug treatment, although the cholelitholytic efficacy of each drug or the combination is probably similar.

Patients suitable for cholelitholytic treatment should have a functioning gall bladder as shown by oral cholecystography; if stones are radiolucent this suggests that they are formed mainly of cholesterol. The stones should be less than 15 mm in diameter, and the patient should not be suffering from acute symptoms. Women who are fertile should be using an adequate contraceptive. The likelihood of success in compliant patients is about 60%. "Floating stones" seen on oral cholecystograms have a high cholesterol content and are successfully dissolved in 80-90% of patients. Large stones that occupy much of the volume of the gall bladder are less likely to respond to bile acids. Contraindications to bile acid treatment include a non-functioning gall bladder and gall stones that are radio-opaque.

About one third of the stones that appear radiolucent on conventional radiographs contain appreciable admixtures of calcium salts and pigment. Calcium and pigment gall stones do not generally respond to bile acid dissolution, which is probably why response rates are so low in apparently radiolucent stones.

MODE OF ACTION

Although chenodeoxycholic acid and ursodeoxycholic acid are both effective in dissolving gall stones that contain cholesterol, their effects on cholesterol and bile acid metabolism and their mechanisms for dissolving cholesterol in bile differ. Both reduce the cholesterol saturation in bile. Chenodeoxycholic acid reduces the secretion and synthesis of cholesterol but has no effect on cholesterol absorption. Ursodeoxy-

cholic acid reduces cholesterol secretion but has little effect on cholesterol synthesis whereas it reduces cholesterol absorption. Hepatic synthesis of bile acids from cholesterol is moderately increased or unchanged by therapeutic doses of ursodeoxycholic acid whereas chenodeoxycholic acid noticeably reduces the ability of the liver to synthesise bile acids from cholesterol.

Chenodeoxycholic acid and ursodeoxycholic acid differ greatly in their mode of cholesterol solubilisation. Chenodeoxycholic acid solubilises cholesterol in micelles whereas ursodeoxycholic acid enhances the transport of cholesterol in liquid crystalline form, which is why the bile acids have been combined to treat cholesterol gall stones.

ADVERSE EFFECTS

Both drugs have proved to be safe in clinical practice. Chenodeoxycholic acid causes moderate changes in liver biochemistry, minor increases in serum low density lipoprotein cholesterol concentration, and diarrhoea. In contrast, ursodeoxycholic acid has been shown to be very safe and causes no adverse effects or signs of toxicity. For this reason, ursodeoxycholic acid has replaced chenodeoxycholic acid as a single agent in treating gall stones.

RESPONSE TO TREATMENT

Stones of 5-10 mm diameter usually dissolve within 1-2 years, and smaller stones within 6-12 months. A low cholesterol diet and taking single bedtime doses of the bile acids enhance complete dissolution. Obese patients are more resistant to treatment and may require larger doses of the bile acids. Regular six monthly ultrasound or cholecystography follow up is required. At least six months elapse before there is any change in the size of gall stones, but treatment is unlikely to be effective if no reduction in size is seen after one year. The risk of gall stone complications is not increased during stone dissolution.

DISADVANTAGES

Cholelitholytic drugs have not proved popular in clinical use for several reasons. Firstly, fewer than 30% of all patients with gall stones fulfil the criteria for oral dissolution treatment, and when such factors as obesity and compliance are considered the figure may be as low as 10%. Secondly, the duration of treatment is a problem because stones in most patients take 18-24 months to dissolve. Radiolucent stones sometimes calcify during bile acid treatment, more commonly with ursodeoxycholic acid, but also with chenodeoxycholic acid. Whether this is new rather than previously undetected calcification unmasked during dissolution is not yet known, but it does prevent further dissolution of gall stones.

Recurrence is also a problem as the abnormality of bile acid and cholesterol metabolism returns once drug treatment is discontinued, and within 4-6 weeks the patient secretes bile that is supersaturated with cholesterol. Thus gall stones tend to recur when treatment stops. The recurrence rate is 10% a year for the first five years, after which stones do not recur. There is therefore an overall recurrence rate of 50%, or treatment is effective in half the patients. Unfortunately, there is no way of preventing gall stone recurrence. Low dose bile acid treatment or low cholesterol or high fibre diets are not effective. The newly formed stones are identified more readily by ultrasonography than cholecystography. They do not tend to cause symptoms more than stones that were present before treatment.

The management of patients once stones have been completely dissolved has yet to be established, but they should possibly be followed up every six months with ultrasonography so that small stones can be identified;

patients are then given further ursodeoxycholic acid treatment, which dissolves the small newly formed stones rapidly. The other alternative is to wait until symptoms develop and then offer a course of bile acid treatment to dissolve the stones. Patients receiving bile acid thus require long term surveillance even after their stones have dissolved. This is one of the drawbacks of this treatment compared with cholecystectomy.

Cholelitholysis has not found general favour, although it is safe, convenient, and not associated appreciably with disease or death. It is useful in patients with chronic respiratory or cardiac disease for whom other treatments are unsuitable. It can also be offered as an alternative to patients who want to avoid an operation, such as those who do not wish to take time off work and those awaiting an operation. All patients with radiolucent gall stones should at least be offered the opportunity of considering cholelitholysis as an alternative to an operation when being counselled about treatment for their gall stones.

Other methods of dissolving gall stones

ROWACHOL

Rowachol is an inexpensive preparation of six cyclic monoterpenes (menthol, menthone, pinene, borneol, camphene, and cineol) in olive oil, which has choloretic and spasmolytic properties. It may be used to treat cholesterol stones in the gall bladder and the bile ducts at a dose of one capsule/10 kg/day. The duration of treatment is similar to that for bile acid. Rowachol (one capsule twice a day) can be combined with chenodeoxycholic acid (7-10 mg/kg/day). It could presumably also be combined with ursodeoxycholic acid. A mixture of 4.8 mg/kg/day ursodeoxycholic acid and 4.8 mg/kg/day menthol, one of the components of Rowachol, has been used to treat cholesterol gall stones. Rowachol has not found general acceptance in the management of gall stones and will not be discussed further.

METHYL *tert*-BUTYL ETHER

Methyl *tert*-butyl ether can be used for dissolving gall bladder or bile duct stones. It is an ether with a boiling point of 52.2°C and is liquid at body temperatures. It is a highly effective dissolving agent for cholesterol gall stones and is infused into the gall bladder via a percutaneous transhepatic 5 French gauge pigtail catheter inserted under ultrasonic control. Gall stones can be dissolved within hours after repeated cycles of infusion of methyl *tert*-butyl ether and complete aspiration. The procedure is carried out without anaesthesia. Nausea, vomiting, duodenal erosion, pain, haemolysis, and inadvertent anaesthesia are encountered, although a microprocessor assisted infusion system has been devised to prevent the gall bladder distending and methyl *tert*-butyl ether overflowing into the duodenum. Dissolution is often not complete, and small residual stones may remain to form a nidus for new stone formation. Only patients with cholesterol gall stones can be treated this way, and calcium or pigment stones are not dissolved.

Treatment with methyl *tert*-butyl ether is likely to remain confined to specialist centres and offered to patients who are unsuitable for operation. It is an invasive procedure that can be performed safely by radiologists accustomed to percutaneous transhepatic cannulation of the gall bladder, but it is unlikely to find a wide role in clinical practice.

EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY

Extracorporeal shock wave lithotripsy was first introduced to manage renal calculi, and the technique has now been adapted for gall bladder and common bile duct stones. Since their introduction in 1986, the

machines for lithotripsy have undergone development and refinement. The first generation machines generated shock waves by discharging an underwater spark, which was painful and the patient required general or spinal anaesthesia or at least parenteral opiate analgesia. The anaesthetised patient also had to be completely immersed in a water bath. Second generation systems have been developed with varying combinations of approaches for shock wave generation and target imaging apparatus. The water immersion tank has been replaced with a compressible moveable water bath container that transmits the focused shock wave across the body wall. The techniques for generating shock waves include electrostatic spark discharge, electromagnetic shocks, and pulse piezoelectric shock generation.

The criteria for selecting patients with gall stones for extracorporeal shock wave lithotripsy include a history of biliary colic; a solitary radiolucent gall bladder stone with a diameter of up to 30 mm, or up to three radiolucent stones with a similar total stone mass; gall bladder visualisation on oral cholecystography; identification of the stones and the gall bladder by ultrasonography; a shock wave path that avoids lungs and bone; and no complications from the gall stones. Patients who are pregnant or receiving any treatment that may result in coagulopathy are not suitable for lithotripsy. As with bile acid treatment, only about 30% of all patients with gall bladder stones are suitable for lithotripsy. Stones may be fragmented at one sitting but a few may require a second.

The successful treatment of patients with gall bladder stones requires a combination of mechanical fragmentation plus chemical solvent dissolution. This is because the spiral valves of Heister represent a barrier to the expulsion of fragments from the gall bladder lumen, gall bladder contractility is probably impaired during the formation of the stones, and the choledochoduodenal sphincter presents a second potential barrier to the passage of small fragments. Patients receive oral ursodeoxycholic acid (7.5 mg/kg/day) administered as a single dose at bedtime. This treatment is started 12 days before lithotripsy and continues for three months after the stones disappear.

Although the rate of adverse effects is claimed to be low, they are common and not without their problems. They include cutaneous petechiae, transient haematuria, and mild leucocytosis, and 35% of patients will have some degree of biliary colic and occasionally mild pancreatitis after stone fragmentation. Experience with extracorporeal shock wave lithotripsy is limited, and the optimum follow up period and recurrence rates have still to be assessed. Management of patients treated by lithotripsy will probably be similar to that of patients whose gall stones have been dissolved by conventional bile acid treatment. Furthermore, stones will also probably recur in this group of patients. Thus the issues of recurrent medical surveillance and courses of treatment will need to be faced and it remains to be seen whether gall stone lithotripsy will be more cost beneficial than conventional cholecystectomy. At present the instruments are extremely expensive. Furthermore, the long term effects of this treatment have yet to be assessed. The emergence of complications some months or years after renal lithotripsy suggests that extracorporeal shock wave treatment for gall stones should be evaluated further before the technique is widely accepted.

Influence of diet

No evidence exists that any particular diet influences gall bladder or gall stone disease. A low fat diet is often prescribed but has not been evaluated satisfactorily. How much beneficial effect such a diet has on symp-

toms or the underlying disorder of hepatic metabolism or gall bladder function remains to be assessed. Similarly, the results of treating patients with a high fibre diet have been disappointing, and the careful observation of patients who have undergone gall stone dissolution using bile acid treatment suggests that a high fibre diet does not prevent the recurrence of gall stones.

Asymptomatic gall stones

The management of patients with asymptomatic gall stones remains controversial. The debate exists over whether the stones should be left alone or whether they should be treated by either cholecystectomy or the newer forms of non-operative treatment. The issues have become clearer with the publication in recent years of several studies of patients with asymptomatic gall stones who were followed up for long periods. Stones that have been present for a long time do not give rise to symptoms or complications as often as had been believed. In one study the cumulative probability of developing biliary pain was only 18% after 20 years. The risk of developing pain appeared to diminish with increasing duration of follow up. Furthermore, biliary complications are always preceded by episodes of biliary pain, and the initial development of symptomatic illness is not as severe as had been feared. Many authorities therefore believe that asymptomatic stones should not be treated. The other approach is to offer the patient bile acid or some other form of non-operative treatment for the gall stones, though this may lead to more cholecystectomies because patients in whom litholysis has been unsuccessful or whose stones have recurred may eventually have operations. For this reason I do not treat patients with stones that are truly asymptomatic.

Stones in the common bile duct (choledocholithiasis)

The introduction of endoscopic sphincterotomy has revolutionised treatment for stones in the common bile duct. Before endoscopy was used to remove common bile duct stones, they were generally accepted as an indication for laparotomy, cholecystectomy, and exploration of the common bile duct. Preoperative preparation included giving parenteral vitamin K if jaundice was present (5-10 mg a day for three days) and antibiotics. Administering 500 ml mannitol 10% intravenously one hour before the operation helps to reduce the risk of a patient with deep jaundice developing acute renal failure. An operative cholangiogram is always recommended. The usual procedure is a supraduodenal choledochotomy drained with a T tube that is left for 7-10 days; and a cholangiogram is usually obtained before its removal. Transduodenal sphincterotomy may be attempted if the gall stones are impacted at the lower end of the common bile duct, in which case T tube drainage may be unnecessary.

Endoscopic sphincterotomy to remove common bile duct stones is now accepted as a very useful technique, which in many centres has replaced operations on the common bile duct. In general endoscopic sphincterotomy is simpler and cheaper than abdominal operations and is preferred by patients. It is of particular value in frail and elderly patients with stones remaining after cholecystectomy. In experienced hands success rates of over 95% are reported. Sphincterotomy may be difficult to achieve when the papilla is within a large diverticulum or if a Billroth II partial gastrectomy has been performed. Stones may not be extracted when sphincterotomy is followed by an immediate complication, such as bleeding or perforation or, most often, if the stones are too large. Stones smaller than 10 mm in diameter are usually removed

easily, but increasing difficulty is experienced with those over 15-20 mm in diameter. Smaller stones may pass spontaneously once a sphincterotomy has been performed or may be extracted using a balloon catheter or metal basket.

Complications of endoscopic sphincterotomy are rare; they include bleeding, pancreatitis, cholangitis, and retroperitoneal perforation. Surgery is needed in under 2% of patients with complications, and the overall death rate is around 1%. This compares favourably with the outcome of biliary operation, which carries a death rate of 5% to 12%. Long term complications include stenosis and occasionally cholangitis. About two thirds of patients have air in the biliary tree and free reflux of barium into the bile duct, but this does not cause problems. Because experience of endoscopic removal of bile duct stones remains limited, however, the technique should be restricted to elderly and frail patients. The outcome for young and fit patients remains uncertain, and many authorities prefer to remove common bile duct stones by abdominal operation rather than endoscopic sphincterotomy.

Endoscopic sphincterotomy is being used increasingly often in patients with the gall bladder in situ. In particular, those with acute biliary disorders such as cholangitis or gall stone pancreatitis can be treated initially with endoscopic duct decompression followed by an elective cholecystectomy when their general medical condition has become satisfactory. A second group of patients are elderly and frail people with chronic symptoms caused by stones in the bile duct as well as the gall bladder whose bile duct stones can be cleared. A decision can then be made whether the stones in the gall bladder warrant treatment. In one study only 10% of such patients required cholecystectomy for biliary pain or cholecystitis during follow up for one to six years.

Endoscopic treatment of gall stones is cheaper than abdominal operation, the procedure can be completed in 30 minutes, and the patient is usually discharged from hospital in two to six days. Most patients prefer this form of treatment to surgery. Bile duct stones will probably be managed increasingly by endoscopic sphincterotomy and by surgery only in selected circumstances or when endoscopic sphincterotomy is not readily available.

OTHER ENDOSCOPIC TECHNIQUES

About 90% of all bile duct stones can be removed using endoscopic sphincterotomy. Very hard stones or those that are impacted at the terminal bile duct may not be amenable to this form of treatment. Alternative developments include electrohydraulic, ultrasound, or mechanical lithotripsy. Even laser technology has been applied to fragmenting common bile duct stones. The earliest lasers used a continuous wave neodymium-YAG laser, which is used to treat general tumours and haemostasis. This form of laser technology melts the stones and carries the danger of thermal injuries to surrounding tissue. More recently a flashlight pulsed neodymium-YAG laser has been introduced. Light energy is transmitted along a highly flexible quartz fibre with a diameter of 0.2 mm. Initial reports suggest that this form of treatment is safe and without complications. Laser technology for managing gall stones is available in very few centres. The development of laser systems is improving, however, and with modifications of endoscopic equipment makes laser lithotripsy likely to become economical, efficient, and safe. It is probably an area of growth.

LITHOTRIPSY

Stones in the common bile duct are amenable to fragmentation by extracorporeal lithotripsy. At

present, this form of treatment is unlikely to be used in preference to endoscopic sphincterotomy. Care must be exercised in locating the stone correctly and avoiding shock trauma to the head of the pancreas. Lithotripsy is unlikely to be of value in patients who require urgent treatment, such as those with cholangitis, pancreatitis, or jaundice. In any event endoscopic sphincterotomy is required from time to time to facilitate the passage of stone fragments in patients who have undergone lithotripsy, and it seems reasonable to offer lithotripsy only to patients who have been treated unsuccessfully by sphincterotomy and who require shock wave fragmentation of large persistent stone.

DISSOLUTION OF STONES IN THE COMMON BILE DUCT

Bile acid or Rowachol can be used to dissolve gall stones in the common bile duct but are not recommended because the course of treatment is too prolonged and the outcome too uncertain. Any form of dissolution is undertaken on the basis of direct infusion of an agent into the common bile duct by a T tube or a catheter positioned by endoscopic sphincterotomy or by percutaneous transhepatic placement. The earlier agents to be infused were heparin and sodium cholate, the success of which almost certainly depended simply on a mechanical flushing effect. Direct infusion of either ursodeoxycholic acid or chenodeoxycholic acid is of limited efficiency.

Methyl *tert*-butyl ether has been infused into the common bile duct and will dissolve cholesterol stones, but it is relatively ineffective, probably because it leaks from the common bile duct into the duodenum. Using methyl *tert*-butyl ether to dissolve retained radiolucent common bile duct stones carries an increased risk of toxicity because of its absorption.

At present only the semisynthetic vegetable oil, mono-octanoin, has found favour as an effective and safe solvent for dissolving cholesterol stones in the biliary tract. Mono-octanoin (Capmul, Mactanin) consists of about 70% glyceryl mono-octanoate and 30% glyceryl di-octanoate with traces of glyceryl tri-octanoate and caprylic acid. Before use mono-octanoin is diluted with water in a ratio of 10 parts water:90 parts oil. The solution is infused at a rate of 3-5 ml an hour using a drip or infusion pump, and an overflow manometer is placed in the tubing between the pump and the patient to ensure that pressure does not exceed 12 cm of mono-octanoin. The drug is non-toxic to the liver. Mono-octanoin can be administered via a T tube drain, a nasobiliary catheter, or a catheter positioned in the bile duct via the percutaneous transhepatic route. Treatment usually lasts for about seven days, but some clinicians have continued infusion for up to two weeks.

Despite initial enthusiasm for using an intraductal infusion of mono-octanoin recent reports suggest that it is not particularly effective. A large study of 343 patients showed unequivocal success in only 26%; in a further 20% the calculi became smaller but remained in the biliary tree. Mono-octanoin was useful in only 54% of patients. Side effects include abdominal pain, nausea, vomiting, and diarrhoea but are related to dose and can be reduced or abolished by diminishing the rate of infusion or amount of mono-octanoin.

Mono-octanoin is unlikely to become widely employed in clinical practice. The increased use of endoscopic sphincterotomy will almost certainly replace this agent, which will be reserved mainly for dissolving residual fragments of stones.

The emulsifiability of mono-octanoate is limited and can be improved by using glycerol mono-octanoate modified by adding *N*-(2-hydroxyethyl)-palmitamide (Palmidrol) and the poloxamer, Pluronic F-68. Some reports suggest that this modified solution is clinically more effective than mono-octanoin alone.

Treatment of calcium and pigment stones

No effective method yet exists for dissolving calcium gall stones or those composed primarily of brown or black pigment. Glyceryl mono-octanoate, Palmidrol, Pluronic F-68, and bile salts may all contribute to the disruption of the organic matrix and may be infused via a catheter placed in the biliary tree. Successes are few and side effects such as nausea and diarrhoea occur in up to 40% of patients, comparable with the incidence of side effects to mono-octanoate. Other agents that have been used include methylhexyl ether and urea-EDTA (ethylenediaminetetra-acetic acid) solutions, but the problems with these treatments are that the solutions are not readily available, the regimens are complicated, and experience is limited at present to only one or two centres. It is too early to say whether such forms of treatment will replace conventional endoscopic sphincterotomy or operation on the common bile duct.

Conclusion

Cholecystectomy presently remains the best option for a patient with stones in the gall bladder. In good hands the operation is safe, effective, and if properly indicated is associated with very few postoperative problems. Under certain circumstances litholysis with bile acids may be offered as an alternative. Extracorporeal lithotripsy, though attractive, is expensive and to some extent experimental. More experience of this technique is needed to ensure that it is safe in the long term. Non-operative management of stones in the gall bladder requires surveillance after dissolution, and further treatment may be required if stones recur. Many patients will therefore feel that the best option

remains cholecystectomy unless an operation is contraindicated for a medical reason.

Cholelithiasis is best managed in the first instance by endoscopic sphincterotomy, at least in older patients or those in whom an operation is contraindicated. Sphincterotomy alone may be sufficient, but mechanical extraction of the stones may be necessary. In certain circumstances infusion of a litholytic agent may be required to dissolve a stone or fragments of a stone; extracorporeal shock wave lithotripsy may also be used. No effective drug treatment is available for stones composed primarily of calcium or bile pigment, which are either removed by operation or, when present in the common bile duct, by endoscopic sphincterotomy. Mechanical procedures can enhance the removal of a stone that does not pass spontaneously.

The variety of procedures now available to clinicians for managing stones in the biliary tract has increased greatly the range of options when deciding what treatment to offer patients. Treatment has to be tailored to each patient and will depend on the site and nature of the gall stones, the age of the patient, and the presence of any associated diseases that might add a risk to anaesthesia and operating.

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Lesson of the Week

Toddlers, teapots, and kettles: beware intraoral scalds

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The possibility of intraoral damage, which is potentially lethal, must be considered in all cases of scalds around the mouth; when it occurs observation in an intensive care unit is recommended

The association of teapots and surface scalds in small children is well known. Damage inside the mouth and pharynx is potentially lethal yet not always recognised. A recent report highlighted the dangers: a 1 year old girl suffered brain damage as a result of obstruction of her upper airway after a delay in transferring her to hospital after she had received intraoral scalds from a teapot spout.¹ This case occurred nine years ago and has only just been settled in court.²

Two cases recently referred to this regional burns unit illustrate the dangers and the need for doctors in general practice and accident and emergency departments to be aware of the potential problems in children with facial scalds.

Case reports

CASE 1

A 2 year old infant applied a teapot spout to her lips and suffered superficial and deep dermal scalds to the lips, chin, and chest totalling about 1.5% of her body surface area. She was taken to a local hospital, where it proved impossible to examine the inside of her mouth. She did not have respiratory distress but was kept in the intensive care unit for observation. During the night (some eight hours after the scald) she developed inspiratory stridor and had difficulty in swallowing. A

FIG 1—Swollen epiglottis (arrowed) secondary to ingestion of hot water (case 1)

difference of opinion arose about the need to support her airway, although a lateral neck x ray film showed an epiglottitis the size of a ripe cherry (fig 1). The decision was made not to intubate the trachea but to continue to observe the child in the intensive care unit.

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