Progress report

Cannulation of the papilla of Vater by endoscopy and retrograde cholangiopancreatography (ERCP)

New fibreoptic duodenoscopes allow an experienced endoscopist to visualize and cannulate the papilla of Vater in conscious patients with at least an 80% chance of achieving retrograde cholangiopancreatography—a technique with obvious diagnostic potential. The historical aspects have already been adequately covered.¹⁻⁴ This review concerns the rapidly increasing world experience, with particular regard to technical problems, clinical relevance, and safety.

Instruments

Current forward-viewing panendoscopes, while excellent for routine oesophago-gastro-bulboscopy⁵, do not allow reliable views of the descending duodenum or papilla. To provide the face-on papillary views required for cannulation, the Olympus JFB³,⁶ and Machida FDS⁷ duodenoscopes view laterally rather than forwards, are even more flexible, and the distal tip can be manoeuvred in four directions under control. Biopsy forceps or teflon cannulae (1·6 mm diameter) may be passed through the instrument channel and out into the field of view over a small controllable bridge (Fig. 1). The cannula must be withdrawn to allow suction, which is frequently needed to remove bile and spilt contrast material. Machida instruments have been difficult to obtain and maintain outside Japan. The latest FDS duodenoscope closely resembles the Olympus instrument, but still lacks push-button control of air and suction. American Cystoscope Makers are developing a thicker lateral viewing gastroduodenoscope (model 5008) with a larger channel; this allows suction with the cannula in place. Preliminary experience with a

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Fig. 1  Tip of Olympus JFB duodenoscope, with metal-tipped teflon cannula passing out over bridge next to the viewing lens and light port.
Prototype shows that it is an adequate gastroscope, and is sufficiently manoeuvrable to be passed into the descending duodenum without difficulty. Good papillary views and cannulation have been achieved. Minor modifications are in hand.

Metal-tipped cannulae are not generally available but these may facilitate cannulation and their radioopacity is useful. A number of cannulae are being developed using radioopaque materials, with distance markers, which are of different shapes and have manoeuvrable tips. The most serious drawback to all current fibrescopes is that radiation may cause irreparable damage to the fibre bundle causing it to turn yellow.

Preparation

Successful ERCP depends on the cooperation of an experienced endoscopist, an enthusiastic radiologist (with high quality radiographic equipment), and at least one technical assistant; ill prepared attempts fail.

Recent acute pancreatitis and Australia antigenaemia appear to be the only major contraindications.

Some workers routinely examine outpatients but because of rare complications we prefer to maintain observation for 36 hours. Patients are examined in the X-ray Department.

Our usual medication consists of intramuscular atropine (0.6-6 mg) and pethidine (100 mg) followed by intravenous diazepam (Valium 0-30 mg). Hyoscine n-butyl bromide (Buscopan) is given intravenously later in increments of 40 mg to maintain duodenal ileus. Similar regimes have found favour elsewhere. Japanese patients appear satisfied with combinations of atropine, Buscopan, and/or trihydroxy propiophenone (Cospanon) with little or no sedation or analgesia. Buscopan is not available in the USA: combinations of atropine and probanthine or of atropine and dicyclomine hydrochloride (Bentyl) are reported to give adequate duodenal ileus, although complications have resulted from high dosage. General anaesthesia has been used but is not necessary and removes an important safeguard. Patients cannot complain of pain due to inexpert instrumentation, overdistension, or excessive injection of contrast material into the pancreatic duct.

Endoscopic Examination

It is customary to introduce endoscopes with the patient on the left side. However, to obtain good radiographs during ERCP, the patient must be supine or prone. Since there is a risk of aspiration in the supine position, we start in a semi-prone, left lateral position, rotating the patient fully prone immediately before or after cannulation. The endoscopist can expect to reach the papillary region (in every case) within a very few minutes, having briefly surveyed the stomach and duodenal bulb and aspirated secretions. The duodenal loop is fully examined for distortion, mucosal ulceration or infiltration, and diverticulae. Biopsy and cytology specimens and photographs are taken as necessary. Frothing in the lumen is suppressed by installing silicone preparations down the instrument channel.

The major papilla is usually obvious, lying slightly posteriorly, half way down the medial wall of the descending duodenum. Its exact site varies, being within 50 mm of the pylorus in 6% of cases, and rarely in the third
part of the duodenum.\textsuperscript{17} The papilla is characterized by a proximal semi-circular hooding fold, a small glans (with a pink or blue reticular pattern), and a longitudinal fold or folds running down the medial wall for several centimetres. This fold is a useful landmark since the usual fault is to search too far distally. Fluoroscopy may occasionally be needed to help in orientation. Immediately proximal to the papilla itself, there is often a short submucosal elevation: this represents the underlying bile duct, and may be pathologically enlarged. Early workers in this field\textsuperscript{8,18} described three main papillary shapes: papillary (tall), hemispherical, and flat (with respective relative frequencies of about 42\%, 36\%, and 22\%). However, the shape of the papilla may vary during examination, probably due to changing muscular tone, and the distinction between shapes is neither clear nor apparently helpful. Occasionally the papillary structure may be entirely intramural and the glans inconspicuous. With experience, failure to find the papilla is rare (18 cases in 310\textsuperscript{11}, six in 211\textsuperscript{19}, 12 in 144\textsuperscript{20}) and is then usually due to gross distortion by pancreatic disease, diverticulum, or surgery. A small accessory papilla has been seen in 24\% of our patients, lying 2-3 cm proximally and slightly anteriorly to the main papilla. Other workers report higher percentages, and up to three accessory papillae in the same patient. Tumours of the papilla are easy to recognize and biopsy\textsuperscript{23} but the normal or inflamed papilla may sometimes show confusingly prominent prolapsed mucosal folds.

\textbf{Cannulation Technique}

Success in cannulation depends upon obtaining a close face-on view of the papilla; this may involve rotating or tipping the patient, the use of suction, air, silicone, and Buscopan, as well as manipulation of the instrument and its distal tip. The teflon cannula is attached to a 50-ml syringe and filled with contrast material so as to exclude all air from the system. Cannulae are provided with metal stilettes, which facilitate their passage. However, subsequent removal of the stilette allows air to enter and it can be flushed out only at the expense of spilling contrast in the duodenum; this may obscure the field and it stimulates peristalsis. Hence we do not use a stilette and pass the full cannula through the instrument and out over the distal bridge into the field of view.

Dense contrast materials are required for good radiographic opacification of the pancreatic duct system. Most workers have followed Oi\textsuperscript{3} in using 60\% Urografin (sodium and methyl-glucamine diatrizoate, Renografin); 50\% and 70\% Urografin, 50\% Hypaque (sodium diatrizoate), and Conray 280 (meglumine iothalamate) are also satisfactory. Kasugai\textsuperscript{10} believes that sodium-free 50\% Angiografin (meglumine diatrizoate) may be safer. However, these dense media may obscure small stones in a dilated biliary system, and 30\% Urografin or 25\% Hypaque are preferable in this situation.

The full cannula is advanced into the papilla under direct vision. The orifice is usually at the apex of the glans, its exact site being deduced from the reticular pattern of its folds. A definite hole, voiding bile or pancreatic juice, has been evident in only 19\% of our patients. Occasionally, the intravenous injection of cholecystokinin may be useful in provoking a flow of bile and demonstrating an unusually placed orifice but this obscures the view and stimulates peristalsis. Indocyanine green has also been used.

In about one-third of our patients the cannula passes rapidly through the
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papilla deeply into one or other duct system. More commonly, the cannula tip sticks less than 5 mm into the papilla; this may be adequate for opacification of one or both ducts and contrast is injected slowly under fluoroscopic control. If contrast refuses into the duodenum the cannula has either entered a papillary valve recess and should be re-positioned, or papillary muscle relaxation must be induced by further intravenous injections of Buscopan (or aminophylline). The application of local anaesthetic directly onto the papilla may be helpful. With incomplete cannulation and duct filling, layering of contrast may give a false impression of stenosis or obstruction. When cannulation succeeds, further contrast is injected under fluoroscopic control until branch ducts are opacified, and relevant radiographs are taken in different positions.

Success Rates in Cannulation and Selective duct Opacification

Published success rates for endoscopic papillary cannulation, ie, opacification of a duct, vary between 75% and 96% (Table I). These figures are not strictly comparable. Indications and criteria vary: some figures refer to numbers of patients rather than to examinations, and others only to most recent experience (shown in brackets). Failure may of course be due to disease.

The most useful figures are those for selective cannulation, ie, opacification of the clinically relevant duct (or ducts). Filling the bile duct in a patient suspected of pancreatic disease is a cannulation success but a clinical failure. The few available selective success rates are also shown in Table I; some are remarkably high. Most groups appear to share our own experience that it is easier to fill the pancreatic duct than the biliary system. The practical problem, therefore, in selective cannulation is more often an attempted change from pancreatic to biliary system (unless both fill simultaneously) than vice versa.

Extensive anatomical studies have provided figures for a common pancreatobiliary channel in the papilla ranging from 5 to 90%; Hand gave a consensus figure of 85%, and reported 13% of patients to have separate duct openings on the major papilla and 2% on separate papillae. Separate orifices were visualized and cannulated in only 4% of our patients although rates of 13.5% and 23.5% have been reported. When only one papilla and

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Table I Overall experience of cannulation success

*Figures in brackets indicate most recent experience
orifice are apparent, the cannula should gradually be withdrawn from the wrong duct into the tip of the papilla while slowly injecting further contrast under fluoroscopic control. If this does not effect a successful transfer, it only remains to recannulate the same orifice from different directions. The pancreatic duct may be prefentially entered when the papilla is approached perpendicularly at close range; to seek the biliary system, the cannula should be pointing acutely upwards almost parallel with the duodenal wall. In our own series, the change from pancreatic to biliary duct cannulation was achieved in 16 out of 21 attempts, and the reverse change in five out of a further eight.

Endoscopy and retrograde cholangiopancreatography is more difficult after Polya partial gastrectomy, but Safrany succeeded in cannulating via the afferent loop in nine out of 11 attempts and Oi in nine out of 13. Sphincterotomy and sphincteroplasty facilitate cannulation unless surgical scarring or restenosis has occurred.

Retrograde Cholangiography

The normal biliary system may accommodate up to 40 ml of contrast, and posturing outlines the whole intrahepatic tree, cystic duct, and gallbladder. Emptying is usually sufficiently slow for radiographs to be taken after complete withdrawal of the cannula and instrument. Biliary tract radiology is familiar, and interpretation is usually simple, assuming adequate filling and exclusion of air. The upper normal limit for the common bile duct diameter is around 10 mm; in 34 normal cases Hara and Ogoshi found a maximum diameter of 8.6 mm (SD ± 1.5). Although the bile duct may normally be larger following cholecystectomy, the exact significance of a diameter of, say 15 mm, is debatable. Endoscopy and retrograde cholangiopancreatography have not yet provided hard data on patterns and timing of biliary emptying (which can be studied using cineradiography) or on bile duct pressures; this type of information is essential in any discussion of papillary stenosis ('papillitis', 'Odditis'). When the gallbladder does not fill, despite good bile duct opacification and correct posture (Fig. 2), this has been found to indicate gallbladder or cystic duct disease in all of a series of 26 patients who came to operation.

Retrograde Pancreatography

Contrast medium runs rapidly to the tail of the gland, and usually outlines the main branches: 2-5 ml is usually adequate. After the cannula has been withdrawn emptying from the normal duct is rapid, and has been complete within five minutes in all our cases. However, Kasugai reports occasional delays of up to 10 minutes in the aged. Despite large necropsy and operative series, pancreatograms are largely unfamiliar and may be more difficult to interpret than they are to obtain. The main duct is most commonly 'pistol shaped' with an acute bend between head and body. Many normal variations have been described, which make it almost impossible to diagnose pathological displacement.

The main pancreatic duct normally tapers from head to tail, and there are a number of measurements available from ERCP (Table II). They are corrected (as far as possible) for radiographic magnification by reference to the size of the overlying instrument. The size of the main duct increases slightly with
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<table>
<thead>
<tr>
<th>Total No. of Patients</th>
<th>Duct Diameter (mm)</th>
<th>Length (cm)</th>
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<td></td>
<td>Head</td>
<td>Body</td>
<td>Tail</td>
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<tr>
<td>25</td>
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<td>48</td>
<td>3-8</td>
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<tr>
<td>110</td>
<td>3-6</td>
<td>2-7</td>
<td>1-6</td>
</tr>
<tr>
<td>41</td>
<td>3-7 ± 0-8</td>
<td>2-7 ± 0-5</td>
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</tr>
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</table>

Table II Diameter and length of main pancreatic duct (mean ± 1 SD) in subjects without evidence of pancreatic disease\textsuperscript{1}

\textsuperscript{1}Classen's figures are medians

... age\textsuperscript{10}, but this is much less marked at ERCP than at necropsy studies, which give upper limits for a normal duct of 9 mm\textsuperscript{33} and even 11 mm\textsuperscript{32}. In life it seems safe to take 6 mm as the upper limit of normal.

Although the degree of filling of branch ducts depends partly on the volume and pressure of contrast injection (and is controlled by fluoroscopy) in practice it varies considerably. Kasugai\textsuperscript{10} filled main branches in 78 of 92 cases, and fine ducts in 21 of 92. This means that it is rare to be able to diagnose pathological lack of filling of even a major branch, such as that to the uncinate process. Since pancreatic tumours do not necessarily involve the main duct, this severely restricts the technique as a diagnostic tool. Opacification of the whole pancreatic parenchyma would provide an attractive extension of the technique if it were shown to be safe, and indeed if the factors determining acinar filling were understood. It is not simply a question of increased volume or pressure of contrast injection, nor is easy opacification necessarily a sign of pancreatitis. But even if the whole gland is opacified, variations in length and shape make it possible to miss or misdiagnose a tumour. Until the results of further careful studies are available, the interpretation of retrograde pancreatograms must rely on major changes in the main duct—complete obstruction, strictures, great variations in calibre (beading), and gross distortion. With regard to variation in calibre, measurements for minimum as well as maximum duct diameters have been reported.\textsuperscript{10,31} However, these measurements come from relatively small series, and Birnstingl\textsuperscript{18} has pointed out that the normal pancreatic duct may show some strictureing (especially at the neck).

Although this has not yet been our experience in 63 pancreatograms, it should evoke no surprise that the main pancreatic duct may appear entirely normal despite extensive pancreatic disease. In chronic pancreatitis, the percentage of normal ducts will depend on the operator's definition, and alternative methods of diagnosis. Classen\textsuperscript{34} found normal ducts in about 30% (some of this group had only recurrent acute pancreatitis), and Liquory\textsuperscript{35} in eight out of 33 patients. In chronic pancreatitis, great variations in calibre and localized stenoses are the most common abnormal findings.\textsuperscript{34,10} The origin and extent of pseudo-cysts can also be defined.

Normal main ductograms have also been described in pancreatic cancer: three out of 13 cases\textsuperscript{38} and three (one 5 cm in diameter) out of eight\textsuperscript{35}. Hara and Ogoshi\textsuperscript{31} reported abnormalities in all of 21 cases of three main types—complete obstruction, stenosis with proximal dilatation, and a gradual tapering. The diagnostic yield and clinical relevance of ERCP in different clinical situations will be further discussed after consideration of potential complications.
Potential Complications

In practice these have been acceptably few, but possibilities include the rare hazards of endoscopy itself, reactions to additional medication (anticholinergics), damage by the cannula to the papilla or ducts, cholangitis and septicaemia, transmission of hepatitis, and pancreatitis.

There have now been several reports of severe febrile reactions, cholangitis, or septicaemia following ERCP: two cases out of 142 patients, two cases (one fatal) out of 144, three out of 283, and three out of 310. Infection has only been described following cholangiography, and when contrast has been injected past an incomplete stricture due to carcinoma or stones. The onset of illness can be rapid and catastrophic but may also be delayed at least 24 hours, and close observation is essential. Specific antibiotic therapy has usually been successful, but early surgical intervention may also be appropriate. It is not yet clear if infection is introduced by the catheter, which cannot be sterile after it has passed through the endoscopic channel and the duodenum; if so, local instillation of antibiotics might be logical. It seems more likely that septicaemia occurs by dissemination of bacteria already present in the stagnant biliary system. Similar infections follow percutaneous and transjugular cholangiography.

The routine prophylactic use of parenteral broad-spectrum antibiotics has been advocated but remains controversial on both theoretical and practical grounds. The introduction of infection into a pancreatic cyst or pseudo-cyst is catastrophic. No attempt should be made to outline the entire cyst, except perhaps immediately before operation; detection of its presence and site of origin is sufficient information.

Although transmission of infectious hepatitis from patient to patient (or staff) via gastrointestinal endoscopes has not been described; it has probably occurred and certainly deserves more consideration. The risk must be greater when examining jaundiced patients, some of whom will eventually be found to have hepatitis. Attempted sterilization of endoscopes by means of prolonged exposure to gases or chemicals raises severe practical problems. Our present practice is to test the serum of all jaundiced patients for hepatitis-associated antigen, and to decline examination of any patient with a positive result.

The papillary area could obviously be damaged, with potentially serious long-term results, especially if attempts are made to inject contrast material when the cannula is incorrectly placed, or when biopsies are taken from close to the orifice. Transient submucosal injection of contrast near the papilla has occurred in four patients. The cannula perforating the pancreatic duct has resulted in the formation of transient pseudo-cysts and extravasation of contrast into the omentum. Free bile has been found in the peritoneal cavity following retrograde cholangiography. Metal tips have become detached from cannulae but happily not within either duct system.

Acute pancreatitis is the more feared complication. Its occurrence following operative cholangiography has restricted the use of this technique. At operation, however, there are additional important factors: pancreatography may be preceded by sphincterotomy and gland manipulation, and the contrast injection is not monitored by fluoroscopy or discomfort of the patient.

Despite earlier reports to the contrary, it is now common experience that serum and urinary amylase levels often rise significantly following successful retrograde filling of the pancreatic duct by this technique. Reported frequency...
of the pathological rise varies from 20 to 30%\(^\text{48}\), 53%\(^\text{9}\), 61%\(^\text{10}\), and 73%\(^\text{28}\). Peak levels are achieved with a few hours and return to normal in one to four days. Serum amylase levels have been serially measured in 52 of our patients; a pathological rise, sometimes to impressive heights, occurred in 38% of cases in which pancreatograms were achieved. The highest figures were for patients with normal ducts, and when parenchymal opacification occurred (like Kasugai\(^\text{10}\), but unlike Gauchier\(^\text{48}\)). However, there appeared no obvious correlation between serum amylase levels (or parenchymal filling) and the intensity or duration of any discomfort on the part of the patient.

The dividing line between amylasaemia and pancreatitis is one of semantics. By acute pancreatitis we mean a clinical illness of pain, fever, and amylasaemia (although a raised amylase level may be absent in a patient with a fibrotic pancreas). Three episodes of acute pancreatitis have occurred in our 132 examinations\(^\text{25}\); all were mild and partly predictable in patients with frequently relapsing acute pancreatitis and the radiographs obtained were clinically useful. Mild episodes of acute pancreatitis have previously been described in the Japanese literature\(^\text{9}\). During 1972, there have been reports suggestive of acute pancreatitis in eight patients\(^\text{9,18,28,48}\), with one death\(^\text{59}\)—a total incidence of pancreatitis in these centres of 1 to 2%.

Possible aetiological factors include the type and concentration of contrast material, the volume and pressure of its injection, delay in contrast emptying from the gland, the role of bile, duodenal juice, and infection introduced into the duct, the physiological and pathological state of the gland itself, and the possibility of sphincter damage or spasm following cannulation. Many of these factors have been extensively discussed and reviewed\(^\text{44,10}\), but there are no data from published studies or reports of pancreatitis to suggest which if any of them are important. One of our patients, and that of Galvan and Klotz\(^\text{42}\), developed pancreatitis despite the opacification of only a few centimetres of the main duct, up to a complete obstruction. Our own controlled study in 40 patients of the prophylactic administration of Trasylol has so far shown no benefit to the patient in terms of discomfort or amylase elevation; two patients who developed pancreatitis were receiving Trasylol. The possibility of long-term damage to the pancreas cannot be ignored. Radiation exposure to the patient is negligible.

Hazards have been discussed at length, because they have not previously received sufficient attention. However, it should be emphasized that actual complications have in fact been rare.

**Clinical Relevance**

Endoscopy and retrograde cholangiopancreatography involves a significant commitment of valuable resources\(^\text{50}\). The instrument is expensive (about £2500) and it breaks down. However, it should in my view already be available as part of the basic set for routine 'dyspeptic' endoscopy. Learning the procedure requires endoscopic experience, special instruction, and persistence. Although cannulation itself may sometimes be achieved in a few minutes, the whole procedure may take up to an hour (and still fail). Is it worth while?

There are four possible indications: persistent or recurrent jaundice; biliary type problems with failed orthodox cholangiography; known pancreatic disease; suspected pancreatic disease.
Fig. 2  Retrograde cholangiogram showing dilated ducts with a stone near the cystic duct opening and nonfilling of gallbladder. The cannula and metal tip can be seen in the lower half of the common bile duct.

Fig. 3  Carcinoma of the pancreatic head causing complete obstruction of the common bile duct and bowing of the distal pancreatic duct. The cannula metal tip is in the papilla.

Fig. 4  Stricture of the common bile duct following cholecystectomy. A splinting tube has become displaced below the strictured area.

Fig. 5  Retrograde pancreatogram demonstrating a mid-duct stricture with small cyst; dilated duct in the tail, with contrast spilling into a large cyst (only partly filled). Man aged 35 after two attacks of acute pancreatitis.
Cholangiograms in 74 patients yielded diagnostic information of both intra- and extrahepatic cholestasis (albeit in only 70-80% of patients). When both techniques are available, it would seem reasonable to use the transhepatic approach only if ERCP fails or demonstrates a complete obstruction (Fig. 3). Laparoscopy should not be forgotten.

The second smaller group is of non-jaundiced patients with persistent biliary type symptoms, in whom orthodox cholangiography fails; this will include patients with pain following biliary surgery (Fig. 4), and some with presumed primary biliary cirrhosis. In this situation, ERCP may be the only alternative to exploratory laparotomy. Classen et al. has shown that diagnostic information can be obtained by endoscopy and retrograde radiology in patients with recurrent problems following biliary-digestive anastomosis.

In patients with known chronic or relapsing pancreatitis, ERCP is an excellent method of demonstrating the anatomy of the papillary region and main duct, and may help considerably in deciding on the advisability of surgery and the correct operative approach (Fig. 5). Diagnostic radiographs were obtained in 19 out of our series of 22 such patients: two normal, nine mid-duct strictures (six with cysts, and one of which had been previously suspected), three complete mid-duct obstruction, four dilated throughout, one duct draining into a duodenal diverticulum. Already we have mentioned 54 patients with chronic pancreatitis examined by Classen et al. 31 of these patients were shown to have biliary tract pathology (24 diagnosed by ERCP).

Retrograde cholangiopancreatography should not be used alone as a screening test for pancreatic pathology. It can provide definite endoscopic or radiographic evidence of disease but cannot exclude it. Failure of cannulation cannot be taken as evidence of local disease. Generalized duct changes and multiple cysts are strong evidence of chronic pancreatitis, but localized stricture or obstruction may also be seen in carcinoma. Endoscopy itself may provide visual or histological evidence of cancer of the head of the pancreas. In other cases the distinction between pancreatitis and cancer can only be made by cytology or laparotomy. Preliminary results suggest that radiographic and functional abnormalities correlate poorly. Further collaborative studies are in progress to define the relationships between endoscopy and pancreatography, enzyme studies, and isotope imaging.

There are several potential future developments. Pure pancreatic juice can be aspirated with difficulty (five out of 17 attempts for biochemical and cytological study. Pancreatic cytological samples have also been obtained by direct needling through the duodenal wall. We can expect to hear more of endoscopic attempts to dilate the papilla, remove stones, and visualize the...
ducts themselves. Operative fibreoptic choledochoscopes are already available, and percutaneous transhepatic cholangioscopy has been described.

Conclusion

In experienced hands, endoscopy of the papillary region and retrograde cholangiopancreatography (ERCP) is sufficiently practicable and safe to constitute a major advance in the diagnosis and management of biliary and pancreatic disease. The technique is not easy to learn and involves a significant commitment of resources which may be inappropriate in smaller hospitals. For the present, ERCP is likely to be used mainly in specialist centres for the investigation of complicated problems, eg, of symptoms in patients after biliary tract surgery and of those with painful and recurrent pancreatitis.

In this review of a rapidly changing field, where formal publications are scarce, it has been thought reasonable to refer to a number of personal communications and unpublished observations. Attempts have been made to check these references, but any error is my own. It is a pleasure to thank my colleague, Dr John Beales, for his help and encouragement.

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