Progress in determining the nature of bile duct strictures

It is surprising that in 1993 patients can still be treated with radical radiotherapy, chemotherapy, or surgery, including liver transplantation, without establishing a definitive diagnosis. This happens, however, in patients with obstructive jaundice caused by a bile duct stricture where there is difficulty in obtaining a tissue diagnosis. The age and frailty of this patient group are often used as justifications for limiting investigations and employing palliative methods of treatment such as endoscopic balloon dilatation or stenting. Although this may sometimes be inappropriate, the lack of a tissue diagnosis undoubtedly results in some patients being inappropriately treated for malignant disease when a benign stricture is present and vice versa. It also hampers any objective assessment of the value of treatment in these patients. The adage of 'a diagnosis is not required because it does not affect management' is now outdated when many treatment options are available.

Malignant bile duct strictures are mainly the result of cancer of the ampulla of Vater, pancreas, or bile duct and account for about 75% of patients presenting with extrahepatic bile duct obstruction. In the remainder strictures are caused by benign conditions such as gall stones, surgical trauma, chronic pancreatitis, or rarer disorders such as sclerosing cholangitis or Caroli's disease.¹

How are we to separate benign from malignant strictures?
Unfortunately, the patient's history and presentation, usually of clinical jaundice, pruritus, vague abdominal pain, anorexia, and weight loss are of limited value in determining the underlying aetiology. Baron et al compared the value of ultrasound and computed tomography in patients with suspected biliary obstruction. Both imaging modalities were effective for determining the presence of obstruction, computed tomography alone accurately determines the level of the obstruction, but neither can reliably predict the cause.² Since imaging cannot accurately predict the aetiology of a biliary stricture it is illogical to base treatment on external imaging alone and most patients then undergo either endoscopic or percutaneous cholangiography.

Does cholangiography establish the nature of a biliary stricture?
Cholangiography accurately locates the site of a stricture in the biliary tree and radiological features may suggest the presence of malignant disease. External imaging (ultrasound or computed tomography) and cholangiography cannot, however, differentiate benign from malignant biliary strictures. For example, it is not possible to differentiate a hilar stricture caused by focal sclerosing cholangitis from one resulting from a cholangiocarcinoma, or a distal stricture due to cancer of the pancreas from a stricture caused by chronic pancreatitis.³ A tissue diagnosis is clearly required to provide a rational basis for treatment.

Biliary exfoliative cytology
Bile sampling at the time of endoscopic or percutaneous cholangiography, with subsequent cytological examination, has been carried out for over 20 years. Surprisingly the sensitivity reported for this technique is frequently less than that for duodenal aspiration cytology, although this may be related to differences in the stage of disease being investigated. Unlike duodenal aspiration cytology, bile exfoliative cytology is generally 100% specific (no false positive results). However, it allows only about one third of patients to be diagnosed and therefore a negative result has little value.⁴ This low sensitivity rate has encouraged the use of instruments to enhance cell exfoliation.

Diagnosing malignancy by percutaneous sampling
In patients with obstructive jaundice secondary to extrahepatic bile duct obstruction, about one third have a focal lesion detected on initial ultrasound and about two thirds on computed tomography.⁵ Whether this lesion should be biopsied percutaneously at the time of initial imaging remains controversial. The morbidity and mortality associated with percutaneous biopsy is very low, and with the use of a fine needle for aspiration cytology is negligible (about 0.16% and 0.006% respectively⁶). The major objection to the percutaneous approach is the possibility of tumour dissemination in the track. The reported incidence after fine needle aspiration is very low (about 1 in 20000). A recent report has suggested, however, that malignant cells are frequently disseminated in the peritoneal cavity after percutaneous fine needle aspiration. Their viability and importance have yet to be established but may be a contributory factor to peritoneal recurrence.⁷ Despite this theoretical risk, the possibility of safely establishing a tissue diagnosis in about two thirds of patients with a focal lesion on imaging justifies percutaneous aspiration cytology as a first line investigation.⁸ Percutaneous fine needle aspiration cytology is, however, highly operator dependent.

**Leading article**

**Alternative methods**
Before percutaneous fine needle aspiration cytology was attempted many groups had shown that a tissue diagnosis could be achieved in some patients with obstructive jaundice caused by malignancy by detecting neoplastic cells in duodenal aspiration. In 1949 Lemon and Byrne reported a large series of patients undergoing duodenal aspiration cytology with a test sensitivity of over 70%.⁹ Despite these encouraging results this technique was not widely adopted because it proved time consuming, generally insensitive, did not localise the neoplastic lesion, and was associated with false positive results.¹⁰ The ability to collect samples directly from the biliary tree at the time of either percutaneous or endoscopic cholangiography has superseded the use of duodenal aspirates and provides a better sample for cytological examination. The possible dissemination of tumour by percutaneous fine needle aspiration cytology may result in these becoming the diagnostic techniques of choice.
generally better than with exfoliative bile cytology alone, with a sensitivity over 60%. Although brush sampling produces more cellular samples than exfoliative bile cytology, radiologists and gastroenterologists have been reluctant to perform brush cytology because of the time involved in carrying out the procedure. This problem was largely overcome in 1989 by Foucht et al, who demonstrated a technique that allowed brush cytology of the biliary tree to be performed without removing the guide wire inserted across the biliary stricture. This technique should result in its more widespread application. Further improvement in the diagnostic accuracy may be obtained by repeated sampling. Although this becomes a time consuming procedure, several negative brushings effectively exclude a diagnosis of biliary neoplasm. In certain patient groups, such as those with sclerosing cholangitis who are being considered for liver transplantation, repeated brushings to exclude the development of a cholangiocarcinoma seem justified or essential.

**Endobiliary biopsy and fine needle aspiration cytology**

Despite the application of exfoliative bile and brush cytology, some 20–30% of patients with malignant biliary strictures will remain undiagnosed either because of a lack of cell exfoliation from the tumour or because the tumour is producing extrinsic compression on the biliary tree and has not affected the biliary epithelium. In these patients two novel cytology methods, endobiliary biopsy and endobiliary fine needle aspiration, may be suitable. Endobiliary biopsy has only recently been introduced after the manufacture of biopsy forceps that are small enough to enter the biliary tree without a sphincterotomy. The tissue obtained may be too small for histological examination but satisfactory for cytology. Reports on the clinical use of endobiliary biopsy forceps are limited and their place in the investigation of biliary strictures remains to be established. Initial studies, however, suggest the technique is safe and effective. In this regard, it is important to stress that the endobiliary biopsy is performed with a needle which is introduced into the biliary tree either percutaneously or endoscopically, has potential advantage over other methods of diagnosing biliary strictures in that the needle may be inserted through the strictured area and thereby obtain tissue from outwith the wall of the bile duct. This might therefore be useful in diagnosing strictures caused by extrinsic compression on the bile ducts. The results of this technique are also preliminary but encouraging. Both endobiliary biopsy and endobiliary fine needle aspiration cytology are likely to establish a role in the investigation of patients in whom a tissue diagnosis is elusive by standard methods.

A wide variety of safe and effective methods is now available for obtaining a cytological diagnosis in patients with biliary strictures. Some are still awaiting adequate clinical evaluation but even with currently available techniques it should be possible to obtain a tissue diagnosis in most patients. Until this is achieved it is impossible to carry out a useful evaluation of the many alternative treatments available for patients with the complex problem of extrahepatic bile duct stricture.

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