potassium iodide 60 mg. daily for three weeks (five subjects), lysine vasopressin 10 pressor units intravenously over two hours (five subjects), and acute lowering of central body temperature by 3.6° F. (2°C.) (one subject).

Administration of thyrotrophin-releasing hormone causes a rise in serum T.S.H. and so should provide a useful test of the function and reserve capacity of the thyrotroph cells of the anterior pituitary. The clinical and laboratory diagnosis of minor degrees of pituitary T.S.H. deficiency can be particularly difficult. All thyroid function tests may be within the conventional normal range and yet the patient may benefit from thyroid hormone medication. Failure of serum T.S.H. levels to rise in response to thyrotrophin-releasing hormone should therefore provide a more refined diagnosis of T.S.H. deficiency. Since thyrotrophin-releasing hormone acts directly on the pituitary it could also be used to distinguish between pituitary and hypothalamic lesions affecting T.S.H. release, a distinction which cannot be made with available tests.

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Medical Memoranda

Congenital Dilatation of Intrahepatic Biliary Ducts with Cholangiocarcinoma

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Congenital dilatation of the intrahepatic ducts is rare. The condition was first described by Caroli *et al.* (1958). The following account of a further case records three features not previously described: obstructive jaundice, the development of severe osteoporosis during the latter part of the illness, and the occurrence of a cholangiocarcinoma arising from one of the dilated ducts.

CASE REPORT

In September 1959 the patient (then aged 23) developed recurrent attacks of painless obstructive jaundice. In 1962 a cholecystectomy was performed at another hospital but no definitive evidence of cholelithiasis was found. She continued to have attacks of jaundice, now accompanied by epigastric and right subcostal pain. In 1964 a laparotomy showed no abnormality of the biliary tree. Because of the continuance of symptoms she was admitted to Manchester Royal Infirmary in September 1965. Percutaneous

cholangiography showed a fistula between the biliary tree and the proximal duodenum. Review of x-ray films showed air in the biliary tree previous to cholecystectomy. At laparotomy a fistula was found between the proximal duodenum and a large cystically dilated biliary duct at the porta hepatis; this contained 400 ml. of colourless mucus. Digital exploration showed considerable dilatation of the intrahepatic biliary ducts. A Roux-en-Y anastomosis was fashioned between the dilated biliary duct and the jejunum. Over the next four months her serum bilirubin subsided from 27 to 2.4 mg./100 ml., and she first complained of backache. In 1967 she noticed a loss in height of 5 cm. Because of continuing jaundice and pyrexia she was readmitted to hospital in April 1968. She was icteric and had one-finger-breadth hepatomegaly and kyphosis of the lower thoracic and upper lumbar vertebrae.

Investigations.—Haemoglobin 11.7 g./100 ml.; serum iron 65 µg./100 ml.; white cell count 14,300/cu. mm.; E.S.R. (Wintrobe) 49 mm. in 1 hour; serum bilirubin 1.4 mg./100 ml.; serum alkaline phosphatase 200 King-Armstrong units/100 ml.; 5-nucleotidase 190 units; serum albumin 3.4 g./100 ml.; serum globulin 6.3 g./100 ml.; electrophoresis showed a pronounced rise of gamma-globulin; serum cholesterol 200 mg./100 ml., with normal lipid pattern; serum electrolytes normal; serum calcium 9.0 and serum inorganic phosphorus 3.4 mg./100 ml.; and 24-hour urine calcium was 56 mg. Faecal fat excretions varied between 13 and 23 g./day at the above serum bilirubin level. X-ray examination of

the spine showed loss of bone density and collapse of the lower thoracic and upper lumbar vertebrae. Iliac crest bone biopsy showed gross osteoporosis only. On barium meal examination an equal flow of contrast medium was observed along both the duodenum and the fistulous communication with the dilated biliary tree.

The patient continued to have a low-grade pyrexia attributed to cholangitis which was not affected by ampicillin or tetracycline. The bilirubin rose in two weeks to 15.2 mg./100 ml. and was unaffected by phenobarbitone 120 mg. daily. After eight weeks in hospital she developed severe upper abdominal pain and vomiting. Two days later signs of peritonitis became manifest and she died the same day.

Necropsy.—The immediate cause of death was generalized peritonitis due to perforation of two acute gastric ulcers on the greater curvature. The anastomosis of the biliary tract and jejunum was intact and widely patent. The dilated biliary tract immediately above the anastomosis communicated with the proximal part of the duodenum. The fistula measured 2 cm. in diameter. The right and left hepatic ducts, together with their segmental branches, were enormously dilated (Fig. 1), measuring from 2 to 4.5 cm. in di-

FIG. 1.—Cut surface of left lobe of liver showing dilated biliary ducts and tumour filling one of the peripheral ducts.

ameter. The ducts, lined by mucus-secreting cells, were filled mainly with colourless viscid mucus admixed with some bile and necrotic tissue. The extrahepatic duct below the short cyst-dilated segment was of normal calibre. It joined the dilated part above the fistula but below the porta hepatis (Fig. 2). The sphincter of Oddi

FIG. 2.—Diagrammatic representation of the anatomy as seen at necropsy.

was normal. Arising from the periphery of one of the dilated ducts was a partially necrotic well-differentiated cholangiocarcinoma, which filled the duct lumen and invaded the surrounding liver. Metastases were found in three paraoesophageal lymph nodes.

DISCUSSION

The presenting symptom, and main complaint, in this patient was obstructive jaundice, which during the early part of the illness may have been due to impaction of an intrahepatic stone at the upper end of the undilated extrahepatic duct and which was probably responsible for producing the fistula between the biliary tree and the duodenum. A mechanical cause of the jaundice would appear to be unlikely after the establishment of the fistula and the later surgical formation of the Roux-en-Y anastomosis. Thereafter the recurrent jaundice was ascribed to ascending cholangitis. A striking feature of the ducts was the presence of the extremely viscid colourless bile; this is in contrast to the finding of Turnberg *et al.* (1968), whose patient secreted a large daily volume of bile of low concentration.

Good radiological visualization of the intrahepatic and extrahepatic biliary system is necessary for the diagnosis of this condition. This is obtained by giving morphine at the same time as the contrast medium during intravenous cholangiography and thus producing spasm of the sphincter of Oddi. Percutaneous or T-tube cholangiography produces even better visualization of the biliary tree in this condition.

Sporadic accounts of pre-existing congenital abnormalities of the biliary tree complicated by cholangiocarcinoma have been reported. Willis (1943) described the case of a man aged 32 with a polycystic liver in which cholangiocarcinoma developed. Two young adults with congenital hepatic fibrosis developed cholangiocarcinoma (Parker, 1956; McCarthy *et al.*, 1965), and nine cases of carcinoma in congenital choledochal cysts have also been described (Macfarlane and Glenn, 1967; Thistlethwaite and Horwitz, 1967). It appears that the biliary tract epithelium in conditions where there are congenital abnormalities of the biliary tree is very liable to carcinomatous change.

The present patient had progressive osteoporosis without concurrent osteomalacia. This has long been recognized in chronic liver disease (Atkinson *et al.*, 1956), but the mechanism is uncertain.

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