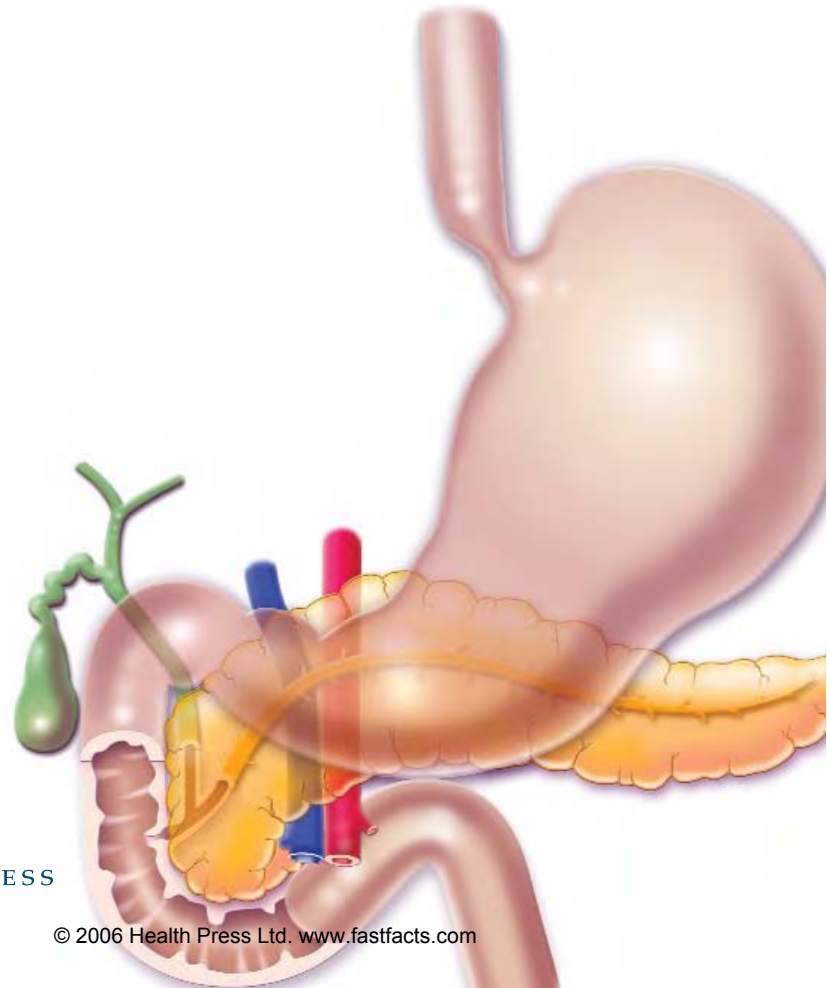
Fast Facts

Fast Facts: Diseases of the Pancreas and Biliary Tract

John P Neoptolemos and Manoop S Bhutani



HEALTH PRESS

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Declaration of Independence
This book is as balanced and as practical as we can make it. Ideas for improvement are always welcome: feedback@fastfacts.com

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Glossary of abbreviations

AIDS: acquired immunodeficiency syndrome

ALT: alanine aminotransferase

APACHE: Acute Physiology And Chronic Health Evaluation

AST: aspartate aminotransferase

CA: cancer antigen

C_5A: complement $_5$A

CBD: common bile duct

CCK: cholecystokinin

CEA: carcinoembryonic antigen

CINC: cytokine-induced neutrophil chemoattractant

CFTR: cystic fibrosis transmembrane conductance regulator [gene]

CRP: C-reactive protein

CT: computed tomography

ENA: epithelial neutrophil-activating [protein]

ERCP: endoscopic retrograde cholangiopancreatography

EUS: endoscopic ultrasonography

5-FU: 5-fluorouracil

GGT: gamma-glutamyltransferase

GI: gastrointestinal

GRO: growth-related [protein]

HAART: highly active antiretroviral therapy

HIDA: hydroxyiminodiacetic acid

ICAM: intercellular adhesion molecule

IL: interleukin

MEN-1: multiple endocrine neoplasia type 1

MIBG: meta-iodobenzylguanide

MODS: multi-organ dysfunction syndrome

MRCP: magnetic resonance cholangiopancreatography

MRI: magnetic resonance imaging

NF-1: neurofibromatosis type 1

PAF: platelet-activating factor

PET: positron-emission tomography

PP: pancreatic polypeptide

PRSS1: protease serine 1 [gene]

PSC: primary sclerosing cholangitis

PSTI: pancreatic secretory trypsin inhibitor

SIRS: systemic inflammatory response syndrome

SPINK1: serine protease inhibitor, kazal type 1 [gene]

TNFα: tumor necrosis factor α

TSC: tuberous sclerosis

VHL: von Hippell–Lindau (syndrome)

VIP: vasoactive intestinal polypeptide

Introduction

The pancreas is important for the production of digestive enzymes (from the acinar cells), bicarbonate (from the duct cells) to neutralize gastric acid, and insulin (from the cells of the islets of Langerhans), essential for sugar control. It is the shape of a small flat fish, 6–8 inches long and salmon pink in color, and lies behind the stomach, stretching between the duodenum on the right to the center (hilum) of the spleen on the left (Figure 1). It is conventionally divided into the head, uncinate process, neck, body and tail.

The main pancreatic duct joins the bile duct to form the common channel or ampulla of Vater (also known as the major papilla or nipple). In 90% of people, the embryonic dorsal and ventral pancreatic ducts have fused to make this pancreatic duct, meeting in the head of the pancreas. In the other 10% the ducts drain separately into the duodenum (pancreas divisum), the dorsal duct (known as the accessory duct) draining through the minor papilla. Small sphincters around the

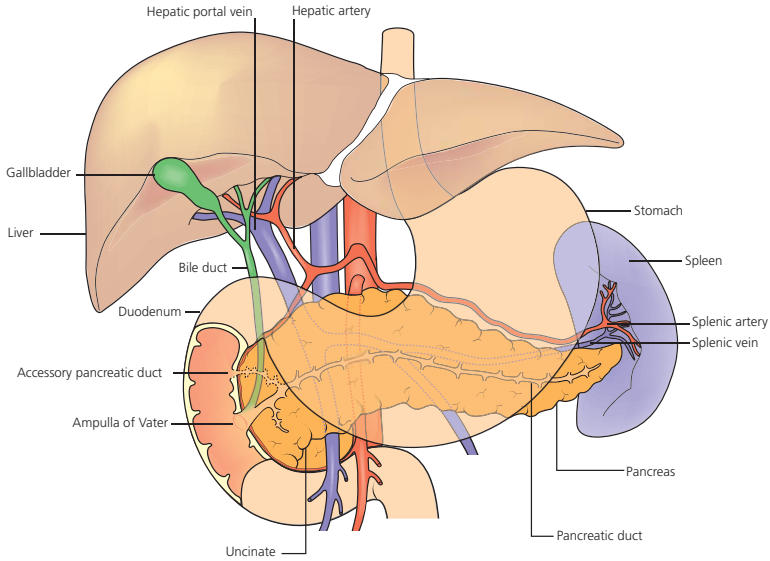

Figure 1 The anatomy of the pancreas and biliary tract.

ends of the main bile and pancreatic ducts control the flow of bile and pancreatic juice, respectively; the sphincter of Oddi controls the outflow from the ampulla of Vater.

Bile acids, essential for the absorption of fats and fat-soluble vitamins, are made in the liver and travel in canaliculi to reach the bile ducts. The intrahepatic bile ducts drain into the right and left hepatic ducts which fuse to form the common hepatic duct. The gallbladder is tucked under the right-hand side of the liver and is connected via the cystic duct to the common hepatic duct to become known as the common bile duct.

The various disorders of these systems will be encountered in any primary care practice. Gallstones are prevalent worldwide and a significant cause of morbidity and mortality. They may cause acute biliary colic, acute cholecystitis or chronic cholecystitis, acute pancreatitis or choledocholithiasis. Gallbladder carcinoma is the fifth most common gastrointestinal (GI) cancer in the USA and the most common GI cancer in Native Americans. Incidence and mortality are very high in certain Latin American countries, especially Chile. Bile duct cancer or cholangiocarcinoma may arise in the intra- or the extrahepatic biliary system, usually in those 50–70 years of age. Sclerosing cholangitis affecting the biliary system may occur in association with diseases such as ulcerative colitis and in secondary form due to conditions such as AIDS. The gallbladder and the biliary system may also be affected by dyskinetic conditions such as sphincter of Oddi dysfunction and gallbladder dyskinesia.

At least 45 000 North Americans will die every year from diseases of the pancreas, even excluding individuals with sugar diabetes. Each year 32 000 North Americans are newly affected with pancreatic cancer. Around 125 000 people in the USA will suffer an attack of acute pancreatitis each year and, separately, there are at least 100 000 long-term sufferers with chronic pancreatitis. All patients with pancreatic disease need to be seen and assessed by specialist doctors.

We have written this book with the intention of providing a clear and simple guide to the diagnosis and management of disorders of the pancreas and biliary tract. We hope that you will find that it helps you to help your patients.

1 Diseases of the gallbladder

Gallstones (cholelithiasis)

Etiology and pathogenesis. Gallstones are mainly composed of cholesterol, bilirubin and calcium salts. In Western populations, the majority of gallstones are the cholesterol type. These form when the cholesterol concentration in the bile exceeds the ability of bile to keep the cholesterol soluble by association with bile salts and phospholipids in the form of mixed micelles and vesicles. Non-cholesterol stones are black- or brown-pigmented stones made up of calcium salts of bilirubin. Black-pigmented stones are more common in patients with cirrhosis or chronic hemolytic states, whereas brown-pigmented stones occur more commonly as primary bile duct stones in association with infection.

Gallstones are a significant cause of morbidity and mortality worldwide. In the USA, gallstones occur in 5–8% of men and 13–26% of women. Native Americans have the highest prevalence in North America, with more than 70% of Pima Indian women having gallstones; African-Americans have the lowest prevalence. European studies have reported the prevalence of gallstones to be about 10% in men and about 20% in women, increased to 30% and 40% respectively in older patients.

Risk factors for gallstones. The prevalence of gallstones is greater in people over 40 years of age, and women are at higher risk than men. Other risk factors for gallstones are given in Table 1.1.

Symptoms and signs. Symptoms may arise from acute or chronic cholecystitis or choledocholithiasis (see Chapter 2, Bile duct stone disease). However, the majority of gallstones are asymptomatic and do not generally require treatment.

Some patients present without complications of gallstones but with mild symptoms of intermittent right upper quadrant pain (biliary colic). These patients are at increased risk for gallstone-related complications.

TABLE 1.1
Risk factors for gallstones

- Age > 40 years
- Female sex
- Estrogen replacement therapy
- Pregnancy
- Family history
- Obesity
- Diabetes mellitus
- Cirrhosis
- Crohn's disease
- Increased serum triglyceride levels
- Lack of exercise
- Drugs: octreotide, clofibrate, ceftriaxone
- Total parenteral nutrition
- Gastric bypass surgery

Diagnosis

Laboratory studies are generally normal in patients with uncomplicated or asymptomatic gallstones.

Plain abdominal radiography is usually unhelpful, as 85–90% of gallstones are radiolucent, but may reveal calcified gallstones in 10–15%; air in the biliary tree suggests a communication (fistula) between the gallbladder and bowel (usually the duodenum); air in the gallbladder wall and sometimes accompanied by an air–fluid level indicates emphysematous acute cholecystitis, often in association with diabetes mellitus; and rarely a calcified ('porcelain') gallbladder indicates a premalignant condition.

Abdominal ultrasound is the preferred test for diagnosis of gallstones. Gallstones characteristically have a highly echogenic focus with a typical acoustic shadow. The accuracy is 95–98%.

Endoscopic ultrasonography (EUS) is able to detect even small gallstones missed by regular abdominal ultrasound.

Magnetic resonance imaging (MRI) has an accuracy of 90–95% in detecting gallstones.

Computed tomography (CT) scan. Although CT scans, like MRI, are not the preferred test for the diagnosis of gallstones, gallstones may be detected in around 30% of patients when a CT scan is performed for other reasons, such as abdominal pain or jaundice.

2 Bile duct stone disease (choledocholithiasis)

Epidemiology and pathogenesis

Stones within the common bile duct (CBD) are usually formed in the gallbladder and pass on to the CBD. They may be of the cholesterol or hard black-pigmented type (see Chapter 1, Diseases of the gallbladder). Primary stones form within the bile duct and are commonly of the soft brown-pigmented type; they are promoted by stasis.

Around 10% of younger patients with stones in the gallbladder have CBD stones at the time of cholecystectomy, rising with age to around 20%.

Clinical features

Symptoms include right upper quadrant pain, jaundice, clay-colored stools and dark urine. Cholangitis may be present, with fever, chills and right upper quadrant pain.

Signs include jaundice, fever and right upper quadrant tenderness. The presence of intermittent fever, jaundice and right upper quadrant pain (Charcot's triad) indicates infection of the bile ducts (acute cholangitis). Shock may also be present, with hypertension and tachycardia.

Diagnosis

Laboratory evaluation may reveal elevated serum levels of bilirubin, alkaline phosphatase, gamma-glutamyltransferase, aspartate aminotransferase and alanine aminotransferase, although these tests may occasionally be normal in patients with CBD stones. Leukocytosis is seen in patients with cholangitis.

Transabdominal ultrasound is non-invasive and is generally the first imaging modality used when a stone in the CBD is suspected. Its sensitivity for detection of a dilated bile duct is 55–90%, and higher in

jaundiced patients. Its sensitivity for detection of stones in the CBD is lower, about 25%.

Endoscopic ultrasound (EUS) is a minimally invasive endoscopic imaging modality for CBD stones with an accuracy of around 98% and is now the preferred method of investigation. Intraductal ultrasound during endoscopic retrograde cholangiopancreatography (ERCP) has a similar accuracy and is marginally superior to ERCP alone. These diagnostic ERCP techniques are invasive and should generally not be used in preference to conventional EUS.

Magnetic resonance cholangiopancreatography (MRCP) is a non-invasive technique for imaging the extra- and intrahepatic biliary system (Figure 2.1). Contraindications include claustrophobia and implanted metal devices and fragments. MRCP is a useful and a reliable test for CBD stones but its accuracy is not quite as good as that of EUS. Most of the stones missed by MRCP are less than 6 mm in diameter.

Computed tomography cholangiography involves imaging the biliary ductal system after injection of contrast medium. The accuracy for CBD stones is around 85% less than that of either of EUS or MRCP.

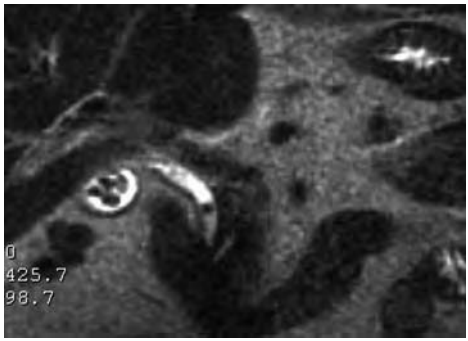

Figure 2.1 Thin-slice (5 mm) single-shot fast-spin echo coronal magnetic resonance cholangiopancreatography sequence showing a small filling defect in the mid-common bile duct. Multiple stones in the gallbladder and a normal-sized pancreatic duct near the ampulla can also be seen. Reproduced courtesy of Aytekin Oto MD, University of Texas Medical Branch.