4 Pancreas, Duodenum, Ampulla of Vater and Extrahepatic Bile Ducts

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4.1 Anatomy

4.1.1 Duodenum

The small intestine is divided into three parts: duodenum, jejunum, and ileum. The duodenum is C-shaped and joins the gastric pylorus to the proximal jejunum by curving around the head of the pancreas. It is 25 cm long and receives the openings of the common bile and pancreatic ducts. The proximal 2.5 cm is covered on its anterior and posterior surfaces by peritoneum, the remainder being retroperitoneal. The duodenum, for purposes of description, is divided into four parts (D1–4). At the duodenojejunal junction, the intestine turns forward—this being called the duodenojejunal flexure.

The mucosa of the duodenum is thick and thrown into numerous circular folds called *plicae circulares*. The common bile duct and the major pancreatic duct pierce the medial wall of D2, approximately halfway along its length. At this point, there is a small elevation called the major duodenal papilla (see below).

Lymphovascular drainage:

The arterial supply originates from the coeliac artery and the superior mesenteric artery (SMA). Venous drainage is to the portal system. The lymphatics follow the course of the arteries, i.e., those from the proximal half drain to the coeliac nodes and those from the distal duodenum drain to the superior mesenteric nodes via the periduodenal nodes.

4.1.2 Pancreas, Ampulla of Vater, and Extrahepatic Bile Ducts

The pancreas is a soft lobulated retroperitoneal organ which is both an endocrine and exocrine gland. The exocrine portion produces enzymes (lipases, proteases) which are conveyed to the duodenum by the pancreatic duct and are concerned with digestion. The endocrine portion (including the islets of Langerhans) produces hormones such as insulin and glucagon. The pancreas is subdivided as follows (Fig. 4.1):

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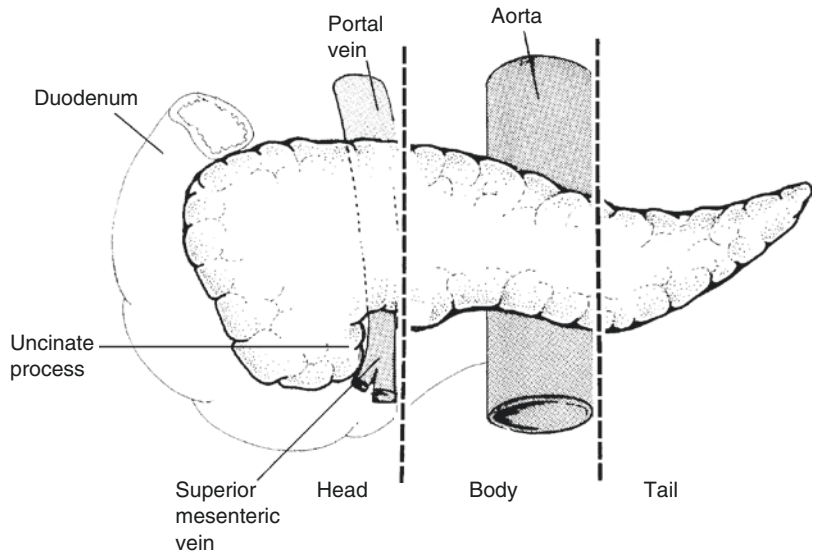


Fig. 4.1 Pancreas (Used with the permission of the Union for International Cancer Control (UICC), Geneva, Switzerland. The original source for this material is from Wittekind et al. (2005))

Head—that part to the right of the left border of the superior mesenteric vein (SMV). It lies within the concavity of the duodenum. The *uncinate process*, a part of the head, extends to the left posterior to the superior mesenteric vessels.

Body—lies between the left border of the SMV and the left border of the aorta.

Tail—lies to the left of the aorta and comes into contact with the hilum of the spleen. Anteriorly the pancreas has a thin covering capsule.

The extrahepatic bile ducts consist of the right and left hepatic ducts, common hepatic duct, and common bile duct (Fig. 4.2). The hepatic ducts emerge from the porta hepatis of the liver and converge to form the common hepatic duct. This descends for 4 cm until it is joined from the right side by the cystic duct when it becomes the common bile duct. This has an extrapancreatic portion of approximately 2 cm following which it enters the pancreas posteriorly, close to the pancreatic neck. The common bile duct then travels through the pancreatic head in a curved fashion before reaching the ampulla of Vater. The main pancreatic duct runs the length of the gland and often merges with the common bile duct to form the ampulla of Vater, which is a small flask-shaped dilated channel situated in the duodenal wall. The ampulla opens into the duodenal lumen by the major duodenal papilla (Fig. 4.2). The distal part of both ducts and the ampulla are surrounded by muscle fibers, this being termed the sphincter of Oddi. It is worth noting that the anatomy of the ampulla of Vater can vary greatly between individuals. In some individuals a minor ampulla can be recognized. This is smaller, connects Santorini's duct with the duodenum and is located approximately 2 cm cranial to the ampulla of Vater/duodenal papilla.

The extrahepatic bile duct system may be subject to a number of variations in its anatomy between individuals.

Lymphovascular drainage:

The arterial supply of the pancreas is from the same vessels that supply the duodenum, and venous drainage is to the portal system. The lymphatics follow the arteries to the peripancreatic, pancreaticoduodenal, and pyloric nodes, and ultimately to the coeliac and superior mesenteric nodes (Fig. 4.3).

The arterial supply to the bile ducts is complex, originating from both the coeliac and SMAs. The lymphatics flow to the infrahepatic, peripancreatic, periduodenal, coeliac, and superior mesenteric nodes.

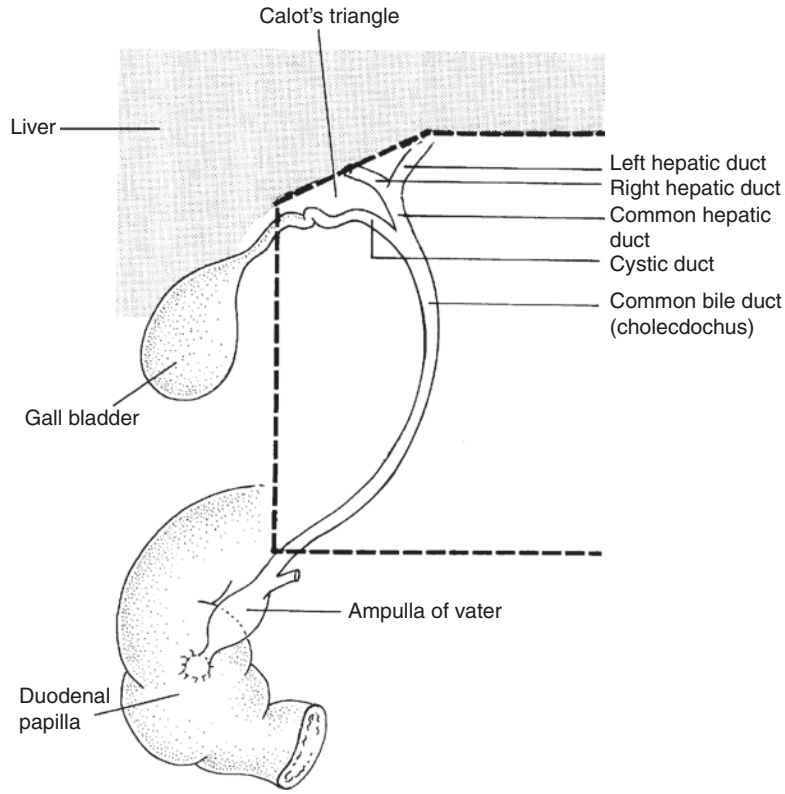


Fig. 4.2 Ampulla of Vater and extrahepatic bile ducts (Used with the permission of the Union for International Cancer Control (UICC), Geneva, Switzerland. The original source for this material is from Wittekind et al. (2005))

4.2 Clinical Presentation

The symptomatology of duodenal peptic ulceration has been discussed in Chap. 3. Duodenal neoplasms, although rare, may lead to epigastric pain, gastric outlet obstruction, and obstructive jaundice if present in the region of the ampulla.

Classically, acute pancreatitis presents with severe epigastric pain which radiates to the back. Chronic pancreatitis produces less acute, but often intractable, epigastric pain. Complications of acute pancreatitis such as shock, infection of necrotic tissue, bowel ileus, metabolic disturbance, and multiorgan failure produce characteristic clinical features.

Bacterial infection in the bile ducts is usually due to secondary infection of obstructed ducts and leads to cholangitis with pain, fever, rigors, and jaundice. If severe the cholangitis may become "ascending" and may cause liver abscesses.

Neoplasms of the head of pancreas (excluding the uncinate process), ampulla of Vater, and extrahepatic bile ducts often lead to obstructive jaundice. Tumours elsewhere in the pancreas do not and so will present later. Obstructive jaundice, because of a lack of absorption of fat and increased excretion of bilirubin in the urine, leads to light-coloured faeces and dark urine. In general, pancreatic and bile duct neoplasms result in vague, poorly localized epigastric pain, anorexia, and weight loss.

Tumours of the endocrine pancreas may be non-functional or functional, the latter resulting in characteristic clinical features because of the hormones they produce:

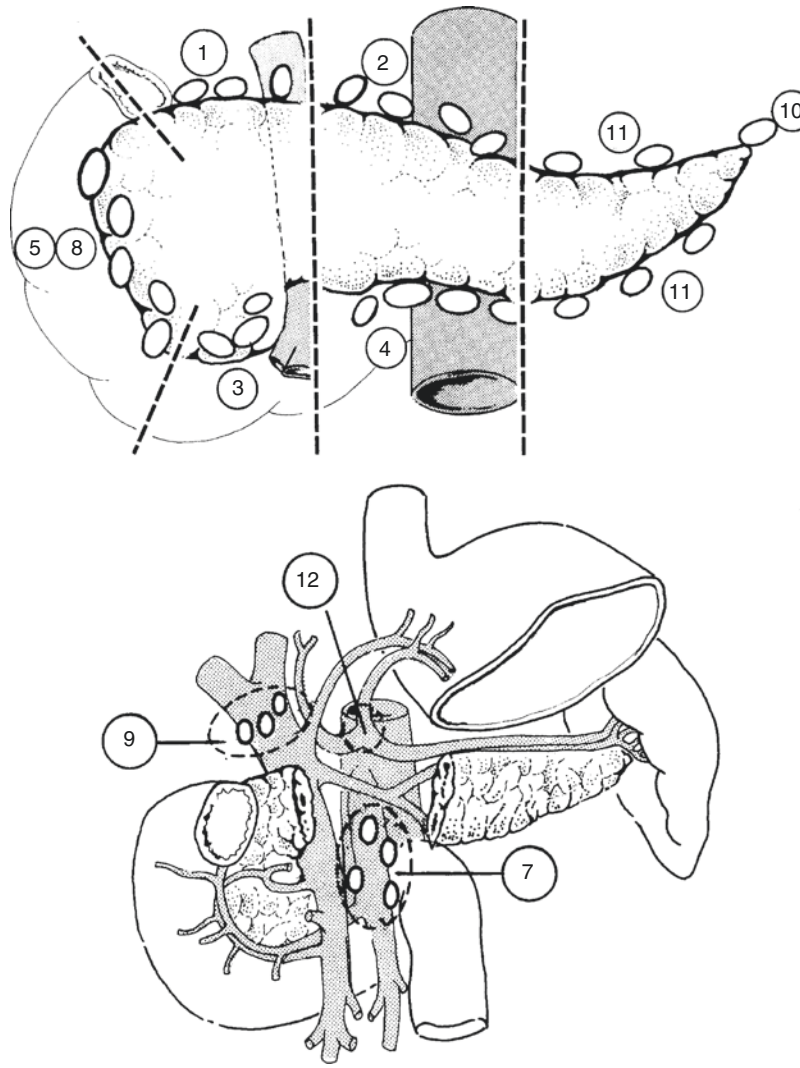


Fig. 4.3 Pancreas and ampulla of Vater: regional lymph nodes are peripancreatic (*1–4*, *11*), pancreaticoduodenal (*5–8*), splenic hilar (*10*), proximal mesenteric (*7*), common bile duct (*9*), and coeliac (*12*) (Used with the permission of the Union for International Cancer Control (UICC), Geneva, Switzerland. The original source for this material is from Wittekind et al. (2005))

- Insulinoma—hypoglycaemic episodes, psychiatric/neurological symptoms
- Gastrinoma—Zollinger–Ellison syndrome
- Glucagonoma—diabetes mellitus and skin rash
- VIPoma—watery diarrhoea, hypokalaemia, and achlorhydria (WDHA) syndrome
- Somatostatinoma—diabetes mellitus, hypochlorhyrdria, gallstones, diarrhoea/steatorrhoea.

4.3 Clinical Investigations

The investigation of duodenal peptic ulcer disease is discussed in Chap. 3.

- Urea and electrolytes (U and E)—electrolyte imbalance may occur in acute pancreatitis and certain endocrine tumours.
- Serum amylase—elevated in acute pancreatitis.
- Clotting screen—may be deranged in obstructive jaundice because of lack of absorption of fat-soluble vitamins which are required in the synthesis of certain clotting factors.
- Liver function tests—obstructive jaundice picture (elevated alk phos and α GT—see Chap. 10).
- CA19–9—serum marker of pancreatic or biliary tract malignancy.

- Serum gut hormone levels and octreotide isotope uptake scan—pancreatic and duodenal neuroendocrine tumours.
- Cyst fluid CEA—usually obtained by endoscopic ultrasound (EUS) and can aid in diagnosis of mucinous lesions of the pancreas for example, intraductal papillary mucinous neoplasms (IPMNs) or mucinous cystic neoplasms (MCNs).
- CXR—to detect pulmonary metastases.
- AXR—10% of gallstones are radio-opaque. Air in the biliary tree may also be seen if there has been previous surgery or a biliary-intestinal fistula.
- USS—to diagnose acute pancreatitis and may detect gallstones in the bile ducts. Tumours less than 1 cm will not be detected. It will also confirm the presence of obstructive jaundice by demonstrating dilated intrahepatic ducts.
- CT (chest, abdomen, and pelvis) and MRI scan—will detect primary tumour and any metastatic spread. Magnetic resonance cholangiopancreatography (MRCP) can be used for non-invasive imaging of the biliary tree.
- Percutaneous transhepatic cholangiogram (PTC)—another method of visualizing the bile ducts is by injecting contrast into the right lobe of the liver. Can be used to obtain bile duct cytology specimens, drain obstructed hepatic and hilar ducts and deploy stents across central strictures.
- OGD/endoscopic retrograde cholangiopancreatography (ERCP)—may be used for both diagnostic (biopsy/biliary brushings) and therapeutic purposes (see below).
- Cholangiopancreatoscopy (e.g. "Spyglass™")—allows direct visualization of bile ducts, including intrahepatic ducts and pancreatic duct. Has diagnostic and therapeutic applications (see below).
- Endoscopic ultrasound (EUS)—used to evaluate abnormalties of the pancreas and lower biliary tree, to evaluate potential resectability of pancreatic tumours and undertake FNA of focal lesions. Can be used in palliative setting to perform a coeliac plexus nerve block for pain.
- Peritoneal aspiration—for malignant cells in ascitic fluid.
- Percutaneous FNAC or needle core biopsy—may provide a preoperative diagnosis.
- Staging laparoscopy with biopsy.
- Doppler studies of the portal vein and angiography may be used to ensure that the vessels are not involved by tumour.

4.4 Pathological Conditions

4.4.1 Non-neoplastic Conditions

Duodenum: Duodenitis and DU have been previously discussed—gastric metaplasia, or nodular gastric heterotopia in D1 and Brunner's gland hyperplasia are also encountered in biopsies of the proximal duodenum. Biopsy for coeliac disease is considered under small intestine.

Ampulla of Vater: Inflammatory polyps of the duodenal papilla are small, pedunculated, and often ulcerated. Partly traumatic in origin due to passage of calculi from the biliary tree. Distinction from neoplasia at OGD/ERCP can be difficult and biopsy is required.

Pancreas: The distal pancreatic duct forms a common channel with the terminal common bile duct in 50–60% of patients resulting in a strong association between pancreatitis and biliary tract disease.

Acute pancreatitis: With an overall mortality of 10–15%, it is rarely biopsied or resected. The commonest causes are gallstones, sphincter spasm, or incompetence with reflux of duodenal fluid and bile, alcohol, trauma, and hypothermia. It is due to release of pancreatic enzymes comprising pancreatic haemorrhage, necrosis, and inflammation with saponification and chalky calcification of abdominal fat. It is usually a self-limiting process, but critical complications include sepsis, shock, bowel paralysis, or perforation. Treatment is resuscitative and supportive—operative intervention can include removal of obstructing gallstones (by ERCP) or infected necrotic tissue (necrosectomy).

Chronic pancreatitis: Commonly due to excess alcohol intake, there is correlation between radiological calcification, pancreatic endocrine and exocrine dysfunction, and the severity of histological changes. Complications include abscess,

systemic fat necrosis and *pancreatic pseudocyst*. Caused by disruption of the duct system due to obstruction by calculus or tumour, a pseudocyst has a thick fibrous wall lined by granulation tissue but no epithelium. It can rupture into the peritoneal cavity or splenic artery. Treatment is by endoscopic or transabdominal drainage either internally to stomach or duodenum or externally to skin. Surgical excision is used if small and localized to the body or tail, or if the pseudocyst is thick-walled and not appropriately sited for drainage.

The commonest biopsy expression of chronic pancreatitis is that seen adjacent to a pancreatic tumour or secondary to an ampullary tumour due to duct obstruction. The acinar and stromal changes can mimic pancreatic carcinoma, making interpretation difficult especially on frozen section. Chronic pancreatitis tends to retain its lobular architecture, lacks malignant cytological changes, and shows no invasion of nerve sheaths or peripancreatic fat.

Autoimmune pancreatitis (AIP): This subtype of chronic pancreatitis can present with abdominal pain or with painless obstructive jaundice and an apparent pancreatic mass on imaging thereby mimicking a pancreatic malignancy. Two subtypes are recognized: Type 1 is associated with elevated serum levels IgG4, a prominence of IgG4 plasma cells in affected tissue, storiform fibrosis and obliterative venulitis. It may occur in association with extrapancreatic IgG4 related diseases. Type 2 tends to have normal IgG4 serum levels and is rarely associated with systemic IgG4 disease. There is an association with inflammatory bowel disease (IBD). Histology typically shows lymphoplasmacytic duct-centric inflammation with granulocytic epithelial lesions, or GELs. Both can be treated by steroids but may come to surgery due to mimicry of malignancy.

Benign pancreatic cysts: retention cysts, lymphoepithelial cysts, squamous lined cysts and pseudocysts may be encountered in surgical practice. These need to be carefully evaluated to ensure that they are not neoplastic mucinous cysts (see below). Developmental cysts can also occur and include duodenal diverticula and foregut cysts.

Extrahepatic bile ducts: Stricture of the common bile duct may be caused by passage of a calculus with or without ascending cholangitis and secondary infection, but is more usually after surgical trauma due to inadvertent injury to or ligation of the duct. Treatment aims to reestablish free drainage of bile to the bowel either by a bypass or stenting procedure (see below).

4.4.2 Neoplastic Conditions

Ampullary adenocarcinoma: Arising from adenomatous dysplasia of either the periampullary duodenal or intra-ampullary duct mucosae, it is one of the commonest causes of death in familial adenomatous polyposis (FAP) in patients who have had a prophylactic colectomy. Adenoma may be amenable to local excision, but radical surgical resection is often required for large lesions and because a surface biopsy showing epithelial dysplasia may harbour underlying invasive adenocarcinoma. Most cases have a well-defined intestinal pattern, but in a minority it can be difficult to separate adenocarcinoma of the duodenal papilla, ampulla, distal pancreatic duct, and distal common bile duct as they can share similar well-to-moderately differentiated tubular and ductular patterns. Detailed examination of the exact anatomical location in the resection specimen is required and the primary site should be determined as duodenal, ampulla of Vater (which includes the duodenal papilla), head of pancreas or distal common bile duct. This distinction is important as the staging system and choice of adjuvant therapy differs for each site. In practice this can be difficult to establish, especially if the tumour is large and involves more than one of these sites. In that scenario, the tumour origin can usually be established at gross examination by determining the epicentre of the tumour. Secondary involvement of the ampulla by pancreatic cancer can occasionally be specified based on the histological features and pattern of mucosal spread. Ampullary adenocarcinomas can have intestinal-type or pancreatobiliary-type differentiation, the latter of which has a worse prognosis. Immunohistochemistry can be used to

make the differentiation (intestinal-type: CK20+, CDX2+, MUC2+; pancreaticobiliary: MUC1+, MUC2−, CDX2−).

Benign pancreatic non-mucinous neoplastic cysts: *serous cystadenoma* (elderly, macro−/microcystic, fluid-filled, central scar, clear cuboidal epithelium). Can occur in Von Hippel-Lindau syndrome. Acinar cell cystadenoma, lymphangioma may also occur.

Cystic pancreatic exocrine lesions of malignant potential: *IPMNs* and *MCNs* can exhibit a benign, borderline, and malignant spectrum of behaviour related to the degree of epithelial dysplasia and extent of invasion into pancreatic parenchyma and peripancreatic fat. MCNs arise almost exclusively in middle-aged females, typically in the pancreatic tail and unconnected to the pancreatic ductal system. They are characterized by the presence of mural ovarian-type stroma. IPMNs are slightly more common in males, aged usually around 60 years, arise within the ductal system but predominantly within the pancreatic head or uncinate process. Intra-ampullary IPMNs can also occur. By definition IPMNs communicate with the ductal system. Three types of ductal involvement are recognized: main, branch duct or combined/mixed type i.e. involvement of both the main duct and its branches. Both MCNs and IPMNs typically show indolent growth but they may harbour small foci of invasive malignancy (identified through careful or complete sampling) or show frank malignant transformation. Resection of MCNs is recommended in fit patients whereas IPMNs are managed according to established guidelines (e.g. Revised Sendai Guidelines) and are resected when certain criteria are met. *Solid pseudopapillary neoplasm*—low grade malignant tumour of uncertain cell origin. An epithelial origin is suspected. Most commonly presents in young females as a mixed solid/cystic lesion composed of pseudopapillae of uniform cells, cystic areas with necrosis and blood lakes.

Pancreatic exocrine carcinoma: Arising from dysplastic pancreatic duct epithelium (referred to as pancreatic intraepithelial neoplasia—PanIN), or a pre-existing mucinous lesion such as an IPMN or MCN as discussed above. Carcinomas form the vast majority of pancreatic tumours, 80–90% are adenocarcinomas which are graded according to the degree of gland formation. Most (70–80%) arise in the pancreatic head with a minority in the body or tail and occasionally multifocal. Perineural invasion is characteristic and diagnostically helpful in biopsies. There is limited suitability for resection (10–20% of cases are resectable at diagnosis). Resectable disease is locally confined with absence of distant metastases and clearance of the main surrounding arterial and venous structures including superior mesenteric artery, vein and portal vein. Partial involvement, distortion of or abutment of some of these vascular structures in the absence of distant metastases suggests borderline resectable disease. Patients with borderline resectable disease may undergo a trial resection or neoadjuvant chemotherapy or chemoradiotherapy. The presence of distant metastases or encasement of the vessels renders a tumour unresectable. Pancreatic head tumours are removed by a Whipple's procedure which results in an average increase in survival of 12–18 months. Tumours of the body and tail of the pancreas are resected via a distal pancreatectomy+/−splenectomy. Adjuvant chemotherapy may be offered post operatively depending on the outcome of pathological evaluation. For those patients with unresectable disease treatment is mainly palliative—palliative chemotherapy (if fit), pain control, nutritional support, and relief of jaundice by open or laparoscopic bypass, or endoscopic stent insertion to combat biliary obstruction.

Other cancers: Unusual but include undifferentiated carcinoma, adenosquamous carcinoma, acinar cell carcinoma, small cell neuroendocrine carcinoma, malignant lymphoma (usually from an adjacent nodal lymphoma), and sarcoma, which often represents spread from a primary sarcoma of gut or retroperitoneum. Renal clear cell carcinomas have a propensity for metastasizing to the pancreas and may come to resection.

Pancreatic neuroendocrine tumours (NET): Single or multiple and forming a minority (3%) of pancreatic tumours, they can be small (<1–2 cm), well circumscribed, and pale or yellow in colour. Occasionally cystic NETs occur.

Pancreatic NETs are positive for general neuroendocrine markers (chromogranin, synaptophysin) and occasionally specific peptides, e.g., insulin, glucagon, gastrin, somatostatin or pancreatic polypeptide. Many (60–85%) are associated with a functional hormonal syndrome, e.g., Zollinger–Ellison syndrome due to pancreaticoduodenal gastrinomas. The pancreas is also involved in 80–100% of type I multiple endocrine neoplasia (MEN) syndrome comprising hyperplasia or tumours of parathyroid, pituitary, adrenal glands, and pancreas (usually gastrinoma). Histology does not reliably predict behaviour and better indicators of potential malignancy are functionality and established metastases—insulinoma (85% benign), gastrinoma (60–85% malignant), size >3 cm, site (e.g., duodenal), tumour grade, invasion of vessels, nodes, adjacent organs, and liver. Detection of metastases is by CT and octreotide scans. Determination of tumour grade on needle core biopsy (mitotic count and Ki-67 index) indicates likely behaviour and influences their oncological management.

Extrahepatic bile duct carcinoma: These are typically adenocarcinomas (often referred to as cholangiocarcinomas) and show an increased incidence in association with various disorders including ulcerative colitis, sclerosing cholangitis, gallstones, and congenital bile duct anomalies. The majority (50–75%) arise in the upper third (including the hilum) with lesser numbers in the middle and distal thirds (10–25% each) or even diffuse and multifocal. Extrahepatic bile duct carcinomas are classified and staged as perihilar (proximal to the origin of the cystic duct to include the right, left and main hepatic ducts) or distal (distal to the insertion of the cystic duct; cystic duct carcinoma is included under gallbladder carcinoma). Sometimes papillary or polypoid but often nodular, ulcerated, sclerotic, or strictured, prognosis relates to the stage of disease, location, and histological grade. There is characteristic perineural invasion often with involvement of regional lymph nodes, peritoneum, or the liver (upper third tumours) at presentation. Other rare cancers are carcinoid tumour, malignant melanoma, lymphoma/leukaemia, and in childhood embryonal rhabdomyosarcoma.

Prognosis: Prognosis of pancreatic ductal adenocarcinoma is poor with an overall 10–20% 5 year survival rate. Chemotherapy has an adjunctive and palliative role for select patients. Cystadenocarcinomas are relatively rare but potentially resectable. Pancreatic neuroendocrine tumours have an indolent time course with a 50% 10-year survival and potential chemoresponsiveness even in the presence of metastases. Increased understanding of the molecular biology of pancreatic NETs has permitted the development of newer drugs such as mTOR inhibitors e.g. everolimus, to treat advanced disease. Ampullary carcinoma has a 5 year survival of 25–50%, improving to 80–85% if early stage (pT1) disease confined to the sphincter of Oddi. Distal bile duct cancers may be potentially resected with 25% 5-year survival. Sclerosing bile duct carcinoma at the hilum (Klatskin tumour) can have an indolent course, but the majority of bile duct cancers present late with very limited survival and only palliative biliary drainage (open bypass or laparoscopic/endoscopic/percutaneous stent insertion) is justified.

4.5 Surgical Pathology Specimens: Clinical Aspects

4.5.1 Biopsy Specimens

The endoscopic technique for the diagnosis of benign lesions of the duodenum has been discussed previously. Endoscopic biopsy of duodenal and ampullary tumours is by OGD, or ERCP. The ERCP scope differs from OGD in that the camera views from the side (lateral view) and not from the end (forward view), as in the gastroscope. This allows the major duodenal papilla to be viewed directly. The papilla is then cannulated and contrast injected at intervals to outline the duct system and radiographs, which appear on a monitor, are taken in real time to check the position of the catheter. The bile duct (cholangiography) and the pancreatic duct (pancreatography) are cannulated in turn and radiographs taken, which may provide clues to the aetiology of the condition, e.g., stones, stricture, etc. ERCP has several diagnostic and therapeutic applications:

The following *diagnostic specimens* can be taken by ERCP:

- Bile and pancreatic juice for cytology.
- Brushings from the ducts for cytology.
- Biopsies from the ampulla

ERCP can also be used for *therapeutic procedures*:

- Sphincterotomy (division of the sphincter of Oddi) can be performed in patients with a history of common bile duct stones to allow free drainage
- Stone extraction can be performed using a balloon catheter or basket
- Dilatation of stricture using a balloon catheter
- Both benign and malignant biliary strictures may be stented (a palliative procedure in the latter) to reduce jaundice.
- ERCP is not without its complications, two of the most common being acute pancreatitis (1–3% of cases) and cholangitis.

Cholangiopancreatoscopy is a more modern technique and allows direct visual diagnostic evaluation of the pancreatic duct and bile ducts using a fibreoptic camera. This overcomes many of the limitations of ERCP and permits more detailed assessment of abnormalties, such as strictures, and targeted sampling of lesions (brushings and direct biopsy using forceps). Similar to ERCP there are several therapeutic applications including stent insertion and removal, endoscopic resection of lesions, tumour ablation therapy, and biliary drainage.

4.5.2 Resection Specimens

4.5.2.1 Neoplastic Lesions: Duodenum, Ampulla, Distal Common Bile Duct, and Exocrine Pancreas

At the time of presentation, pancreatic carcinoma is beyond resection in more than 80% of patients. Also, given the advanced age of presentation in the vast majority of patients, over 95% of cases are treated palliatively. However, if the patient is fit, the tumour locally confined, does not involve major vessels, and has not metastasized on imaging, then a curative procedure may be considered.

Although the type of operation will depend on the site and size of tumour, the curative procedure of choice for duodenal, ampullary, distal common bile duct, and pancreatic head tumours is a standard Kausch–Whipple pancreaticoduodenectomy (PD)—*Whipple's procedure.*

This procedure involves a transverse subcostal incision and initial exploration to assess operability. It then involves the en bloc resection of the pancreatic head (with a variable amount of body depending on the location and size of the tumour), distal two-thirds of the stomach, duodenum (and proximal 10 cm of jejunum), gallbladder, and common bile duct (Fig. 4.4a), which may be extended proximally for distal common bile duct tumours. There are many methods (up to 70!) of reconstruction after PD. One of the most popular is the formation of the following (Fig. 4.4b):

1. Pancreaticojejunostomy (end to end)
2. Hepaticojejunostomy (end to side)—anastomosis of the hepatic duct to the jejunum
3. Gastrojejunostomy (end to side)
4. Jejunojejunostomy (side to side)—this decompresses the proximal jejunal loop and reduces jejuno-gastric reflux

If there is involvement by tumour of the body and tail, the procedure can be modified to a *total* PD which includes resection of the body and tail of the pancreas ± the spleen.

For some small ampullary and periampullary (i.e., head of pancreas, distal common bile duct, and duodenum) tumours, a *pylorus-preserving PD* is performed. This is essentially identical to a standard PD except that the distal stomach and proximal 3 cm of duodenum are left in situ, thus retaining the food storage and release functions of the stomach.

A *distal pancreatectomy* consists of resection of the body and tail of the pancreas, usually including the spleen. This procedure may be used for tumours—many benign—which are located in the distal pancreas.

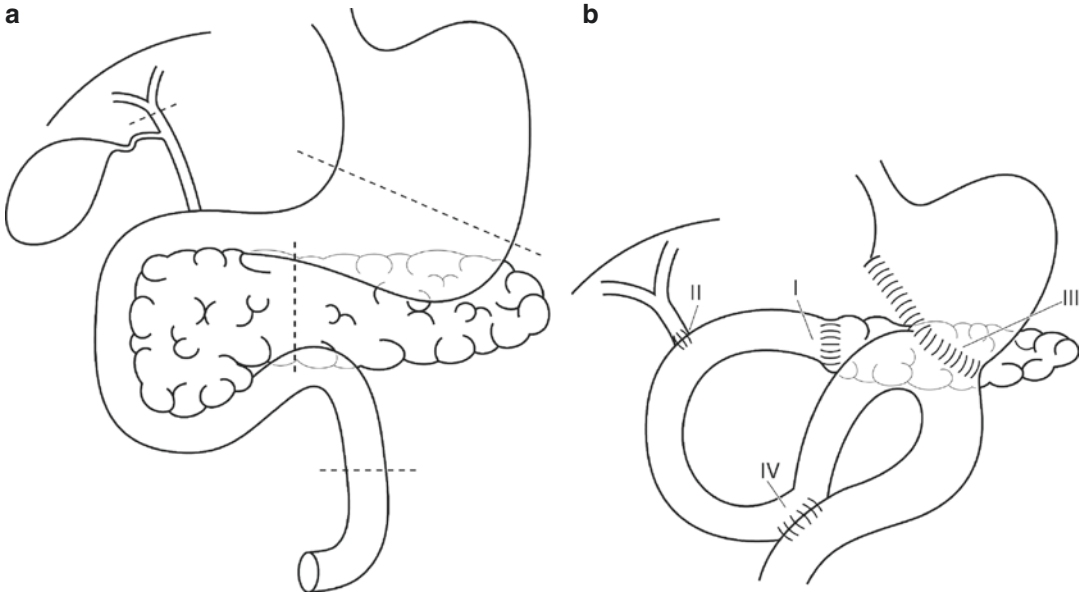


Fig. 4.4 Whipple's procedure: (**a**) limits of resection and (**b**) reconstruction anastomoses (Reproduced, with permission, from Allen and Cameron (2013))

In all the above procedures, the pancreatic resection margin may be sent for frozen section examination to ensure adequate excision.

4.5.2.2 Neoplastic Lesions of the Endocrine Pancreas

The goals of surgery for tumours of the endocrine pancreas are twofold:

- To locate and excise all abnormal tissue
- To differentiate between benign and malignant tumours by conducting a search for metastatic deposits

Localization of tumours may be carried out by a combination of preoperative imaging (MRI, octreotide scanning) and intraoperative palpation and USS. Once the tumour has been localized, there are two main methods of excision:

- Enucleation—Excision of the tumour and a surrounding segment of normal pancreas can be carried out if the tumour is small (<1.5 cm) and superficial.
- Resection—For larger tumours which are deep-seated, a formal pancreatic resection is required, i.e., a distal pancreatectomy for distal tumours or a proximal pancreatectomy (duodenum-preserving resection of the pancreatic head) for proximal tumours. A PD procedure is only rarely required for large tumours in the head of pancreas or duodenum.

4.5.2.3 Neoplastic Lesions of the Extrahepatic Bile Ducts

Cancer of the bile ducts (cholangiocarcinoma) is treated palliatively in 80–90% of cases and resection should only be considered in localized tumours without metastatic spread. When surgical resection is considered, the type of procedure will depend on the site of tumour:

- Tumours in the distal common bile duct (i.e., lying behind the duodenum and pancreas)—Whipple's procedure.
- Tumours proximal to this and distal to the confluence of the right and left hepatic ducts—wide excision of the supraduodenal biliary tree, gallbladder, and related nodes. A length of jejunum is isolated in a Roux-en-Y loop and an end-to-side hepaticojejunal anastomosis allows biliary drainage.
- Tumours proximal to the hepatic confluence require the above plus a relevant liver resection (see Chap. 10).

Palliation for distal common bile duct tumours is most commonly done by ERCP stenting. Other methods of operative palliation (i.e., "by-pass" techniques) are:

- Choledochoduodenostomy—proximal common bile duct is anastomosed to D1.
- Hepaticojejunostomy—can be used in more proximal biliary tumours (i.e., common hepatic duct/proximal common bile duct).

For proximal biliary (hilar) tumours, a segment III hepaticojejunostomy can be used. In this the liver is divided to the left of the falciform ligament until the segment III duct is visualized. An anastomosis is then fashioned between this and a Roux-en-Y loop of jejunum.

4.5.2.4 Non-neoplastic Lesions

Two of the most common complications of *acute pancreatitis* requiring surgical intervention are:

- Necrotizing pancreatitis—Surgical intervention has a mortality rate of 60% and involves removal of necrotic tissue from the pancreas and retroperitoneal spaces, and drainage of fluid collections.
- Pancreatic pseudocyst—cystogastrostomy—a pseudocyst in the lesser sac is drained into the stomach via an opening in the posterior wall of the stomach.
- In *chronic pancreatitis*, the following procedures may be employed:
- The pain associated with chronic pancreatitis is caused by obstruction of the pancreatic duct leading to duct hypertension. The *Frey operation* (localized resection of the pancreatic head and side to side pancreaticojejunostomy) is designed to decompress the duct.
- When there is disruption of the duct distal to the head, a distal pancreatectomy is indicated.
- Occasionally, when the disease is maximal in the head, a Whipple's procedure may be employed, possibly when investigations are equivocal regarding malignancy. Another option would be a duodenum-preserving resection of the pancreatic head or total pancreatectomy.

Bile duct stones may be removed laparoscopically or by an open procedure if they cannot be removed by ERCP. Strictures may be stented or bypassed using one of the techniques described above.

4.6 Surgical Laboratory Specimens: Laboratory Protocols

4.6.1 Biopsy and Local Mucosal Resection Specimens

See Chap. 1.

4.6.2 Resection Specimens

Specimen

- Most pancreatic resections are for neoplastic conditions, although operative intervention may be indicated for debridement of necrotic tissue in acute pancreatitis, trauma to a major duct, or removal of the pancreatic head or pseudocyst in chronic pancreatitis. Resections are either local for pseudocyst or cystic neoplasms, or radical for ampullary, pancreatic head or bile duct cancers. Radical excision is also undertaken for many cystic lesions due to concerns regarding neoplasia. Carcinoma of the body and tail usually presents late and is typically irresectable.
- To demonstrate the lesion and its relationship to the surgical margins, the pancreas is cut into multiple parallel slices, preferably in the horizontal plane (to allow correlation with CT scan cross-sectional images). In some cases vertical or coronal planes can be used. Specimens may be opened longitudinally through the stomach and duodenum to aid fixation prior to complete dissection. A small number of axial incisions may be made, if required for biobanking etc., taking care to assess for potential margin involvement.
- The presence of any stent or surgically labeled structures, e.g., portal vein, SMV, should be noted.

4.6.2.1 Local Resection of Cystic Lesions

- Weight (g) and maximum dimension (cm).
- Capsule: intact/deficient/smooth/nodular/adhesions/circumscribed/lobulated.
- Cut surface: uni−/multilocular/septate/solid areas (cm)/contents—fibrin, mucoid, serous fluid.
- Photograph.
- Paint the external surface.
- Fixation by immersion in 10% formalin for 48 h.
- Sample at least one block per centimetre diameter of the tumour/cyst to include thin, nodular, and solid areas of its wall and internal aspect. If the cystic lesion is suspected to be an IPMN or MCN and there is no obvious macroscopic invasive disease it is preferable to submit the entire lesion for histological evaluation to exclude or identify microscopic invasion.
- Sample adjacent tissues to include the resection margins and any other structures.

4.6.2.2 Local Resection of Pancreatic Head in Chronic Pancreatitis

- Weight (g) and dimensions (cm): then fix in 10% formalin for 48 h.
- Serially slice perpendicular to the pancreatic duct.
- Inspect and describe, e.g., haemorrhage, abscess, necrosis, calculi, calcification.
- Select five representative blocks, assuming no suspicion of malignancy on macroscopic examination.

4.6.2.3 Necrosectomy Specimen

- Number of pieces, total weight (g), and maximum dimension (cm).
- Fix in 10% formalin for 48 h.
- Serially slice, inspect, and describe, e.g. haemorrhage, abscess, necrosis, calculi, calcification, tissues present.
- Select five representative blocks.

4.6.2.4 Distal Pancreatectomy (Fig. 4.5)

- Orientate—cut end is proximal, distal end is uncut ± spleen.
- Weight (g) and measurements—length × width × depth (cm).
- Paint the proximal cut margin and the external surfaces using different colours of ink for the various anatomical and surgical aspects—superior, inferior, anterior capsule, posterior retroperitoneal.
- Fixation by immersion in 10% formalin for 48 h.
- Transverse section the proximal margin to include the duct.
- Serially section the pancreas at 3–4 mm intervals in a perpendicular plane to its long axis. If a cystic neoplasm is suspected a probe can be inserted into and along the main pancreatic duct and the specimen sliced parallel along the probe. This can aid the assessment of the relationship of the cystic lesion to the pancreatic ductal system. It is perfectly acceptable to slice the specimen using the perpendicular slicing method above.
- Lay the slices out in sequence and photograph.
- Tumour: size (cm), edge (circumscribed/irregular), appearances, consistency, relationship to the pancreatic duct, distances (mm) to the specimen edges.
- Sample a minimum of five blocks of tumour in relation to pancreas, pancreatic duct, peripancreatic fat and its margins, and spleen. If a cystic lesion is identified it is preferable to submit the entire lesion as invasive disease (early carcinomas) and ovarian–type stroma (MCNs) may be missed using a limited sampling protocol.
- Sample all regional lymph nodes, non-neoplastic pancreas and spleen (if present).

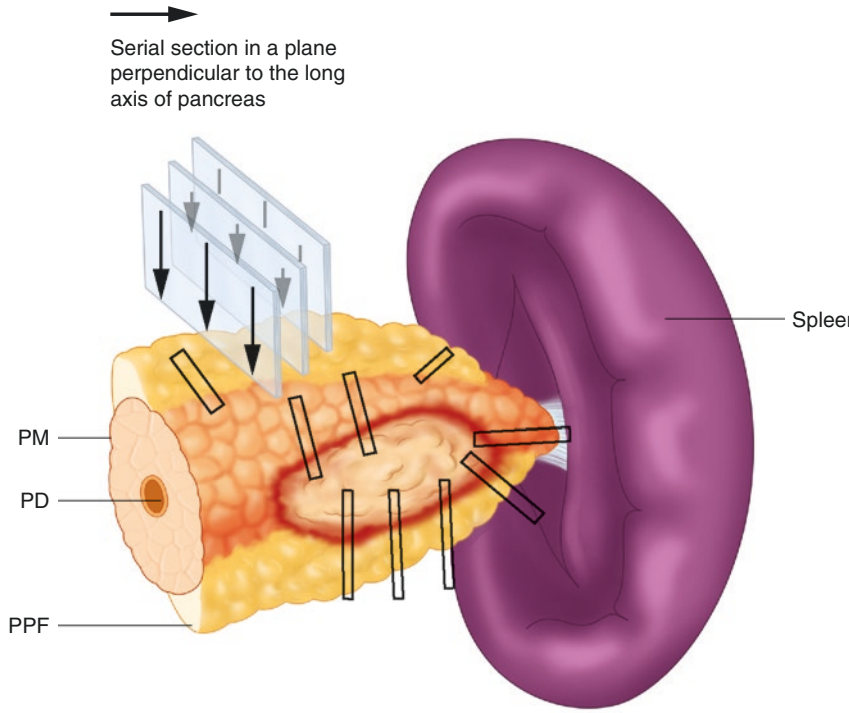


Fig. 4.5 Distal pancreatectomy (Reproduced, with permission, after Allen and Cameron (2013))

4.6.2.5 Whipple's Procedure (Figs. 4.6 and 4.7)

Initial procedure:

- Open with scissors by cutting along the lesser curvature of the stomach and the free border of the duodenum.
- Measurements:
  Lengths (cm) of distal sleeve of stomach and duodenum, and parts present (D1–4).
  Dimensions (cm) of pancreas, and parts present (head, body, attached named vessel, e.g., SMV).
  Lengths of gallbladder (if attached) and bile duct (cm).
- Fixation by immersion in 10% formalin for 24 h.
- Paint the external anatomical and surgical margins using different colours of ink and labeled appropriately—anterior, posterior, SMV, SMA and pancreatic transection margin. The surgical margins should be identified and inked prior to slicing (see Fig. 4.6). It is also advisable to sample the bile duct and pancreatic transection margins prior to slicing.
- Sample the following surgical margins: proximal gastric, distal duodenal, pancreatic transection margin taking care to include the pancreatic duct, and, proximal common bile duct.
- Trim off the uninvolved, "excess" parts of the duodenal and gastric wall to leave a small cuff around the pancreas. This renders the specimen more compact and easier to slice and examine. Do not remove duodenal tissue if involved by tumour (Figs. 4.6 and 4.7).
- Place the specimen flat on the bench and with a long, sharp knife horizontally slice the specimen into parallel slices 4–5 mm thick (Fig. 4.7). Lay the slices out in order from superior to inferior, number/label and photograph (if possible to aid sign out and tumour board/multidisciplinary meeting discussion). It

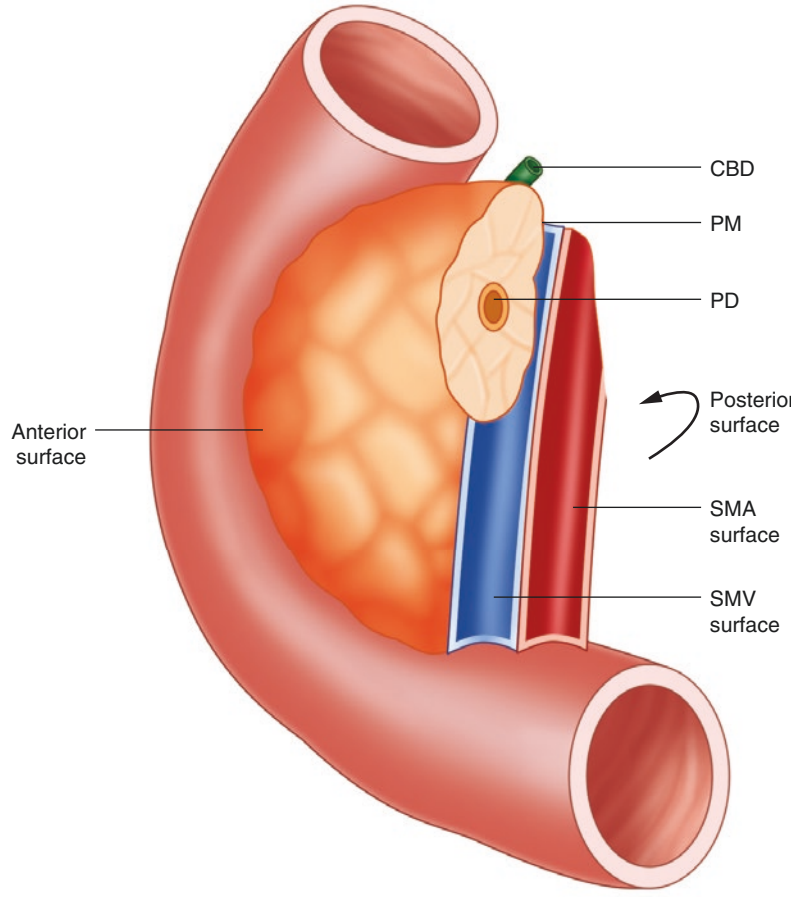


Fig. 4.6 "Trimmed" specimen demonstrating important margins in a Whipple's procedure (Reproduced, with permission, Royal College of Pathologists and Paul Brown, Medical Illustrator, Leeds Teaching Hospitals NHS Trust). *CBD* common bile duct, *PD* pancreatic duct, *PM* pancreatic transection margin

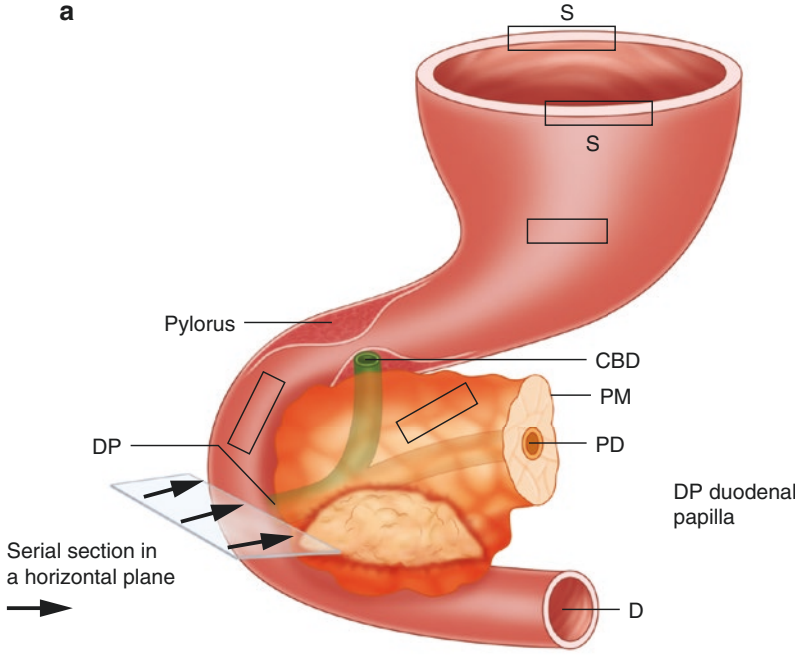
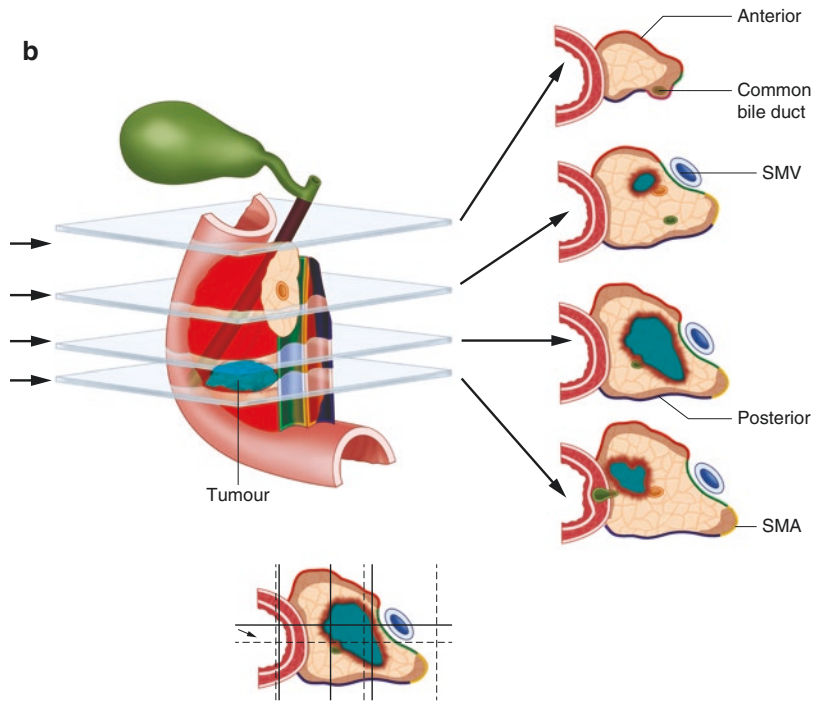


Fig. 4.7 (**a**, **b**) Whipple's procedure for carcinoma of ampulla of Vater, head of pancreas or distal common bile duct. Modified and reproduced with permission after Allen and Cameron (2013), Verbeke (2008, 2013). (**b**) Serial horizontal slices and number slices for photography, subdivision and harvesting of blocks

Fig. 4.7 (continued)



is useful to identify the common bile duct and pancreatic duct in each slide, as appropriate, and assess the relationship of the tumour mass to these structures to determine the tumour origin.

- Further 24 h fixation may be required.

Description:

- Tumour
  - Site: duodenum/ampulla/pancreas (duct/parenchyma)/bile duct
  - Size: length × width × depth (cm) or maximum dimension (cm)
    Appearance:
    Polypoid/diffuse/ulcerated—ampullary/bile duct tumours.
    Cystic/papillary/mucoid/scirrhous/thickening—pancreatic exocrine tumours.
  - Circumscribed/pale/homogeneous—pancreatic neuroendocrine tumours
  - Edge: circumscribed/irregular
- Pancreatic and bile ducts: dilatation/stenosis/extrinsic or intraduct tumour/stent
- Pancreas: indurated/oedematous/fat necrosis
- Peripancreatic lymph nodes: location/number/size
- Other organs: involvement of SMV, duodenum or stomach etc.

Blocks for histology (Fig. 4.7):

- Resection margins (see above).
- Sampling is best performed by following the numerical or sequential order of the slices (see above under *"Initial procedure")*. This makes it easier to evaluate the 3-dimensional profile and verify the origin of the tumour during microscopic evaluation.
- Tissue samples are best taken to include the tumour and neighbouring structures such as margins and lymph nodes. In this regard it is often helpful to submit the most representative slices from the pancreas in their entirety (as composite blocks, or megablocks, if local resources permit). Lymph nodes should not be dissected out from the pancreatic tissue at this stage but instead sampled along with adjacent pancreatic parenchyma. The position of the node in the specimen i.e. slice number and closest margin, can also be recorded and will facilitate identification of duplicate nodes (which may straddle multiple slices) and assignment of lymph node station, if required.
- Perigastric lymph nodes will not be represented in the slices above. The perigastric fat should be separately examined for nodes and those identified submitted.
- Sample non-neoplastic pancreas, stomach, and duodenum.

- The peripancreatic fat often contains numerous small lymph nodes that may not be visible or palpable during macroscopic examination. After sampling all other blocks as outlined above it can be useful to submit the remaining peripancreatic fat separately.
- If other organs are present (total or regional pancreatectomy—PD, gastrectomy, splenectomy, portal vein, transverse colectomy, mesocolon, omentum, and regional nodes): describe, weigh, measure, paint, and block according to the macroscopic degree of tumour spread. Label the blocks as to their site of origin.

4.6.2.6 Distal Extrahepatic Bile Duct Cancer Resection

- Bile duct segment
  - Site: common bile duct/common hepatic duct/cystic duct. For main right, main left or common hepatic duct refer to perihilar staging system (Chap. 10). For tumours of the cystic duct refer to gallbladder staging system (Chap. 9).
  - Length × diameter (cm)
  - Dilated/ulcerated/strictured/cyst and maximum dimension (cm) of lesion
  - Calculi
- Tumour
  - Maximum dimension (cm)
  - Site: common bile duct/common hepatic duct/right or left hepatic duct/cystic duct/intraduct/mural/extramural/involvement of liver
  - Appearance: strictured/ulcerated/nodular/polypoid/multifocal
- Hepatic resection (more commonly encountered in perihilar bile duct cancers)
  - Segment(s)
  - Dimensions (cm) and maximum dimension (cm) of tumour present
  - Identify bile duct margins
- Biliary stent
  - Not present/present/placement (within or outside the lumen).
- Gallbladder
  - Present/not present/involved by tumour.
- Sample the distal bile duct limit (circumferential transverse section) and the proximal bile duct limit or the hepatic resection margin (two or three blocks).
- Paint the external adventitial CRM.
- Serially section the specimen transversely at 3–4 mm intervals.
- Sample five or six blocks to demonstrate the worst point of tumour invasion in relation to the CRM, liver, gallbladder, proximal and distal surgical limits. If liver resection with perihilar tumour, identify and sample obvious infiltration of the main portal vein or hepatic artery branches (Chap. 10).
- Sample all lymph nodes.

Histopathology report:

- Tumour type
  - Ampulla/bile duct: adenocarcinoma (subdivide as intestinal-type or pancreatobiliary type using immunohistochemistry; see section "Neoplastic Conditions").
  - Pancreas: adenocarcinoma/neuroendocrine tumour/other. If other, please specify type e.g. adenosquamous
- Tumour differentiation/grade:
  - Ampullary/bile duct adenocarcinoma: well/moderate/poor.
  - Pancreatic carcinoma:

Well/grade 1	>95% glands
Moderate/grade 2	50–95% glands
Poor/grade 3	5–50% glands
Undifferentiated/grade 4	<5% glands

- Tumour edge
- Pushing/infiltrative/lymphoid response.
- Assessment of response to neoadjuvant therapy, if relevant.
- *Extent of local tumour spread: TNM 8 for carcinoma Ampulla of Vater.*

pTis	Carcinoma in situ
pT1	Tumour pT1a. limited to the ampulla or sphincter of Oddi, or, pT1b. perisphincteric invasion and/or into duodenal submucosa
pT2	Tumour invades muscularis propria of duodenum
pT3	Tumour invades pancreas: pT3a. ≤0.5 cm, or, pT3b. >0.5 cm or peripancreatic tissue/duodenal serosa

pTis	Carcinoma in situ
pT4	Tumour invades superior mesenteric artery or coeliac axis, or common hepatic artery

Pancreas—carcinoma of exocrine pancreas or high-grade neuroendocrine carcinoma (well differentiated neuroendocrine tumours should be staged according to ENETS TNM system; TNM8 staging may be supplied for comparison. ENETS is European Neuroendocrine Tumour Society).

pTis	Carcinoma in situ
pT1	Tumour limited to the pancreas, ≤2 cm maximum dimension
pT2	Tumour limited to the pancreas, >2 cm and ≤4 cm dimension
pT3	Tumour >4 cm dimension
pT4	Tumour involves coeliac axis, SMA and/or common hepatic artery

Distal extrahepatic bile ducts—(for tumour distal to the insertion of the cystic duct; perihilar tumours are classified separately—chap. 10)

pT1	Tumour invades bile duct wall <5 mm depth
pT2	Tumour invades bile duct wall 5–12 mm depth
pT3	Tumour invades bile duct wall >12 mm depth
pT4	Tumour involves the coeliac axis, SMA and/or common hepatic artery

- Lymphovascular invasion—present/not present. Perineural space or lymphovascular invasion is present in up to 50% of pancreaticobiliary carcinomas with spread to regional nodes at diagnosis. Involvement of large named vessels, e.g., SMV, portal vein, is a major determinant of postoperative survival.
- Regional lymph nodes:
  Peripancreatic, pancreaticoduodenal, pyloric, pericholedochal, SMV/SMA (right lateral wall) and proximal mesenteric. Also coeliac (for head of pancreas tumour) and tail of pancreas/splenic hilum/retroperitoneal nodes (for body/tail of pancreas tumours). A regional lymphadenectomy will usually include 12 or more lymph nodes.

pN0	No regional lymph node metastasis
pN1	Metastasis in 1–3 regional lymph node(s)
pN2	Metastasis in 4 or more regional lymph nodes

- Ampulla of Vater: pN1 = 1–2nodes, pN2 ≥ 3nodes
- Excision margins
  Proximal gastric and distal duodenal limits of tumour clearance (cm).
  Distal pancreatic surgical margin/common bile duct margin of tumour clearance (mm)—also comment on pancreatic intraepithelial neoplasia (PanIN).
  Peripancreatic edge tumour clearance (mm)—transection margin, superior mesenteric vein, superior mesenteric artery/uncinate, anterior capsule, posterior.
  For extrahepatic bile duct cancer—tumour clearance (mm) of the distal and proximal bile duct, hepatic and radial resection margins.
- Other pathology
  Duodenal adenoma (s), secondary pancreatitis, fat necrosis, calculi, ulcerative colitis, sclerosing cholangitis, choledochal cysts.

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