JAUNDICE

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The term jaundice, derived from the French (meaning yellow), refers to the yellowish-orange discoloration of skin, sclerae, and mucous membranes that results from excessive deposition of bilirubin in the tissues. The jaundiced patient has been documented in the literature from the time of the earliest medical records. Symptoms were first recorded on clay tablets from ancient Mesopotamia, dating back to the third millennium BC. However, doctors first described the clinical details of jaundice and recognized it as related to a pathologic condition of the liver in the Hippocratic Corpus.2,3

In what follows, we outline a problem-based approach to the jaundiced patient that involves assessing the incremental information provided by successive clinical and laboratory investigations, as well as the information obtained by means of modern imaging techniques. Current decision making in the approach to the jaundiced patient should include not only careful evaluation of anatomic issues but also close attention to patient morbidity and quality-of-life concerns, as well as a focus on a cost-effective diagnostic workup. For optimal treatment, an integrated approach that involves the surgeon, gastroenterologist, and radiologist is essential.

Terminology and Epidemiology

Jaundice represents an important clinical sign that can be related to many different disease processes. It develops when serum bilirubin levels rise above 2 mg/dL (34.2 mmol/L); however, the appearance of skin discoloration depends on multiple factors, including how long the episode lasts and whether it results from a predominantly direct (conjugated) or indirect (unconjugated) hyperbilirubinemia. Varying terminology is used to refer to the causes of jaundice, but for the purposes of this review, it is described as prehepatic, hepatic, or posthepatic.

Prehepatic jaundice is due to increased turnover of red blood cells and will present with an indirect hyperbilirubinemia. However, a detailed discussion of prehepatic jaundice is mostly outside the scope of this review [see Sidebar Indirect (Unconjugated) Bilirubin and Table 1]. Hepatic jaundice represents the majority (around 60%) of all cases of jaundice and may be due to direct or indirect hyperbilirubinemia. About half of these cases result from injury to hepatic cells, whereas the remaining half are due to biliary obstruction within the liver.5–7 The most common cause of hepatic jaundice is alcohol-induced liver disease, which is responsible for 10 to 17% of all cases of jaundice. Viral hepatitis is the second most common cause of hepatic jaundice [see Sidebar Hepatic Jaundice and Table 2].5,8

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**Approach to the Jaundiced Patient**

- **Patient has confirmed hepatic jaundice**
  - [See Sidebar Hepatic Jaundice.]

- **Patient has confirmed posthepatic jaundice**
  - Proceed according to clinical scenario present.

- **Patient has presumed posthepatic jaundice**
  - Obtain ultrasonogram to confirm posthepatic jaundice and identify level of biliary obstruction.
  - In some unusual clinical situations, ultrasonography may not detect the posthepatic cause of jaundice, and magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP), percutaneous transhepatic cholangiography (PTC), repeat ultrasonography, or endoscopic ultrasonography (EUS) may be necessary. If all these situations are ruled out, seek a hepatic cause and consider liver biopsy.

**Suspected cholangitis**

- Choledocholithiasis is the most likely diagnosis.
- Resuscitate, correct any coagulopathy, and give appropriate antibiotics.
- Perform ERCP for definitive diagnosis and treatment. If ERCP cannot be done, consider transhepatic drainage or surgery.

**Suspected choledocholithiasis**

- Perform preoperative MRCP or ERCP and laparoscopic cholecystectomy.
- Alternatively, perform laparoscopic cholecystectomy with intraoperative cholangiography.
Perform physical examination and obtain history. Confirm icterus by examining oral mucous membranes, palms, soles, and sclerae in natural light. Distinguish indirect (unconjugated) from direct (conjugated) hyperbilirubinemia: normal-colored urine and stools suggest indirect hyperbilirubinemia; dark urine, pale stools, and signs or symptoms of a cholestatic syndrome suggest direct hyperbilirubinemia. Measure total serum bilirubin and percentage of conjugated bilirubin.

Perform clinical assessment

Distinguish hepatic (“medical”) jaundice from posthepatic (“surgical”) jaundice. Acute hepatitis, alcohol abuse, and physical evidence of cirrhosis or portal hypertension suggest hepatic jaundice. Abdominal pain, rigors, itching, and a palpable liver >2 cm below costal margin suggest posthepatic jaundice.

Suspected lesion other than choledocholithiasis

The most common single cause is pancreatic cancer; many of the other possible causes also involve malignancy. Perform spiral computed tomography (CT) or magnetic resonance imaging with MRCP to diagnose lesion and assess resectability. Consider EUS with biopsy for distal-third obstruction. Perform Doppler ultrasonography to stage lesion further; CT angiography or magnetic resonance angiography may be considered if ultrasonogram is abnormal. Perform MRCP to assess intrahepatic biliary system in patients with middle-third or upper-third obstruction.

Upper-third obstruction

**Palliation:** bypass with left (segment III) hepaticojejunostomy

**Resection for cure:** resection of tumor, possibly with hepatectomy or segmentectomy, and reconstruction with hepaticojejunostomy or choangiojejunostomy

Middle-third obstruction

**Palliation:** bypass with hepaticojejunostomy

**Resection for cure:** resection of tumor and reconstruction with hepaticojejunostomy

Lower-third obstruction

**Palliation:** bypass with Roux-en-Y choledochojunostomy

**Resection for cure:** resection of tumor with pancreaticoduodenectomy or local ampullary excision

Patient presents with skin discoloration suggestive of jaundice

Patient has indirect hyperbilirubinemia

[See Sidebar: Indirect (Unconjugated) Bilirubin.]

Patient has direct hyperbilirubinemia

Distinguish hepatic (“medical”) jaundice from posthepatic (“surgical”) jaundice. Acute hepatitis, alcohol abuse, and physical evidence of cirrhosis or portal hypertension suggest hepatic jaundice. Abdominal pain, rigors, itching, and a palpable liver >2 cm below costal margin suggest posthepatic jaundice.

Patient has direct hyperbilirubinemia

Distinguish hepatic (“medical”) jaundice from posthepatic (“surgical”) jaundice. Acute hepatitis, alcohol abuse, and physical evidence of cirrhosis or portal hypertension suggest hepatic jaundice. Abdominal pain, rigors, itching, and a palpable liver >2 cm below costal margin suggest posthepatic jaundice.

Patient has indirect hyperbilirubinemia

[See Sidebar: Indirect (Unconjugated) Bilirubin.]

Patient has presumed hepatic jaundice

[See Sidebar: Hepatic Jaundice.]

Patient has confirmed hepatic jaundice

Proceed according to clinical scenario present.

Patient has confirmed posthepatic jaundice

Treat with ERCP or PTC and drainage. For advanced malignant disease, supportive care alone may be indicated.

Lesion appears unresectable, and surgical palliation is not indicated

Treat with ERCP or PTC and drainage. For advanced malignant disease, supportive care alone may be indicated.

Lesion appears resectable, or surgical palliation is indicated

Treat with surgical bypass or resection as appropriate for level of obstruction. Perform laparoscopy to confirm resectability before laparotomy.

Upper-third obstruction

**Palliation:** bypass with left (segment III) hepaticojejunostomy

**Resection for cure:** resection of tumor, possibly with hepatectomy or segmentectomy, and reconstruction with hepaticojejunostomy or choangiojejunostomy

Middle-third obstruction

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**Resection for cure:** resection of tumor and reconstruction with hepaticojejunostomy

Lower-third obstruction

**Palliation:** bypass with Roux-en-Y choledochojunostomy

**Resection for cure:** resection of tumor with pancreaticoduodenectomy or local ampullary excision

Scientific American Surgery
Hepatic Jaundice

Hepatic jaundice may be either acute or chronic and may be caused by a variety of conditions [see Table 2].

Acute hepatic jaundice may arise de novo or in the setting of ongoing liver disease. Although specific therapies exist for certain clinical problems (e.g., acetylcysteine for acetaminophen ingestion and penicillin plus sildinib for *Amanita phalloides* poisoning), treatment in most cases remains supportive. Patients in whom encephalopathy develops within 2 to 8 weeks of the onset of jaundice are usually classified as having fulminant hepatic failure. Evidence of encephalopathy, renal failure, or a severe coagulopathy is predictive of poor outcome in this setting.13 The most common causes of fulminant hepatic failure are viral hepatitis and drug toxicity. The mortality from fulminant hepatic failure remains high even though liver transplantation has favorably affected the prognosis.136

In cases of chronic hepatic jaundice, the patient may have chronic hepatitis or cholestasis, with or without cirrhosis. Causes include viral infection, drug-induced chronic hepatitis, autoimmune liver disease, genetic disorders (e.g., Wilson disease and α1-antitrypsin deficiency), chronic cholestatic disorders, alcoholic liver disease, and steatohepatitis.137 Treatment, once again, is usually supportive depending on the clinical presentation; whether more specific therapy is needed and what form it takes depend on the cause of the liver disease. Although physiologic tests have been developed to quantify hepatic reserve, for many years, the most widely used and best validated prognostic index was the Child-Pugh classification (see below), which correlates with individual survival and has been shown to predict operative risk.13 However, the Model for End-Stage Liver Disease (MELD) score is now used to prioritize the allocation of organs for liver transplantation by the United Network for Organ Sharing (UNOS). This score is based on the serum bilirubin and creatinine concentrations, the international normalized ratio (INR), and the presence of hepatocellular carcinoma; it does not make use of some of the more subjective components of the Child-Pugh score (e.g., ascites and encephalopathy). The MELD score ranges from 6 to 40, with higher scores corresponding to more advanced liver disease. The score is primarily used to allocate liver transplants; however, it has also been shown to have prognostic value in other clinical settings, for example, predicting mortality in patients with acute alcoholic hepatitis, fulminant hepatic failure, or cirrhosis.138 Liver transplantation is the treatment of choice in most cases of end-stage liver disease.

**Child-Pugh Classification Numerical Score**

<table>
<thead>
<tr>
<th>Variable</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy</td>
<td>Nil (0)</td>
<td>Slight to moderate (1, 2)</td>
<td>Moderate to severe (3–5)</td>
</tr>
<tr>
<td>Ascites</td>
<td>Nil</td>
<td>Slight</td>
<td>Moderate to severe</td>
</tr>
<tr>
<td>Bilirubin, mg/dL (mmol/L)</td>
<td>&lt; 2 (&lt; 34)</td>
<td>2–3 (34–51)</td>
<td>&gt; 3 (&gt; 51)</td>
</tr>
<tr>
<td>Albumin, g/dL (g/L)</td>
<td>&gt; 3.5 (&gt; 35)</td>
<td>2.8–3.5 (28–35)</td>
<td>&lt; 2.8 (&lt; 28)</td>
</tr>
<tr>
<td>Prothrombin index</td>
<td>&gt; 70%</td>
<td>40–70%</td>
<td>&lt; 40%</td>
</tr>
</tbody>
</table>

Modified Child-Pugh risk grade (depending on total score): 5 or 6 points, grade A; 7 to 9 points, grade B; 10 to 15 points, grade C.

*Système International d’Unités, or SI units.

Posthepatic jaundice makes up about 35% of jaundice cases, with the most frequent causes being obstruction due to malignancy of the extrahepatic biliary tree and choleodocholithiasis [see Table 3]. Malignancies account for the greatest individual fraction (20 to 35%) of all jaundice cases, with pancreatic cancer being the most common.9–11 Choleodocholithiasis is the most common cause of benign biliary obstruction and the underlying cause of symptoms in 13 to 16% of patients presenting with jaundice.5,9,12

Although we have attempted to simplify much of the terminology related to the jaundiced patient here, the term *cholestatic* is important to understand in the context of this review. It refers to decreased delivery of bilirubin into the intestine (and subsequent accumulation in the hepatocytes and in the blood), irrespective of the underlying cause (i.e., hepatic or posthepatic). When it is mild, it may not be associated with clinical jaundice. However, as it worsens, the chronic lack of bile delivery to the intestine results in a “cholestatic” syndrome with signs and symptoms related to conjugated hyperbilirubinemia and chronic malabsorption of fat-soluble vitamins (i.e., vitamins A, D, E, and K).

Finally, sepsis and bacterial infection are responsible for up to 20% of the cases of jaundice by a variety of mechanisms that may result in a combination of hemolysis, hepatic injury, and cholestasis.13

**Clinical Evaluation and Investigative Studies**

**HISTORY AND PHYSICAL EXAMINATION**

When a patient presents with a skin discoloration suggestive of jaundice, the first step is to confirm that icterus is indeed present. To this end, the mucous membranes of the mouth, the palms of the hands, the soles of the feet, and the sclera should be examined in natural light. Because such areas are protected from the sun, photodegradation of bile is minimized; thus, the yellowish discoloration of the elastic tissues may be more easily detected. Occasionally, deposition of a yellowish pigment on skin can mimic jaundice but may, in fact, be related to the consumption of large quantities of

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**Table 2 Causes of Hepatic Jaundice**

<table>
<thead>
<tr>
<th>Hepatitis</th>
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</thead>
<tbody>
<tr>
<td>Viral</td>
</tr>
<tr>
<td>Autoimmune</td>
</tr>
<tr>
<td>Alcoholic</td>
</tr>
<tr>
<td>Drugs and hormones</td>
</tr>
<tr>
<td>Liver infiltration and storage disorders</td>
</tr>
<tr>
<td>Systemic infections</td>
</tr>
<tr>
<td>Total parenteral nutrition</td>
</tr>
<tr>
<td>Postoperative intrahepatic cholestasis</td>
</tr>
<tr>
<td>Cholestasis of pregnancy</td>
</tr>
<tr>
<td>Benign recurrent intrahepatic cholestasis</td>
</tr>
<tr>
<td>Infantile cholestatic syndromes</td>
</tr>
<tr>
<td>Inherited metabolic defects</td>
</tr>
<tr>
<td>Gilbert syndrome</td>
</tr>
<tr>
<td>Crigler-Najjar syndrome types I and II</td>
</tr>
<tr>
<td>No identifiable cause (idiopathic hepatic jaundice)</td>
</tr>
</tbody>
</table>

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**Table 3 Causes of Hepatic Jaundice**

<table>
<thead>
<tr>
<th>Causes of Hepatic Jaundice</th>
<th>137</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral hepatitis</td>
<td></td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td></td>
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<tr>
<td>Alcoholic hepatitis</td>
<td></td>
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<tr>
<td>Drugs and hormones</td>
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<tr>
<td>Liver infiltration and storage disorders</td>
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<td>No identifiable cause (idiopathic hepatic jaundice)</td>
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</tr>
</tbody>
</table>
food containing orange pigments, such as lycopene or carotene, or drugs such as rifampin or quinacrine. In these cases, the skin is usually the only site of coloration, and careful inspection of the sclerae and mucous membranes generally reveals no icteric pigmentation.

Any cause of organic liver injury can result in jaundice; therefore, a careful history of drug and alcohol use should always be assessed. Questions about drug use should include all prescribed medications, over-the-counter drugs, supplements, and illicit drug use as these can be directly hepatotoxic. Intravenous (IV) drug use is also an associated risk factor for viral hepatitis due to hematogenous spread via toxic. Intravenous (IV) drug use is also an associated risk factor for viral hepatitis due to hematogenous spread via

**Table 3 Causes of Posthepatic Jaundice**

<table>
<thead>
<tr>
<th>Upper third obstruction</th>
<th>Polycystic liver disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caroli disease</td>
<td>Hepatocellular carcinoma</td>
</tr>
<tr>
<td>Oriental cholangiopapillitis</td>
<td>Hepatic arterial thrombosis (e.g., after liver transplantation or chemotherapy)</td>
</tr>
<tr>
<td>Hemobilia (e.g., after biliary manipulation)</td>
<td>Iatrogenic bile duct injury (e.g., after laparoscopic cholecystectomy)</td>
</tr>
<tr>
<td>Cholangiocarcinoma (Klatskin tumor)</td>
<td>Sclerosing cholangitis</td>
</tr>
<tr>
<td>Papillomas of the bile duct</td>
<td>Benign idiopathic bile duct stricture</td>
</tr>
<tr>
<td>Middle third obstruction</td>
<td>Cholangiocarcinoma</td>
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<tr>
<td>Cholangiocarcinoma</td>
<td>Sclerosing cholangitis</td>
</tr>
<tr>
<td>Papillomas of the bile duct</td>
<td>Gallbladder cancer</td>
</tr>
<tr>
<td>Choledochal cyst</td>
<td>Choleodochal cyst</td>
</tr>
<tr>
<td>Intrabiliary parasites</td>
<td>Mirizzi syndrome</td>
</tr>
<tr>
<td>Extrinsic nodal compression (e.g., from breast cancer or lymphoma)</td>
<td>Iatrogenic bile duct injury (e.g., after open cholecystectomy)</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>Benign idiopathic bile duct stricture</td>
</tr>
<tr>
<td>Lower third obstruction</td>
<td>Cholangiocarcinoma</td>
</tr>
<tr>
<td>Cholangiocarcinoma</td>
<td>Sclerosing cholangitis</td>
</tr>
<tr>
<td>Papillomas of the bile duct</td>
<td>Gallbladder cancer</td>
</tr>
<tr>
<td>Pancreatic tumors</td>
<td>Ampullary tumors</td>
</tr>
<tr>
<td>Chronic pancreatitis</td>
<td>Sphincter of Oddi dysfunction</td>
</tr>
<tr>
<td>Papillary stenosis</td>
<td>Duodenal diverticula</td>
</tr>
<tr>
<td>Penetrating duodenal ulcer</td>
<td>Retroduodenal adenopathy (e.g., lymphoma, carcinoma)</td>
</tr>
</tbody>
</table>

Cirrhosis can present with signs such as spider nevi, palmar erythema, gynecomastia, caput medusa, and ascites. Asterixis, a flapping tremor of the hands with the wrist extended, also suggests the presence of hepatic encephalopathy. Dupuytren contractures, parotid gland enlargement, and testicular atrophy have been associated with alcoholic cirrhosis in particular. Lymph node enlargement, including the Virchow node (left supravacular node) and Sister Mary Joseph nodule (palpable node bulging into the umbilicus), may be suggestive of metastatic abdominal malignancy. Kayser-Fleischer rings on a slit-lamp examination will suggest Wilson disease, although most physical examination findings will not be as suggestive of specific causes.

**Direct versus Indirect Hyperbilirubinemia**

The history and physical examination can also help determine direct versus indirect hyperbilirubinemia in a patient with jaundice. If the patient has normal-colored urine and stools, indirect bilirubin [see Sidebar Indirect (Unconjugated) Bilirubin] will be predominant [see Table 1]. If the patient has dark urine, pale stools, or any other signs or symptoms of a cholestatic syndrome (pruritus, bruising, steatorrhea, night blindness, osteomalacia, and neuromuscular weakness), the serum bilirubin fractionation usually indicates that direct bilirubin is predominant.

Therefore, with a thorough history and physical examination, it is often possible to distinguish between direct and indirect hyperbilirubinemia on clinical grounds alone. Direct hyperbilirubinemia is the type most relevant to the surgeon and therefore is the focus of the remainder of this review.

**Hepatic versus Posthepatic Jaundice**

Once the presence of direct hyperbilirubinemia is confirmed, the next step is to determine whether the jaundice is hepatic or posthepatic. A number of authors have studied the reliability of clinical assessment for making this determination. The sensitivities of the history, physical examination, and blood tests alone range from 70 to 95%, whereas the specificities are approximately 75%. The overall accuracy of clinical assessment of hepatic and posthepatic causes of jaundice ranges from 87 to 97%. Clinically, hepatic jaundice is most often signaled by acute hepatitis, a history of alcohol abuse, or physical findings reflecting cirrhosis or portal hypertension [see Table 2]. Posthepatic jaundice is most often signaled by abdominal pain, rigors, itching, or a palpable liver more than 2 cm below the costal margin.

By using discriminant analysis in a pediatric patient population, two investigators were able to isolate three biochemical tests that differentiated between biliary atresia and intrahepatic cholestasis with an accuracy of 95%: total serum bilirubin concentration, alkaline phosphatase (ALP) level, and γ-glutamyltransferase (GGT) level. In a separate study, a multivariate analysis model demonstrated that patients with posthepatic jaundice were younger, had a longer history of jaundice, were more likely to present with fever, and had greater elevations of serum protein concentrations and shorter coagulation times than patients with hepatic jaundice.
model, however, despite its 96% sensitivity (greater than that of any single radiologic diagnostic modality), could not accurately predict the level of a biliary obstruction. Other investigators have reported similar findings, and most agree that strategies that omit ultrasonography are clearly inferior. In summary, a clinical approach supported by simple biochemical evaluation displays good predictive ability to distinguish hepatic from posthepatic jaundice; however, a clinical approach alone does not accurately identify the level of biliary obstruction in a patient with posthepatic jaundice.

**LABORATORY TESTS**

As part of the initial patient evaluation, basic laboratory tests should also be drawn to confirm hyperbilirubinemia and assess liver function. Important liver function tests that can aid in the diagnosis include bilirubin with fractionation, aminotransferases, ALP, albumin, and prothrombin time. Bilirubin fractionation will confirm the clinical findings suggesting either a direct or an indirect hyperbilirubinemia, and it has been suggested that total bilirubin levels may be useful in diagnosing malignant versus benign causes of posthepatic jaundice. Possibly due to the slower onset of obstruction, higher bilirubin levels may be found in malignant obstruction. One study found that in the presence of a biliary obstruction, extremely elevated bilirubin levels (> 5.8 mg/dL or 100 mmol/L) are suggestive of a malignant process and the sensitivity and specificity for malignancy increase as bilirubin levels continue to rise. However, this is just one clue in helping to determine the diagnosis.

Following confirmation of hyperbilirubinemia, the first distinction should be made between patients with isolated bilirubin elevations versus those with abnormal values in other liver tests. Jaundice in the presence of normal liver function tests suggests that the cause is not due to hepatic injury or biliary disease and therefore carries a limited diagnosis. Possible causes include inherited disorders such as Dubin-Johnson and Rotor syndromes in the case of direct hyperbilirubinemia or Gilbert and Crigler-Najjar syndromes in the case of indirect hyperbilirubinemia. In addition, hemolytic disorders may result in hyperbilirubinemia without a change in liver enzymes.

In the presence of elevated liver function tests, the next step should be to determine the pattern of elevation. Using liver enzyme values, such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and ALP, can help distinguish hepatic from posthepatic causes. Often both aminotransferases and ALP may be elevated, but the magnitude of elevation will be useful in determining the etiology. Predominantly elevated ALP suggests cholestasis and therefore most likely a posthepatic cause. In this case, the next steps should include imaging to verify posthepatic jaundice and to determine the level of obstruction.

ALP is present in many tissues, particularly the liver and bones. Therefore, an elevation of ALP can be due to a number of causes; however, alongside a rise in GGT, it strongly suggests that the elevation is due to ALP release from liver cells. When hepatic jaundice is suspected, further laboratory tests are indicated to determine the cause of hepatic injury. These subsequent tests should include a toxicology screen with acetaminophen level, viral serologies, and autoimmune markers. To screen for viral hepatitis, anti-hepatitis A IgM, hepatitis B surface antigen and core antibody, and hepatitis C RNA should be tested. An anti-hepatitis C antibody test may also be used, but it often takes weeks for levels of antibody to become detectable; therefore, the test is less reliable in an acute process. Identification of autoimmune hepatitis requires antinuclear antibodies or other specific immunoglobulin markers. In specific circumstances, one may wish to check for hepatitis D and E antibodies, cytomegalovirus, Epstein-Barr virus, or ceruloplasmin levels if Wilson disease is suspected.

An increased prothrombin time, as measured by the international normalized ratio (INR), may be present in patients presenting with jaundice. The increased INR may result from hepatocellular injury and impairment of synthetic function or secondary to vitamin K deficiency. As a result of bile duct obstruction, fat-soluble vitamins, including vitamin K, may undergo decreased intestinal absorption, leading to defects in the extrinsic clotting cascade and increased INR. Therefore, patients with jaundice and increased INR should be administered vitamin K to help distinguish between vitamin K deficiencies resulting from obstructive jaundice and hepatocellular disease.

**IMAGING**

Imaging techniques are most useful in cases involving posthepatic causes of jaundice. Once a thorough history has been obtained and bedside and laboratory assessments have been completed, the next step is imaging, the goals of which in a case of posthepatic jaundice are (1) to confirm the presence of an extrahepatic obstruction (i.e., to verify that the jaundice is indeed posthepatic rather than hepatic), (2) to determine the level of the obstruction, (3) to identify the specific cause of the obstruction, and (4) to provide complementary information relating to the underlying diagnosis (e.g., staging information in cases of malignancy). The following approach is an efficacious, cost-effective, and safe way of obtaining such information in a patient with presumed posthepatic jaundice.

Ultrasonography should be the first imaging technique undertaken in any patient presenting with jaundice. It is the least invasive and lowest cost option available while providing a large amount of information to guide the subsequent workup. The presence of dilatation of the extrahepatic biliary system confirms that a posthepatic cause is responsible for the jaundice. Ultrasonography detects ductal dilatation with an accuracy of 95% (sensitivity of 55 to 95% and specificity of 71 to 96%), although the results are, to some extent, operator dependent.

If ultrasonography does not reveal bile duct dilatation, it is unlikely that an obstructing lesion is present, and the findings may point to a specific hepatic cause of jaundice (e.g., cirrhosis or infiltration of the liver by tumor). However, there are a few specific instances in which ultrasonography may fail to detect a posthepatic cause of jaundice. For instance, very early in the course of an obstructive process, not enough time may have elapsed for biliary dilatation to
occur. In this setting, a hepatoiminodiacetic acid (HIDA) scan has often helped identify bile duct blockage. The yield from this test is highest when the serum bilirubin level is lower than 5.85 mg/dL (100 mmol/L). Occasionally, the intrahepatic biliary tree is unable to dilate; possible causes of this include extensive hepatic fibrosis, cirrhosis, sclerosing cholangitis, and liver transplantation. If one of these diagnoses is suspected, then endoscopic retrograde cholangiopancreatography (ERCP), magnetic resonance cholangiopancreatography (MRCP), or percutaneous transhepatic cholangiography (PTC) will eventually be required to confirm the diagnosis of biliary obstruction. Occasionally, the biliary tree dilatation may be intermittent; possible causes of this condition include choledocholithiasis and some biliary tumors. In a patient with gallstones, transient liver test abnormalities by themselves may suggest an intermediate to high likelihood of common bile duct (CBD) stones even if there is no biliary ductal dilatation. If one of these diagnoses is suspected, ultrasonography may be repeated after a short period of observation (when clinically applicable); biliary ductal dilatation then generally becomes apparent. False negative results may also arise due to a failure to visualize the biliary tree accurately, most often due to bowel gas. In the unique instance of jaundice when the ALP and GGT are both elevated, indicating a cholestatic pattern consistent with posthepatic jaundice, but no dilatation can be identified, an antimitochondrial antibody (AMA) test should be performed. A positive AMA test in this setting is 95% sensitive and 98% specific for primary biliary cirrhosis. If all of these clinical situations have been ruled out, a hepatic cause for the jaundice should be sought (see Table 2) and a liver biopsy considered. Some centers prefer computed tomography (CT) to ultrasonography as the initial imaging modality, but we, like a number of other authors, find ultrasonography to be the most expedient, least invasive, and most economical imaging method for differentiating between hepatic and posthepatic causes of jaundice, as well as for evaluating the level of obstruction. However, CT may be considered as the initial imaging technique if there is a strong suspicion of a malignant biliary obstruction as it has the ability to give detailed anatomic information that is vital for the accurate diagnosis and staging of a perianpillary malignancy. Traditional imaging techniques, such as oral or IV cholangiography, have a negligible role to play in this setting because of their very poor accuracy and safety, especially in jaundiced patients.

MRCP (see Figure 1) and endoscopic ultrasonography (EUS) are more commonly being used to visualize the biliary and pancreatic ductal systems in various populations of patients with obstructive jaundice. Compared with direct cholangiography, both are excellent at diagnosing biliary obstruction and establishing its location and nature. MRCP exhibits more modest detection rates when diagnosing small CBD stones. Cytology specimens are readily obtained via fine-needle aspiration (FNA) during EUS. To investigate malignant biliary disease, EUS is useful for perianpillary pathologic conditions, whereas contrast-enhanced CT and MRI with MRCP are useful for both perianpillary and more proximal diseases of the biliary tree.

**Figure 1** Magnetic retrograde cholangiopancreatogram of a dilated extrahepatic biliary tree in a jaundiced patient found to have a distal cholangiocarcinoma.

Given the many imaging modalities available today, the use of direct cholangiography as a diagnostic tool, with either ERCP or PTC, is becoming less common. Unlike other imaging modalities, direct cholangiography poses significant risks to the patient: there is a 4 to 7% incidence of pancreatitis or cholangitis after ERCP, and there is a 4% incidence of bile leakage, cholangitis, or bleeding after PTC. Intraoperative cholangiography at the time of cholecystectomy is commonly used in some centers. This technique allows for intraoperative assessment of the biliary anatomy and allows for the detection of CBD stones, which can then be dealt with immediately via choledoscopy or laparoscopic or open CBD explorations or postoperatively via ERCP. There are also several risks that are particular to the manipulation of an obstructed biliary system (see below). For these reasons, the role of ERCP and PTC is increasingly a therapeutic one; therefore, it is important to gather as much clinical information as possible on the likely cause of the jaundice before performing either investigation.

**Workup and Management of Posthepatic Jaundice**

Once ultrasonography has confirmed that extrahepatic ductal obstruction is present, there are three possible clinical scenarios: acute suppurative cholangitis, suspected choledocholithiasis without cholangitis, or a suspected lesion other than choledocholithiasis, most commonly malignant obstruction. The direction of the subsequent workup depends on which of the three appears most likely.

**Suspected Cholangitis**

If a jaundiced patient presents with jaundice, fever, and right upper quadrant pain (Charcot triad), acute suppurative cholangitis is most likely present. The most common...
etiology is choledocholithiasis, with cholangitis rarely observed with malignant obstruction in a noninstrumented (ERCP or PTC) biliary tree. After appropriate resuscitation, correction of any coagulopathy that may be present, and administration of antibiotics, ERCP is indicated for diagnosis and treatment.\(^59\) If ERCP is unavailable or is not feasible (e.g., because of previous Roux-en-Y reconstruction), transhepatic drainage or operative CBD exploration and drainage may be necessary. It is important to emphasize here that the mainstay of treatment of severe cholangitis is not just the administration of appropriate antibiotics but also the establishment of adequate biliary drainage. The presence of stones with cholangitis has been identified as an important risk factor for the development of more serious, possibly life-threatening disease; therefore, emergency drainage alongside antibiotics is indicated in these patients.\(^57\)

**Suspected Choledocholithiasis without Cholangitis**

Choledocholithiasis should be strongly suspected if the jaundice is episodic or painful or if ultrasonography has demonstrated the presence of gallstones or bile duct stones. In contrast, malignant obstructions more often present without pain in patients with a slower onset of symptoms and higher bilirubin levels.\(^52\) Following the initial ultrasonography, the American Society of Gastrointestinal Endoscopy (ASGE) suggests that follow-up procedures be based on the likelihood of stones in the CBD.\(^58\) Patients with suspected choledocholithiasis should be referred for laparoscopic cholecystectomy with preoperative ERCP, intraoperative cholangiography, or intraoperative ultrasonography.\(^59\) When there is a strong indication of choledocholithiasis, the next steps must include confirmation and clearance of potential CBD stones. For this purpose, ERCP has a high diagnostic yield\(^56,60\); it allows confirmation of the diagnosis preoperatively (thus obviating intraoperative surprises) and is capable of clearing the CBD of stones in 95% of cases. Decision analyses appear to confirm the utility of this strategy when laparoscopic CBD exploration is not an option.\(^61-64\)

When feasible, however, some surgeons favor a fully laparoscopic approach in which choledocholithiasis is detected in the operating room by means of intraoperative cholangiography\(^65,66\) or ultrasonography,\(^67-69\) and laparoscopic CBD exploration for biliary clearance is performed when choledocholithiasis is confirmed. Given that both the ERCP approach and the fully laparoscopic approach have advantages and limitations, the optimal approach in a particular setting should be dictated by local expertise. In cases where the diagnosis of choledocholithiasis is not definitive, MRCP is the most appropriate next step as this strategy limits the periprocedural risks associated with ERCP. EUS is also an option to diagnose choledocholithiasis; however, MRCP is still preferred as it is less invasive and has an equivalent success rate in identifying choledocholithiasis.\(^58,70,71\)

**Suspected Lesion Other Than Choledocholithiasis**

If gallstones are not identified, the clinical presentation is less acute (e.g., progressive abdominal or back pain), or if there are associated constitutional symptoms (e.g., weight loss, fatigue, and long-standing anorexia), the presence of a lesion other than choledocholithiasis should be suspected. Possible causes of posthepatic obstruction (other than choledocholithiasis) may be classified into three categories depending on the location of the obstructing lesion (as suggested by the pattern of gallbladder and biliary tree dilatation on the ultrasonogram): the upper third of the biliary tree, the middle third, or the lower (distal) third \([\text{see Table 3}]\). Consequently, the next step in the workup of the patient is typically contrast-enhanced cross-sectional imaging (CT or MRI/MRCP).

**Malignant Disease as the Cause of Posthepatic Jaundice: Diagnosis and Assessment of Resectability**

Assessment of the resectability of a malignant periampullary tumor hinges on whether the visceral vasculature (superior mesenteric vein, portal vein, superior mesenteric artery, hepatic artery) is free of tumor encasement and on whether there is an absence of distant disease spread. Unfortunately, at the time of diagnosis, the majority of lesions will be clearly unresectable.

For determining resectability and staging lesions before operation, we rely mainly on contrast-enhanced pancreas protocol CT \([\text{see Figure 2}]\). The advent and widespread availability of multidetector CT have made this modality the dominant first-line imaging method in cases of suspected periamplullary masses and is considered to be superior for the diagnosis and staging of lesions such as pancreatic cancer.\(^46,72,73\) For optimal evaluation of the pancreas, a fine-cut triple-phase (arterial phase, late arterial phase, and portal venous phase) scan should be obtained. Oral administration of water allows better
evaluation of the duodenum and the ampulla.\textsuperscript{74,75} CT has been shown to be extremely accurate in differentiating benign from malignant biliary obstruction,\textsuperscript{76} exhibits a high negative predictive value, and has a false positive rate of less than 10%; its sensitivity is optimal for pancreatic lesions larger than 1 cm in diameter. Ascites, liver metastases, lymph nodes larger than 2 cm in diameter, and invasion into adjacent organs are all signs of advanced disease.\textsuperscript{77} On the basis of these criteria, contrast-enhanced pancreas protocol CT can predict whether a lesion will be resectable with an accuracy approaching 90%, which is superior to either ultrasonography or MRI.\textsuperscript{78} However, 10% of tumors that appear to be resectable on CT are found to be unresectable at operation.\textsuperscript{79} Although CT is the method of choice for pancreatic cancer, for other malignant causes of biliary obstruction, it has proven less useful in determining resectability. In cases of cholangiocarcinoma, CT often fails to accurately identify the extent of tumor involvement along the bile duct, therefore making it unreliable for assessing the appropriate margins of resection.\textsuperscript{79} MRI-based staging, along with MRCP, can aid in these cases as it is more successful in detecting the proximal biliary spread of cholangiocarcinoma (see Figure 2).\textsuperscript{80-83}

EUS is a highly sensitive method of imaging the pancreas and the duodenum.\textsuperscript{77,80-85} In two large studies, it was found to be superior to CT and standard ultrasonography in staging periampullary cancers.\textsuperscript{80,85} Subsequent studies indicated that although EUS is superior to CT for detection and staging, it provides similar information regarding nodal status and overall assessment of resectability.\textsuperscript{74,88} From a cost-minimization point of view, the optimal strategy is to begin with a contrast-enhanced pancreas protocol CT and to follow up with EUS only in cases in which further information or a tissue diagnosis is required.\textsuperscript{89,90} EUS has been found useful for identifying small (< 2 cm) pancreatic tumors, which may be suspected in a patient who has an obstruction of the distal third of the bile duct and whose CT scan is normal.\textsuperscript{91}

In patients with a suspected periampullary tumor, direct FNA of the lesion at the time of EUS has become the gold standard method for obtaining a tissue diagnosis. In the case of potentially resectable lesions, however, this measure adds very little to the decision-making process. The limited data currently available suggest that assays of tumor markers in serum and pancreatic fluid are useful, particularly for cystic lesions of the pancreas.\textsuperscript{92}

At this point in the evaluation, patients can be referred for either cholangiography (ERCP or MRCP) to clarify a still unclear diagnosis or biliary decompression (see below). MRI of the pancreas with MRCP continues to improve rapidly. It is a noninvasive modality that evaluates the pancreas, vasculature, and periampullary ductal system in a single examination, with the additional benefit of avoiding ionizing radiation and iodinated contrast agents.\textsuperscript{83} MRCP remains the test of choice for evaluation of middle and upper third lesions in cases in which decompression is not required.

In the event that none of these modalities point to a diagnosis, the use of \textsuperscript{18F}-fluorodeoxyglucose positron emission tomography (FDG-PET) may be considered to help differentiate benign periampullary conditions from malignant ones.\textsuperscript{92,93} Besides facilitating diagnosis, FDG-PET provides information regarding occult metastases and can be useful in detecting recurrent disease.

When a biliary stricture is detected at cholangiography, brush cytology or biopsy is mandatory. Biliary cytology, however, has been disappointing, particularly at ERCP: diagnostic accuracy ranges from 40 to 85%,\textsuperscript{94,95} mostly because the negative predictive value is poor. Accuracy improves with multiple samplings and when a biliary rather than a pancreatic malignancy is detected. In addition, biopsy tends to be more accurate than brush cytology.\textsuperscript{96}

Nonoperative Management: Drainage and Cholangiography

In the majority of patients with malignant biliary obstruction, treatment is palliative rather than curative. At the time of diagnosis, fewer than 20% of patients with pancreatic cancer are eligible for resection.\textsuperscript{96-98} It is therefore especially important to recognize and minimize the iatrogenic risks related to the manipulation of an obstructed biliary system; this is why staging and cholangiography are currently being performed with EUS, CT, and MRCP.

Cholangiography and decompression of the obstructed biliary system: As a rule, we favor ERCP; although PTC may be preferable for obstructions near the hepatic duct bifurcation. In those that require decompression, ERCP is sufficient in 90 to 95% of patients.\textsuperscript{7} Whichever imaging modality is used, the following principles apply:

1. In the absence of preexisting or concomitant hepatocellular dysfunction, drainage of one half of the liver is generally sufficient for resolution of jaundice.\textsuperscript{98}
2. Because of its external diameter, a transhepatic drain, once inserted, does not necessarily permit equal drainage of all segments of the liver, particularly if there are a number of intrahepatic ductal stenoses. Accordingly, some patients with conditions such as sclerosing cholangitis or a growing tumor may experience persistent sepsis from an infected excluded liver segment even when the prosthesis is patent (see Figure 3). An excluded segment may even be responsible for severe, persistent pruritus.
3. Any attempt at opacifying an obstructed biliary tree introduces a significant risk of subsequent cholangitis, even when appropriate antibiotic prophylaxis is provided. Accordingly, when one elects to perform direct cholangiography, there should be a plan for biliary drainage at the time of ERCP or PTC.
4. Even though jaundice is believed to be associated with multiple adverse systemic effects (e.g., renal failure, sepsis, and impaired wound healing),\textsuperscript{99,100} routine preoperative drainage of an obstructed biliary system does not benefit patients who will soon undergo resection.\textsuperscript{101,102} A growing body of evidence suggests that in patients with either periampullary\textsuperscript{103,104} or hepatic\textsuperscript{105} malignancies, routine preoperative direct cholangiography with decompression is associated with a higher incidence of postoperative complications when tumor resection is ultimately carried out.
When direct cholangiography is performed, it should be thought of as more than just a diagnostic test: it is the ideal setting for cytology, biopsy, or even drainage of the obstructed bile duct via a sphincterotomy, a nasobiliary tube, or a catheter or stent. Accordingly, it is essential that the surgeon, the gastroenterologist, and the radiologist discuss the possible need for drainage well before it is required. Early, open communication among all members of the treating team is a hallmark of the modern management of biliary obstruction.

Palliation in patients with advanced malignant disease
When a patient has advanced malignant disease, drainage of the biliary system for palliation is not routinely indicated, because the risk of complications related to the procedure may outweigh the potential benefit. Indeed, the best treatment for a patient with asymptomatic obstructive jaundice and liver metastases may be supportive care alone.106 Biliary decompression is indicated if cholangitis or severe pruritus interferes with quality of life.

A stent placed with ERCP is considered to be the palliative modality of choice for advanced disease,25 although upper third lesions may be managed most easily through the initial placement of an internal or external catheter at the time of PTC. Metal expandable stents remain patent longer than large conventional plastic stents107,108 and are the standard of care.109,110 Whether plastic biliary stents should be replaced prophylactically or only after obstruction has occurred remains controversial; however, the results from a randomized controlled trial (RCT) favor the former approach.111 In another RCT, the use of prophylactic ciprofloxacin did not prolong stent patency but did reduce the incidence of cholangitis and improve quality-of-life scores.112

RCTs suggest that surgical biliary bypass should be reserved for patients who are expected to survive for 6 months or longer because bypass is associated with more prolonged palliation at the cost of greater initial morbidity.113 The role of prophylactic gastric drainage at the time of operative biliary drainage remains controversial,114,115 although two RCTs demonstrated a reduced incidence of subsequent clinical gastric outlet obstruction when this measure was employed. Jaundiced patients with unresectable lesions who also present with duodenal or jejunal obstruction may be candidates for duodenal stent placement. If patients are undergoing surgical palliation, then they should be referred for gastrojejunostomy at the time of biliary bypass surgery. There is evidence to suggest that when a pancreatic malignancy is present, intraoperative celiac ganglion injection should be performed for either prophylactic or therapeutic pain control.116,117

Operative Management at Specific Sites: Bypass and Resection
Surgical treatment of tumors causing biliary obstruction is determined primarily by the level of the biliary obstruction. Posthepatic obstructions are generally divided into thirds based on anatomic markers. The upper third consists of the right and left hepatic ducts down to the confluence with the cystic duct, the middle third consists of the CBD to the upper border of the duodenum, and the lower third consists of the remaining bile duct through the ampulla of Vater.118,119 Current evidence indicates that modern surgical approaches are resulting in lower postoperative morbidity and, possibly, improved 5-year survival.120 At one time, there was considerable enthusiasm for routine use of staging laparoscopy; at present, however, selective use is recommended.121 The high quality of current cross-sectional imaging modalities has obviated the need for staging laparoscopy in the vast majority of cases.
In what follows, only the general principles of resection or bypass at each level of obstruction are discussed; operative technical details are addressed elsewhere.

**Upper third obstruction**

**Palliation** Because the left hepatic duct has a long extrahepatic segment that makes it more accessible, the preferred bypass technique for an obstructing upper third lesion is a left (or segment 3) hepaticojejunostomy. This operation has superseded the Longmire procedure because it does not involve formal resection of liver parenchyma. Laparoscopic bypass techniques that make use of segment 3 have been developed, but their performance has yet to be formally assessed, and they cannot yet be incorporated into a management algorithm.122,123

**Resection for cure** The hilar plate is taken down to lengthen the hepatic duct segment available for subsequent anastomosis. Often a formal hepatectomy or segmentectomy is required to ensure an adequate proximal margin of resection. If the resection must be carried out proximal to the hepatic duct bifurcation, several cholangiojejunostomies will have to be done to anastomose individual hepatic biliary branches. Frozen-section examination of the proximal and distal resection margins is important because of the propensity of tumors such as cholangiocarcinoma to spread in a submucosal or perineural plane.

The results of aggressive hilar tumor resections that included as much liver tissue as was necessary to obtain a negative margin appear to justify this approach.124 In cases of left hepatic involvement, resection of the caudate lobe (segments 1 and 9) is indicated as well.125,126

**Middle third obstruction**

**Palliation** Surgical bypass of middle third lesions is technically simpler because a hepaticojejunostomy can often be performed distal to the hepatic duct bifurcation, which means that exposure of the hilar plate or the intrahepatic ducts is unnecessary.

**Resection for cure** Discrete tumors in this part of the bile duct, although uncommon, are usually quite amenable to resection along with the lymphatic chains in the porta hepatis. Resection of an early gallbladder cancer may, on occasion, necessitate the concomitant resection of segment 5, although the value of resecting this segment prophylactically has not been conclusively demonstrated.127 Sometimes jaundice from a suspected middle third lesion is, in fact, caused by a case of Mirizzi syndrome [see Figure 4]. In such cases, a gallstone is responsible for extrinsic obstruction of the CBD, either by causing inflammation of the gallbladder wall or via direct impingement. Proper treatment of this syndrome may involve hepticojejunostomy in addition to cholecystectomy if a cholecystocholedochal fistula is present.128

**Lower third obstruction**

**Palliation** The preferred bypass technique for lower third lesions is a Roux-en-Y choledocho- or hepaticojejunostomy. Cholecystojejunostomy carries a higher risk of complications and subsequent development of jaundice129; this remains true even when it is performed laparoscopically. Occasionally, it may be done as a temporizing measure before a more definitive procedure in the context of an upcoming transfer to a specialized center.

**Resection for cure** Occasionally, an impacted CBD stone at the duodenal ampulla mimics a tumor and is not clearly identified preoperatively. Because of the growing use of EUS and MRCP, such a situation is increasingly uncommon. Resection of a lower third lesion usually involves a pancreaticoduodenectomy, although transduodenal ampullary resection may be an acceptable alternative for a small adenoma of the ampulla; local duodenal resection without removal of the head of the pancreas has also been described.130 For optimal results, pancreaticoduodenectomy is best performed in specialized centers.131

Figure 4 Endoscopic retrograde cholangiopancreatography demonstrates extrinsic compression of the common hepatic duct by a stone in the Hartmann pouch. A biliary stent has been inserted for drainage.
Multimodality therapy with neoadjuvant or adjuvant chemotherapy with or without radiation has been shown to improve the prognosis after resection of a pancreatic adenocarcinoma, but this debate falls outside the scope of this discussion.

Postoperative Jaundice

A clinical scenario of particular pertinence to surgeons that we have not yet addressed is the development of jaundice in the postoperative setting.

Jaundice develops in approximately 1% of all surgical patients after operation. When jaundice occurs after a hepatobiliary procedure, it may be attributable to specific biliary causes, such as retained CBD stones, postoperative biliary leakage (through reabsorption of bile leaking into the peritoneum) [see Figure 5], injury to the CBD, and the subsequent development of biliary strictures. In most instances, however, the jaundice derives from a combination of disease processes, and only rarely is invasive testing or active treatment required.

A diagnostic approach similar to the one outlined earlier (see above) is applicable to postoperative jaundice. However, as the possible causes of postoperative jaundice vary depending on the time interval between the operation and the development of jaundice, the following diagnostic approach may also be useful:

- Jaundice may develop within 48 hours of the operation; this is most often the result of the breakdown of red blood cells, occurring in the context of multiple blood transfusions (particularly with stored blood), the resorption of a large hematoma, or a transfusion reaction. Hemolysis may also develop in a patient with a known underlying hemolytic anemia and may be precipitated by the administration of specific drugs (e.g., sulfa drugs in a patient who has glucose 6-phosphate dehydrogenase deficiency). Cardiopulmonary bypass or the insertion of a prosthetic valve may be associated with the development of early postoperative jaundice as well. Gilbert syndrome [see Sidebar Hepatic Jaundice] may first manifest itself early in the postoperative period. Occasionally, a mild conjugated hyperbilirubinemia may be related to Dubin-Johnson syndrome, which is an inherited disorder of bilirubin metabolism. This condition is usually self-limited and is characterized by the presence of a melaninlike pigment in the liver.

- Intraoperative hypotension or hypoxemia or the early development of heart failure can lead to conjugated hyperbilirubinemia within 5 to 10 days after operation. The hyperbilirubinemia may be associated with other end-organ damage (e.g., acute tubular necrosis). In fact, any impairment of renal function causes a decrease in bilirubin excretion and can be responsible for a mild hyperbilirubinemia.

- Jaundice may develop 7 to 10 days after operation in association with a medication-induced hepatitis attributable to an anesthetic agent. This syndrome has an estimated incidence of one in 10,000 after an initial exposure. More commonly, the jaundice is related to the administration of antibiotics or other medications used in the perioperative setting.

- After the first week, jaundice associated with intrahepatic cholestasis is often a manifestation of a septic response and usually presents in the setting of overt infection, particularly in patients with multiple organ dysfunction syndrome. Gram-negative sepsis from an intra-abdominal source is typical; if it persists, the outcome is likely to be poor. Jaundice may occur in as many as 30% of patients receiving total parenteral nutrition (TPN). It may be attributable to steatosis, particularly with formulas containing large amounts of carbohydrates. In addition, decreased export of bilirubin from the hepatocytes may lead to cholestasis, the severity of which appears to be related to the duration of TPN administration. Acute cholecystitis or even ductal obstruction may develop as a result of sludge in the gallbladder and the CBD. An elevated postoperative bilirubin level at any time may also result from unsuspected hepatic or posthepatic causes (e.g., occult cirrhosis, choledocholithiasis, or cholecystitis). A rare cause of postoperative jaundice is the development of thyrotoxicosis. Another entity to consider (as a diagnosis of exclusion) is so-called benign postoperative cholestasis, a primarily cholestatic, self-limited process with no clearly demonstrable cause that typically arises within 2 to 10 days after operation. Benign postoperative cholestasis may be attributable to a combination of mechanisms, including an increased pigment load, impaired liver function resulting from hypoxemia and hypotension, and decreased renal bilirubin excretion caused by varying degrees of tubular necrosis. The predominantly conjugated hyperbilirubinemia may reach 40 mg/dL and remain elevated for as long as 3 weeks.

- In the late postoperative period, the development of non-A, non-B, non-C viral hepatitis after transfusion of blood products will usually occur within 5 to 12 weeks of operation.
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