

# The Hospitalized Patient with Abnormal Liver Function Tests

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## KEYWORDS

- Hospitalized • Evaluation • Liver function tests • LFTs
- Operation risk calculation

An inpatient consultation often asks a specific question such as “What is the operative risk in this patient?” Or, on occasion, the inpatient consultation may be a more general request such as “Patient known to you, please evaluate.”

The most useful impression on the consultation form regarding abnormal LFTs in a hospitalized patient should comment on the following: (1) *chronicity*: for example, acute decompensation of chronically abnormal liver function tests (LFTs); (2) *etiology* of the patient’s liver disease: acute ischemic hepatopathy superimposed on chronic nonalcoholic steatohepatitis; (3) *severity* of the process: cirrhosis: Child’s C; Model for End-Stage Liver Disease (MELD) score 22; 80% operative risk in abdominal surgery of mortality; and (4) *complications*: + ascites, + encephalopathy, + esophageal varices, needs screening for hepatocellular carcinoma.

## OVERVIEW OF PROCESS

The evaluation of abnormal LFTs in a hospitalized patient tends to assume more urgency than that in the outpatient setting. The preliminary step is a determination as to whether the abnormal LFTs are associated with the initial reason for the patient’s hospitalization, are secondary to a chronic underlying liver disease preceding the admission, or developed in hospital. A careful history, either directly from the patient or family members, a review of outpatient records, and/or phone calls to the patient’s physician may be critical in providing the necessary information.

Evaluation of the underlying etiology of the liver disease is the second step. If the abnormal LFTs in question is an isolated aminotransferase elevation, then confirmation of the source of the serum enzyme, whether of hepatic origin or elsewhere, is important.

The third step is to determine the acuteness or severity of the dysfunction. The methods for calculating the severity depend on whether the inpatient admission is associated with de novo acute liver failure (ALF) or acute decompensation of *chronic* liver

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disease. If acute, then the King's College Criteria for Liver Transplantation or the MELD score may be most appropriate. Conversely, in the case of a chronic presentation of underlying liver disease, the procedure should be assessing the stage (severity) of fibrosis. If stage 4 fibrosis (cirrhosis) is present, then a MELD score (Fig. 1) is calculated to determine whether the patient needs liver transplant evaluation during this admission.

The final and fourth step is to look for any associated complications resulting from the presence of either the acute or chronic liver disease.

## STEP 1: HISTORY AND PHYSICAL EXAMINATION

### *History*

A meticulous medical history focused on the liver can provide important clues regarding abnormal LFTs in the hospitalized patient. Of utmost importance, yet frequently overlooked, is the determination as to whether the patient had pre-existing abnormal LFTs before the recent illness and hospitalization. In particular, it must be determined whether the liver disease has occurred suddenly, developed gradually, or simply has not been apparent until the hospitalization.

Clues that can be helpful for suggesting specific causes include the presence of right upper quadrant pain, fever, and nausea  $\pm$  vomiting, all of which are suggestive of possible biliary tract disease. A history of intravenous drug use and recent foreign travel, associated with a viral prodrome, would raise the likelihood of an acute viral hepatitis. A history of previous liver disease or surgeries involving the liver can also offer important information. Careful questioning about consumption of alcohol, frequency, and amount from both the patient as well as the family can also be helpful. However, by far, the most important comment of the history is accurate information on medication use (whether prescription, illicit, or herbal) and the time course in relation to the hepatic dysfunction.

Calculation of the model for end-stage liver disease (MELD) score

<b>MELD Score =</b>	0.957 x Loge(creatinine mg/dL)
	+ 0.378 x Loge(bilirubin mg/dL)
	+ 1.120 x Loge(INR)
	+ 0.643*

INR, international normalized ratio

The maximum serum creatinine level in the MELD score equation is 4.0 mg/dL

Multiply by 10 and round to the nearest whole number

Laboratory values less than 1.0 are set to 1.0 for the purposes of the MELD score calculation.

**Fig. 1.** Calculation of the model for end-stage liver disease (MELD) score. The maximum serum creatinine level in the MELD score equation is 4.0 mg/dL. Multiply by 10 and round to the nearest whole number. Laboratory values less than 1.0 are set to 1.0 for the purposes of the MELD score calculation. INR, International normalized ratio.

## **Physical Examination**

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Often forgotten in this age of high technology is that a thorough physical examination can often shed light on the cause, severity, and, occasionally, presence of 1 or more complications of liver disease. It has been said that “One good feel of the liver is worth any 2 LFTs” (F.M. Hanger Jr., 1971). Above all, it should be noted whether the liver is large or small, soft/hard, or nodular and whether tenderness is present over the liver itself or in the region of the gallbladder. A tender liver would suggest acute enlargement secondary to congestion, hepatitis, or cholangitis.

In particular, signs of right-sided heart failure including jugular venous distention, an enlarged tender liver, tricuspid regurgitation murmur, clubbing, an increased pulmonary heart sound, or fixed splitting of the second heart sound (suggestive of pulmonary hypertension), could suggest either acute or chronic hepatic congestion and/or the presence of the hepatopulmonary syndrome. The presence or absence of abdominal scars, palpable abdominal masses, or lymphadenopathy can also be helpful.

Characteristic changes should be sought on physical examination for chronicity of the liver disease, such as jaundice, scleral icterus, muscle wasting, spider angiomas, palmar erythema, splenomegaly, prominent abdominal pains, ascites, pedal edema, and a hepatic encephalopathy (asterixis). Additional findings include gynecomastia, fetor hepaticus, xanthelasmas, Dupuytren’s contractures, and caput medusa.

## **STEP 2: LABORATORY EVALUATION FOR ETIOLOGY**

### **Blood Panels**

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#### **Liver function tests**

**Confirming hepatic origin** Of concern, especially in the case of an isolated enzyme elevation, is to ensure that the abnormal LFT in question is of hepatic origin. Common liver enzymes, such as aspartate aminotransferase (AST) are found not only in the liver but can also derive from cardiac muscle, skeletal muscle, kidneys, brain, pancreas, lungs, and erythrocytes.<sup>1</sup> Other causes of serum AST elevation are rhabdomyolysis, recent vigorous physical activity, or inflammatory muscle disease. In a similar fashion, an elevated alkaline phosphatase may not only indicate a hepatobiliary origin but can also frequently point to a bone or intestinal source (in particular in patients with blood type O or B after the ingestion of a fatty meal).<sup>2</sup> Therefore, the serum alkaline phosphatase level is best determined in the fasting state. A serum albumin level is usually used to indicate overall liver function; an abnormally low serum albumin level may reflect disease in another organ system, such as a protein-losing enteropathy or nephrotic syndrome.

The best approach to an isolated LFT abnormality such as alkaline phosphatase would be to order isoenzymes fractionation.<sup>3</sup> Macroenzymes are molecules of high molecular weight, which are formed by the binding of a normal enzyme to another plasma protein, and have most commonly been described with isolated AST elevations.<sup>4</sup>

**Evaluation of the LFT pattern** Evaluation of the pattern of the initial LFT panel (**Table 1**) in association with serum prothrombin time and platelet count is key.<sup>5</sup> Although characteristic changes are not always present, this can provide a useful initial guidance, which can be confirmed by disease-specific blood testing, radiographic imaging, or liver biopsy.

The first determination is whether the pattern is more characteristic of “hepatitis” or cholestasis.<sup>6</sup> The predominant “hepatitis” pattern with alanine aminotransferase (ALT) and AST elevation out of proportion to alkaline phosphatase is characteristic of viral

	Hepatocellular			Biliary		Infiltration
	Ischemia, & Toxins	Viral Hepatitis	Alcohol	Complete	Partial	Infiltrative Disease
Aminotransferases	50–100×	5–50×	2–5×	1–5×	1–5×	1–3×
Alk phos	1–3×	1–3×	1–10×	2–20×	2–10×	1–20×
Bilirubin	1–5×	1–30×	1–30×	1–30×	1–5×	1–5×
Prothrombin time	Prolonged and unresponsive to vitamin K in severe disease			Responsive to SQ vitamin K		Usually nl
Albumin	Decreased chronic disease			Usually nl		Usually nl
Platelet count	Decrease suggests stage III/IV			Usually nl		Usually nl

*Abbreviations:* Alk phos, alkaline phosphatase; nl, normal; SC, subcutaneous.

*Data from* Aijaz A, Keeffe EB. Liver Chemistry and function tests. In: Feldman, Friedman, Brandt, editors. Sleisenger & Fordtran's gastrointestinal and liver disease. 8th edition. Philadelphia: Saunders Elsevier; 2006. p. 1575–86.

hepatitis, nonalcoholic steatohepatitis, and alcohol- and drug-induced liver disease. A serum ALT to AST ratio greater than 2:1, but where the AST is less than 10 times the upper limit of normal, is consistent with alcoholic liver disease.<sup>7</sup>

If the pattern is cholestatic, then it is important to differentiate extrahepatic biliary tract obstruction from intrahepatic cholestasis. Classical biliary of the alkaline phosphatase elevation includes biliary strictures, choledocholithiasis, primary sclerosing cholangitis, and cholangiocarcinoma. Causes of the intrahepatic cholestasis include drug-induced etiologies, granulomatous disease and primary biliary cirrhosis, and malignant infiltration of the liver.<sup>6</sup> An elevated alkaline phosphatase is not invariable with neoplastic liver disease.<sup>8</sup>

### **Platelet count and prothrombin time**

Jaundice in the face of a high platelet count is suggestive of acute liver disease or metastatic cancer/lymphoma involving liver. An elevation in the AST much greater than that in ALT is suggestive of shock liver as is a rapid rise in the serum prothrombin time, returning to normal over a period of several days. Acute acetaminophen toxicity can present with a significant elevation in the prothrombin time out of proportion to the elevation in the total bilirubin. Subcutaneous vitamin K will normalize the prothrombin time in patients with extrahepatic biliary obstruction but usually not with intrahepatic cholestasis. Chronically low platelet count (in the absence of bone marrow suppression or increased consumption) raises the possibility of liver fibrosis (stage 3 or 4) with portal hypertension and secondary hypersplenism.

### **Serologic testing**

Following the evaluation of the LFTs, other blood tests are ordered to test for various etiologies of liver disease (**Box 1**). Depending on whether the liver test abnormalities were present before admission to the hospital, testing should also be sent for blood toxicology screens (especially on admission to the emergency room), viral liver disease, autoimmune hepatitis, primary sclerosing cholangitis, hemochromatosis, nonalcoholic fatty liver disease (NAFLD), and, if indicated by age, Wilson's disease (**Table 2**).

**Box 1****Initial laboratory testing***Recommended Initial Testing*

Toxicology testing (in emergency room/ day 1 of hospitalization)

Urine and blood toxicology screens

**Viral**

Hepatitis A antibody (IgM)

Hepatitis B surface antigen, hepatitis B core antibody total, and surface antibody

Hepatitis C antibody

**Viral (optional)**

If hepatitis B surface antigen (+)

Hepatitis viral B DNA (PCR)

Hepatitis B antigen and antibody

If hepatitis C antibody (+)

Hepatitis viral C RNA (PCR) and genotype

If immunosuppressed (future: microarray panel testing)

Cytomegalovirus antibody (IgM)

Epstein-Barr viral antibody (IgM)

Herpes simplex antibody (IgM)

**Auto antibodies**

Antinuclear antibody

Antismooth muscle antibody

Antimitochondrial antibody

Perinuclear anti-neutrophil cytoplasmic antibody (atypical)

**Metabolic**

Ceruloplasmin (serum), urine for 24-h copper

Ferritin, iron, total iron-binding capacity

Fasting insulin, lipid profile, hemoglobin A<sub>1c</sub>

*Abbreviations:* IgM, immunoglobulin M; PCR, polymerase chain reaction.

***Noninvasive Evaluation Techniques***

Noninvasive radiographic imaging is the next procedure to supplement the results of blood testing.

***Radiographic imaging***

**Ultrasound/Doppler ultrasound** Abdominal ultrasound (US), with or without a Doppler ultrasound (DUS) component, is usually the initial imaging test in the evaluation of hepatobiliary disease. Important information gleaned from the US report may be the presence of hepatic masses as well as information about the diameter of the extrahepatic biliary tree. A caveat, however, is that patients with significant cirrhosis of the liver, especially due to primary sclerosing cholangitis or primary biliary cirrhosis, may have less biliary tract dilatation than would normally be expected with acute biliary

Table 2 Etiologies of acute and chronic liver disease	
Liver Disease Classification	
Viral (classical)	Metabolic
Hepatitis A	Wilson's disease
Hepatitis B	Hemochromatosis
Hepatitis C	Steatosis (NASH/NAFL)
Hepatitis D	Pregnancy
Hepatitis E	
Viral (other)	Alcohol
Cytomegalovirus	Autoimmune hepatitis
Epstein-Barr virus	Ischemic
Herpes simplex virus	Arterial thrombosis
	Budd-Chiari syndrome
	Veno-occlusive disease
Medications	Malignancy
Prescription	Primary
Illicit	Hepatocellular carcinoma
Herbal	Cholangiocarcinoma
	Metastatic
Biliary	Unknown etiology
Choledocholithiasis	Primary sclerosing cholangitis
Biliary stricture	Primary biliary cirrhosis
Choledochoceles	
AIDS cholangiopathy	

Abbreviation: NASH, nonalcoholic steatohepatitis.

tract obstruction.<sup>9</sup> With these exceptions, nevertheless, the overall sensitivity of US for the detection of biliary obstruction in the presence of jaundice is around 90% with comparable specificity.<sup>10</sup>

**Computed tomography and magnetic resonance imaging** Computed Tomography (CT) is clearly superior to US for detection of intrahepatic and extrahepatic masses, as well as providing superior information about other organs of the abdominal region. However, in a patient with a high suspicion of biliary tract disease, magnetic resonance cholangiopancreatography (MRCP) is clearly superior to CT in the evaluation of the biliary system and determining the cause of possible obstruction.

The contour of the liver, in particular the presence of modularity as well as caudate lobe enlargement, correlates with the presence of cirrhosis on liver biopsy.<sup>11</sup> The presence of splenomegaly, dilatation of the portal vein, paraesophageal, and/or gastric varices can also be useful to suggest the presence of portal hypertension.

### Nuclear medicine

**DISIDA Scan** Previously, hepatobiliary scintigraphy initially with hepatobiliary iminodiacetic acid (HIDA) scan, now more commonly the diisopropyl iminodiacetic acid (DISIDA) scan, was used to seek for biliary tract obstruction. However, given the superior information available with modern CT and MRI/MRCP imaging techniques, it is no longer recommended as an initial examination. In addition, accurate information from a DISIDA scan is limited to patients with a serum bilirubin level less than 20 mg/dL. The DISIDA scan remains sensitive, however, for the evaluation of the presence of acute cholecystitis or for a potential bile leak after biliary tract surgery or an endoscopic retrograde cholangiopancreatography (ERCP) sphincterotomy.<sup>12</sup>

**Liver spleen scans** Ninety percent of sulfur colloid tagged with technetium-99 m is removed by the liver, with the remaining particles extracted by the spleen and bone marrow. The ratio of the sulfur colloid clearance by the spleen and bone marrow increases in proportion to that by the liver with worsening liver function.<sup>13</sup> In addition, abnormal (patchy) distribution of the sulfur colloid is found in patients with severe liver disease. Despite improvements in the technique with Technetium-99 m, single-positron emission computed tomography (SPECT) scanning computer reconstruction of the image, this has fallen out of favor with better imaging of liver by CT and MRI scans.<sup>14</sup>

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### **Endoscopic Techniques**

#### **Endoscopic ultrasound**

Endoscopic ultrasound (EUS) is a newer technique with increasing use over the last several years. Overall, it has a sensitivity and specificity similar to those of MRCP.<sup>15</sup> However, it also has the advantage of permitting biopsy of suspected areas of malignancy.<sup>16</sup>

#### **Endoscopic retrograde cholangiopancreatography**

ERCP is the classic endoscopic method for the evaluation of the biliary system and the associated pancreatic duct. Among its advantages is its high degree of accuracy, with sensitivity rates of 89% to 90% and specificity rates of 89% to 100%.<sup>10</sup> The disadvantage is that it is an invasive procedure with a risk of complications both related to performance of endoscopy as well as specific to the injection and manipulation of the biliary tree and pancreatic duct.<sup>17</sup> A study comparing available techniques found sensitivity and specificity for diagnosis of malignancy in patients: 85% to 75% for ERCP, 85% to 71% for MRCP, 77% to 63% for CT, and 79% to 62% for EUS.<sup>15</sup>

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### **Specific Patterns and Considerations**

#### **Acute biliary tract disease**

**Cholelithiasis and biliary stricture** Acute bile duct obstruction produces an elevation of alkaline phosphatase out of proportion to the serum aminotransferases. However, early in acute biliary obstruction, the AST and ALT may transiently rise as high as 10 to 20 times the upper limit of normal.<sup>18</sup> US is sensitive in the presence of biliary dilatation; however, it is much less sensitive in the presence of a nondilated bile duct. Confirmatory investigations include EUS, MRCP, and ERCP. A National Institutes of Health consensus statement concluded that the EUS, MRCP, and ERCP have comparable sensitivity and specificity in the detection of common bile duct stones.<sup>19</sup>

#### **Specific hepatocellular diseases and patterns**

**Infectious hepatitis** ALF in the United States is most commonly due to drug hepatotoxicity. However, acute viral liver disease including hepatitis A, hepatitis B and, extremely rarely, superinfection with hepatitis D or acute hepatitis E must also be considered.<sup>20</sup>

In patients on immunosuppression, particularly post-transplant, the herpes viruses (Epstein-Barr virus, cytomegalovirus, varicella zoster virus, and the herpes simplex virus) must also be kept in mind. Newer simultaneous DNA microarray technology may make a rapid diagnosis in the future in this setting.<sup>21</sup>

In addition to viral etiologies, abnormal LFTs commonly occur in the inpatient in the presence of disseminated infection, in particular both gram-negative and gram-positive bacterial infection. However, abnormal LFTs with other infections, including spirochetal, protozoal, fungal, and helminthic, can also occur.

**Associated with malignancy** Primary hepatobiliary carcinoma as well as liver infiltration by metastatic disease frequently causes abnormal LFTs. Metastases are more

common than primary malignant tumors of the liver. Standard LFTs do not discriminate between primary and metastatic carcinomas. The various imaging modalities discussed earlier are the best means to further evaluate suspected malignant involvement of the liver.

**Drug-induced liver injury** Although many drugs in the Physician Desk Reference have been associated with abnormal LFTs, certain classes of medication are more frequently linked than others. In addition to prescription medications, herbal medications, illegal recreational substances, and environmental toxins have also been associated with drug-induced liver injury (DILI). The most common class of drug hepatotoxicity encountered during hospitalization is reaction to a medication, especially anti-microbial drugs.<sup>22</sup> However, multiple other classes of drugs have also been implicated. (For further information, please see Chapter 7: Modern Hepatotoxicity) DILI can, in general, be grouped into 1 of 2 presentations: predictable and idiosyncratic hepatotoxicity. Hepatotoxins frequently have a characteristic pattern of liver test abnormality: hepatitis, cholestatic, or mixed.

### ***Predictable hepatotoxicity***

In predictable hepatotoxicity, the presentation is directly related to the dose of the drug received and tends to develop almost immediately with necrosis in zone 3 of the liver.<sup>23</sup> This is not due to the drug itself but most commonly secondary to a metabolite. An example of this would be acetaminophen.<sup>24</sup> The Acute Liver Failure Study Group suggests that the majority of cases (39%) of ALF, one of the most dreaded complications of liver disease, are due to acetaminophen overdose.<sup>24</sup> In the acetaminophen group, there was a 68% chance of spontaneous survival, with only 6% of patients undergoing liver transplantation.

### ***Idiosyncratic (unpredictable) hepatotoxicity***

In contrast, the onset of liver dysfunction associated with an idiosyncratic drug reaction tends to be slower.<sup>25</sup> This reaction occurs rarely, is more common after multiple exposures, and is unrelated to the dose of the drug. Occasionally, it can be associated with fever, rash, and eosinophilia. However, ALF due to idiosyncratic drug reactions clearly has had a more dismal prognosis, with an overall 25% survival and up to 53% of patients requiring liver transplantation.<sup>24</sup>

The best way to determine whether a medication is responsible for the abnormal LFT is to stop that particular medication and determine if the LFTs return to normal.<sup>26</sup> Occasionally, this is not possible in an acute, rapidly deteriorating situation, in which case, a liver biopsy may be necessary to help identify which drug is most likely responsible.

**Ischemic hepatitis** Ischemic hepatitis is a common cause within the hospital of extreme AST elevation greater than 2000 U/L.<sup>27</sup> One of the most common etiologies is cardiovascular disease, which is reported to be responsible for almost 70% of cases.<sup>28</sup> Acute liver ischemia can result from generalized hypotension, particularly in the presence of underlying cirrhosis of the liver. It is not uncommon for the prothrombin time to be acutely prolonged over a rapid return to normal within the space of 2 to 3 days, followed by the serum aminotransferase levels within 7 to 10 days.

In addition, however, hypoxia, hyperthermia, and acute vascular occlusive disease can also present with acute abnormalities in LFTs, resulting in the need for hospitalization. In addition, acute hepatic vein thrombosis (Budd-Chiari syndrome) can result in sudden onset of ascites and hepatic decompensation.

**Alcoholic liver disease** Many patients conceal alcohol abuse, and, therefore, the diagnosis of alcoholic liver disease is not always obvious. Patients present with an AST to ALT ratio of at least 2:1.<sup>29</sup> This should slowly improve during a prolonged hospitalization. In addition, although not commonly used within the hospital after the first few days of admission, is the carbohydrate-deficient transferrin. Although it is a relative specific marker for alcohol abuse, it tends to decline after the patient has been absent for 4 days.<sup>30</sup> (For further information, please see Chapter 8: Management of Alcoholic Liver Disease.)

**Jaundice in the postoperative period** Postoperative jaundice is often multifactorial. However, abnormal LFTs can occur in almost 25% to 75% of patients postsurgery.<sup>31</sup> Although this can happen in patients with completely normal liver function preoperatively, this tends to be more common in patients with compensated cirrhosis (almost 50% of the patients).<sup>32</sup> A number of additional factors include impaired liver perfusion due to intraoperative or postoperative hypotension/hypoxia, blood transfusions, medication reactions, and occult sepsis. (For further information, see Chapter 4: Surgery in the Patient with Liver Disease).

**Chronic liver disease** Finally, all forms of chronic liver disease can, of course, be diagnosed for the first time during admission to the hospital. In fact, the most common etiology of liver disease in the United States at the present time is NAFLD.<sup>33</sup>

### STEP 3: EVALUATION OF SEVERITY

#### *Acute Liver Disease (Prognostic Factors)*

##### *King's College Criteria*

The King's College Criteria were initially reported to be effective in providing prognostic of the need for liver transplantation in ALF due to acetaminophen (**Table 3**).<sup>34</sup> The criteria, however, were later modified to include ALF secondary to other etiologies. Moreover, in nonacetaminophen-related ALF, the presence of even a single adverse prognostic factor (see **Table 3**) predicts mortality of 80%.<sup>35</sup>

##### *Chronic Liver Disease Liver With/Without Acute Decompensation*

Since chemistry panels are commonly ordered as part of the initial admission to the hospital, many chronic liver diseases can be recognized for the first time. The causes of chronic liver disease are listed in **Table 2**.

**Table 3**  
King's College Criteria for transplantation in acute liver failure

Nonacetaminophen Cases	Acetaminophen Cases
INR >6.5 (PT >100 s) or any 3 of the following: Idiosyncratic drug/indeterminant Age <10 or >40 y Acute/subacute presentation Serum bilirubin >17.5 mg/dL INR >3.5 (PT >50 s)	Arterial pH <7.3 or any 1 of the following: Stage III/IV encephalopathy Serum creatinine >3.4 mg/dL INR >6.5 (PT >100 s)

*Abbreviations:* INR, international normalized ratio; PT, prothrombin time.

*Data from* O'Grady JG, Alexander GJ, Hayllar KM, et al. Early indicators of prognosis in fulminant hepatic failure. *Gastroenterology* 1989;97:439-45; and Bernal W, Donaldson N, Wyncoll D, et al. Blood lactate as an early predictor of outcome in paracetamol-induced acute liver failure: a cohort study. *Lancet* 2002;359:558-63.

### **Child-Turcotte-Pugh**

The Child-Turcotte-Pugh (CTP) classification was initially used to predict mortality postcholecystectomy (**Table 4**). Its use has been generalized to the prognosis of patients postabdominal surgery (**Table 5**) of all types.<sup>36</sup> Surgery is always contraindicated in patients with Child's class C cirrhosis unless a life-threatening indication is present, such as bowel infarction, gangrenous cholecystitis, or incarcerated hernia. The estimation of operative risk in patients with cirrhosis was previously based on the Child-Turcotte-Pugh score, which has now been replaced by the Model for End-Stage Liver Disease (MELD).

### **MELD Score**

The MELD scoring system was initially developed to predict 3-month mortality in patients undergoing transjugular intrahepatic portosystemic shunts.<sup>37</sup> The MELD scoring system is based on the serum bilirubin level, international normalized ratio (INR), and the serum creatinine level (see **Fig. 1**). This was adopted in February 2002 as the primary determinant for organ allocation in the United States. MELD is useful in predicting 3-month mortality in patients before and after transplant.<sup>38</sup>

### **Evaluation of Operative Risk**

Elective surgical procedures are contraindicated in the face of active liver disease until a complete evaluation has been undertaken. In general, patients can be classified into those with minimal operative risk and those with increased operative risk, which includes those of active hepatitis and cirrhosis.

### **Child-Turcotte-Pugh**

The CTP classification was initially used to predict mortality postcholecystectomy (see **Table 4**). Its use has been generalized for prognosis of all cirrhotic patients (see **Table 5**).<sup>36</sup>

### **Model for end-stage liver disease**

The MELD scoring system has also been applied to predict the outcome after surgery in cirrhotic patients.<sup>39</sup> It has the advantage of being more objective than the CTP classification, which is limited by subjective grading of some variables, such as ascites and hepatic encephalopathy. In addition, the CTP is unable to provide adequate risk assessment in patients with severely decompensated liver disease. (For further information, see the article by O'Leary and colleagues elsewhere in this issue.)

<b>Table 4</b>			
<b>Calculation of the Child-Turcotte-Pugh classification</b>			
<b>Parameter</b>	<b>Numerical Score</b>		
	<b>1</b>	<b>2</b>	<b>3</b>
Ascites	None	Slight	Moderate/severe
Encephalopathy	None	Slight/moderate	Moderate/severe
Bilirubin (mg/dL)	<2.0	2.1–3	≥ 3.1
Albumin (g/dL)	≥ 3.5	2.8–3.5	≤ 2.7
Prothrombin time (s) <sup>a</sup>	1–4	4.1–6	>6.0

Grade (A): 5–6, grade (B): 7–9, grade (C): 10–15.

<sup>a</sup> seconds increased over control.

**Table 5**  
**Child-Turcotte-Pugh score and predicted operative mortality**

Total Numerical Score	Child-Turcotte-Pugh Class	Operative Mortality Rate
5–6	A	10%
7–9	B	30%
10–15	C	82%

The Mayo Clinic has made a recent modification to the MELD score that calculates the postoperative day 7, day 30, day 90, year 1, and year 5 in patients with cirrhosis for all types of major surgery. This model includes in addition to bilirubin level, creatinine level, and INR, the American Society of Anesthesiologists classification and the etiology of disease (<http://www.mayoclinic.org/meld/mayomodel9.html>).

#### **STEP 4: EVALUATION FOR COMPLICATIONS**

##### ***Acute Liver Failure***

This rare clinical syndrome is defined as development of coagulopathy in association with hepatic encephalopathy within 26 weeks of recognition of liver disease in a patient without pre-existing liver disease. Causes of death include sepsis, hypoglycemia, cerebral edema, multisystem organ failure, acute respiratory distress syndrome, and renal failure (acute tumor necrosis and type 1 hepatorenal syndrome). Bacterial infections develop in as many as 80% of patients.<sup>40</sup>

##### ***Chronic Liver Disease***

Sometimes a complication of chronic liver disease can be one of the major reasons for the patient's admission to the hospital. Alternatively, a patient with chronic liver disease is admitted for another reason. During the hospital admission, the patient may be noted to have thrombocytopenia. If the subsequent evaluation suggests cirrhosis, it is helpful to look for the presence of a complication of cirrhosis. These typically include esophageal or gastric varices, ascites, hepatic encephalopathy, and hepatocellular carcinoma. However, it should not be forgotten that there are additional complications of cirrhosis. These include portopulmonary hypertension, hepatopulmonary syndrome, and hepatorenal syndrome type 2.

##### ***Evaluation for esophageal varices***

Studies have documented that gastroesophageal varices are present in approximately 40% of patients with Child's A cirrhosis and almost 85% of patients with Child's C classification.<sup>41</sup> The platelet count can be a good predictor of the presence or absence of esophageal varices on upper endoscopy. Specifically, a platelet count of 150,000/mm<sup>3</sup> excludes the presence of medium or large esophageal varices with a sensitivity of 90% and negative predictive value of 99%.<sup>42</sup> According to the American Association for the Study of Liver Disease practice guidelines, "screening endoscopy for the diagnosis of esophageal in gastric varices is recommended when the diagnosis of cirrhosis is made."<sup>43</sup> The American Society for Gastrointestinal Endoscopy recommends screening for esophageal varices in "Patients with cirrhosis and portal hypertension but no prior variceal hemorrhage especially those with platelet counts <140,000/mm<sup>3</sup>, or Child's Class B or C."<sup>44</sup>

### **Surveillance for hepatocellular carcinoma**

The incidence of hepatocellular carcinoma (HCC) has been rising in various countries.<sup>45,46</sup> Surveillance for HCC should be routinely performed in patients with a diagnosis of cirrhosis of the liver and in patients with chronic hepatitis B. These patients should be entered into a surveillance program using US every 6- to 12-month intervals.<sup>47</sup>

### **SUMMARY AND FINAL COMMENTS**

In summary, evaluation of abnormal LFTs in the hospitalized patient is similar to that in the outpatient setting but often of a more pressing nature. There are 4 steps in this process. The first is to determine if the abnormal LFTs are associated with the major reason for the admission to the hospital or are of chronic nature. The second is to determine the etiology. The third part of this process is to evaluate the severity of the dysfunction and determine if ALF or acute decompensation of chronic liver failure is present. The fourth and final step is to look for associated complications of either acute or chronic liver failure as appropriate. The recommendations section of the consultation form should highlight any missing diagnostic testing for the cause of the disease and the severity of the dysfunction. In addition, there should be clear management guidelines for treatment of the liver disease, the associated complications, as well as a comment regarding the prognosis for the disease and expected response to therapy. A consultation report that focuses on these issues and their management in the best way will provide the most information and value in the evaluation of abnormal LFTs in the hospitalized patient.

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