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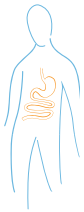

Laboratory Tests in Liver Disease

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INTRODUCTION

The liver is the largest solid organ in the body, and it performs many metabolic, secretory, and nutritional functions that are vital to maintenance of a healthy human physiology. The liver is responsible for glucose homeostasis, plasma protein synthesis, lipid and lipoprotein synthesis, bile acid synthesis and secretion (for absorption of fats and vitamins), and vitamin storage (vitamins B_{12}, A, D, E, and K). In addition, the liver is the major site for biotransformation, detoxification, and excretion of a vast array of endogenous and exogenous compounds (e.g., drugs, toxins). As a result of these diverse roles, the clinical manifestations of liver disease are varied and can be quite subtle. Laboratory tests are designed to assess the various functions of the liver, which are then correlated with patient history and physical examination as part of a broader assessment. These tests may be ordered as part of a screening evaluation or to further evaluate clinical signs and symptoms prompting consideration of liver disease, such as hepatomegaly, ascites, jaundice, dark urine, light-colored stool, or gastrointestinal bleeding.

LIVER FUNCTION TESTS

Colloquially, the term *liver function tests* (LFTs) is used quite often when referring to a panel of measurements to assess the "function" of the liver. This panel typically includes measurements of total protein, albumin, aspartate aminotransferase (AST, formerly called serum glutamic-oxaloacetic transaminase or SGOT), alanine aminotransferase (ALT, formerly called serum glutamic-pyruvic transaminase or SGPT), alkaline phosphatase (ALP), γ-glutamyl transpeptidase (GGT), bilirubin (conjugated and unconjugated), and prothrombin time (PT). Unlike tests used to assess function in other organ systems (e.g., arterial blood gases, creatinine clearance), liver function tests do not directly measure hepatic function and may not accurately reflect the cause or severity of liver disease. Rather, they reflect certain patterns or types of liver and biliary cell injury that warrant further evaluation. The most widely available and useful liver function tests are outlined in Table 39-1.

Hepatocellular Injury

AST and ALT are intracellular enzymes that catalyze the transfer of the α-amino group of aspartate or alanine to the α-keto group of ketoglutaric acid, resulting in formation of pyruvate or oxaloacetic acid, respectively. They are important enzymes that participate in gluconeogenesis. With cell injury, AST and ALT are released into the circulation, and higher values are used primarily as markers of liver inflammation. ALT is found predominantly in hepatocytes, and an elevation in ALT is more specific than an elevated AST for liver disease. AST is found in the liver but also in heart, skeletal muscle, brain, kidney, pancreas, and lungs. After injury or death of liver cells, these enzymes are released into the circulation. They are measured indirectly with the use of a spectrophotometer.

In most hepatocellular disorders (e.g., viral hepatitis, acetaminophen toxicity), ALT levels are higher than or equal to AST levels. In alcoholic liver disease, however, the AST usually is more than two-fold higher than the ALT (AST/ALT ratio >2). An AST/ALT ratio greater than 3 is 97% specific for alcohol as the underlying cause. Extremely high transaminase levels (15 times the upper limit of normal) generally indicate acute hepatocellular necrosis from viral or toxic causes such as acetaminophen; less frequently, they indicate acute bile duct obstruction or hepatic ischemia (shock liver).

Patients who have isolated asymptomatic elevations of AST and ALT (usually ALT > AST) may have nonalcoholic fatty liver disease (NAFLD), which is caused by obesity, insulin resistance and diabetes, hyperlipidemia, or excessive alcohol consumption. However, in some cases, the AST is higher than the ALT, mimicking the pattern seen in alcoholic liver disease. A careful history and evaluation are warranted, although the AST/ALT ratio in NAFLD rarely exceeds 2, thus distinguishing it from alcoholic liver disease.

Infiltrative hepatocellular disease (e.g., hemochromatosis) and chronic viral hepatitis are also part of the differential.

Cholestasis

Serum ALP comprises a group of isoenzymes derived from the liver, bone, intestine, and placenta. Hepatic ALP (isoenzyme ALP-1) is present mainly in the mucosal cells lining the bile ducts; the usual flow of bile into the small intestine maintains the normal serum level of ALP. In cholestasis related to biliary obstruction or duct injury, serum ALP levels rise as a result of retention of bile acids in the liver; the bile acids solubilize ALP from the hepatocyte plasma membrane and also stimulate its synthesis. Various other hepatocyte plasma membrane enzymes are simultaneously released, including 5′-nucleotidase (5′-NT) and GGT, confirming that the elevated ALP is caused by hepatobiliary disease. The measurement of ALP is thus correlated with integrity of the biliary system.

Primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC) are examples of obstructive diseases with predominant elevation of ALP. Other conditions, such as bone regeneration, pregnancy, and neoplastic, infiltrative, and granulomatous liver diseases are also associated with elevated ALP levels.