CME

ACG Clinical Guideline: Evaluation of Abnormal Liver Chemistries

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Clinicians are required to assess abnormal liver chemistries on a daily basis. The most common liver chemistries ordered are serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase and bilirubin. These tests should be termed liver chemistries or liver tests. Hepatocellular injury is defined as disproportionate elevation of AST and ALT levels compared with alkaline phosphatase levels. Cholestatic injury is defined as disproportionate elevation of alkaline phosphatase level as compared with AST and ALT levels. The majority of bilirubin circulates as unconjugated bilirubin and an elevated conjugated bilirubin implies hepatocellular disease or cholestasis. Multiple studies have demonstrated that the presence of an elevated ALT has been associated with increased liver-related mortality. A true healthy normal ALT level ranges from 29 to 33 IU/l for males, 19 to 25 IU/l for females and levels above this should be assessed. The degree of elevation of ALT and or AST in the clinical setting helps guide the evaluation. The evaluation of hepatocellular injury includes testing for viral hepatitis A, B, and C, assessment for nonalcoholic fatty liver disease and alcoholic liver disease, screening for hereditary hemochromatosis, autoimmune hepatitis, Wilson's disease, and alpha-1 antitrypsin deficiency. In addition, a history of prescribed and over-the-counter medicines should be sought. For the evaluation of an alkaline phosphatase elevation determined to be of hepatic origin, testing for primary biliary cholangitis and primary sclerosing cholangitis should be undertaken. Total bilirubin elevation can occur in either cholestatic or hepatocellular diseases. Elevated total serum bilirubin levels should be fractionated to direct and indirect bilirubin fractions and an elevated serum conjugated bilirubin implies hepatocellular disease or biliary obstruction in most settings. A liver biopsy may be considered when serologic testing and imaging fails to elucidate a diagnosis, to stage a condition, or when multiple diagnoses are possible.

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INTRODUCTION

The authors were invited by the Board of Trustees and Practice Guidelines Committee of the American College of Gastroenterology to develop a practice guideline regarding the evaluation of abnormal liver chemistries. We used the following resources:

1. A formal review and literature search of the world literature on MEDLINE and EMBASE databases dealing with the evaluation of abnormal liver chemistries, studies that dealt with normal or reference range for alanine aminotransferase (ALT) levels and what thresholds trigger an evaluation for actionable liver disease. Studies detailing the relationship between ALT and nonalcoholic fatty liver disease, as well as studies assessing the significance of elevated liver chemistries on overall mortality and morbidity.
2. Guideline policies of the American College of Gastroenterology.
3. The experience of the authors and independent reviewers, as well as communication with senior hepatologists across the United States with regard to the threshold for evaluating abnormal liver chemistries.

These recommendations are intended for use by physicians and health care providers and suggest preferred approaches to the diagnoses and evaluation of those with abnormal liver tests (**Table 1**). These guidelines are intended to be flexible and should be adjusted as deemed appropriate when applied to individual patients. Recommendations are evidence-based where possible. On subjects lacking rigid scientific data, recommendations are made based on the consensus opinion of the authors. To more fully characterize the available evidence reporting the recommendations, the ACG

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