

# HOSPITAL PHYSICIAN®

## GASTROENTEROLOGY BOARD REVIEW MANUAL

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The *Hospital Physician Gastroenterology Board Review Manual* is a study guide for fellows and practicing physicians preparing for board examinations in gastroenterology. Each quarterly manual reviews a topic essential to the current practice of gastroenterology.

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## Nonalcoholic Fatty Liver Disease

### Series Editor:

**Richard A. Wright, MD**

*Professor and Chief, Division of Gastroenterology/Hepatology, Department of Medicine, University of Louisville School of Medicine, Louisville, KY*

### Contributors:

**Matthew Cave, MD**

*Fellow, Division of Gastroenterology/Hepatology, Department of Medicine, University of Louisville School of Medicine, Louisville, KY*

**Miriam Vos Louthan, MD, MSPH**

*Fellow, Division of Gastroenterology, Department of Pediatrics, University of Louisville School of Medicine, Louisville, KY*

**Craig J. McClain, MD**

*Professor and Vice Chair for Research, Department of Medicine; Jewish Hospital Distinguished Chair in Hepatology, Division of Gastroenterology/Hepatology; University of Louisville School of Medicine, Louisville, KY*

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# Nonalcoholic Fatty Liver Disease

Matthew Cave, MD, Miriam Vos Louthan, MD, MSPH, and Craig J. McClain, MD

## CASE VIGNETTE

An obese 55-year-old white man with diabetes and hypertriglyceridemia develops right upper quadrant discomfort. He is subsequently diagnosed with symptomatic gallstones and undergoes laparoscopic cholecystectomy at a regional hospital. On intraoperative examination, his liver appears fatty and nodular; biopsy shows steatohepatitis with cirrhosis. The patient is referred to a hepatology clinic.

At the clinic, the patient says he does not drink alcohol excessively and has no family history of liver disease. He is fatigued and reports persistent right upper quadrant fullness. Physical examination reveals nontender hepatomegaly and prominent central obesity with a body mass index (BMI) of 40 kg/m<sup>2</sup>. Results of laboratory tests include alanine aminotransferase (ALT) level of 85 U/L, aspartate aminotransferase (AST) level of 75 U/L, and an albumin level of 2.9 g/dL; results of all other laboratory tests are normal. The patient is diagnosed with nonalcoholic steatohepatitis and is instructed to lose weight and control his diabetes and hypertriglyceridemia.

Over the next 3 years, the patient is noncompliant with the recommended lifestyle modifications, despite input from his physician, a nutritionist, and family members. The patient's liver function deteriorates, and he develops ascites complicated by noncompliance with a low sodium diet. He ultimately requires high-dose spironolactone and furosemide. On a subsequent screening ultrasound, a 3-cm mass is noted; biopsy shows hepatocellular carcinoma. The patient is referred to a liver transplant program; however, the patient's severe obesity is considered to be a major risk factor for complications of liver transplantation.

Faced with imminent mortality, the patient attempts to lose weight and adhere to the low sodium diet. He presents to his local emergency room in pulseless electrical activity arrest with severe hyperkalemia and dies despite aggressive resuscitation attempts. Possibly, this poorly compliant patient used potassium-containing salt substitute, despite medical counseling regarding this risk. He is survived by 2 adult sons, one of whom is

obese and was recently diagnosed with prediabetes and elevated liver enzyme values.

## INTRODUCTION

Obesity-associated fatty liver disease was first described by Westwater and Fainer<sup>1</sup> nearly 50 years ago. Knowledge of the disease progressed little until 1979, when Adler and Scaffner<sup>2</sup> described fatty liver, hepatitis, fibrosis, and cirrhosis mimicking alcoholic liver disease in a group of overweight patients, many of whom were diabetic and had lipid abnormalities. The following year, Ludwig et al<sup>3</sup> introduced the term *nonalcoholic steatohepatitis* to describe similar pathologic findings in a group of obese female patients, many of whom were diabetic, with hepatomegaly and mild abnormalities on liver function tests. Since then, the term *nonalcoholic fatty liver disease* (NAFLD) has been used to describe a larger spectrum of steatotic liver disease generally associated with the metabolic syndrome (**Table 1**).

NAFLD is defined by clinicopathologic criteria. Clinically, patients with NAFLD do not consume significant quantities of alcohol (generally no more than 2 drinks per day). Pathologically, several patterns of disease exist in NAFLD that resemble alcoholic liver disease. The sine qua non of NAFLD is macrovesicular steatosis or fatty liver. If this condition exists in isolation, the patient is diagnosed with simple steatosis or nonalcoholic fatty liver (NAFL). As most patients tolerate this condition well, it is unclear whether simple steatosis represents a disease state or an adaptive response to metabolic stress.<sup>4,5</sup> Some patients with NAFL develop superimposed necroinflammatory activity, often with fibrosis, termed *nonalcoholic steatohepatitis* (NASH). Some patients with NASH develop cirrhosis, which may become complicated by hepatocellular carcinoma, and ultimately die from a liver-related cause.

Primary NAFLD is the hepatic manifestation of the metabolic syndrome and its prevalence is increasing at an alarming rate. Secondary causes of NAFLD are much less common and include drugs and toxins, surgical procedures, and other causes as noted in **Table 2**. This review focuses on primary NAFLD.