

HOSPITAL PHYSICIAN®

ENDOCRINOLOGY BOARD REVIEW MANUAL

STATEMENT OF EDITORIAL PURPOSE

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

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Cardiovascular Risk Factors: Metabolic Syndrome

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Cardiovascular Risk Factors: Metabolic Syndrome

Annaswamy Raji, MD, and Jorge Plutzky, MD

INTRODUCTION

Risk factors for cardiovascular disease often cluster in certain individuals. One such constellation of risk factors is *metabolic syndrome*, the importance of which is underscored by the finding that patients with metabolic syndrome have nearly the same risk for cardiovascular disease as patients with type 2 diabetes.¹

Metabolic syndrome has been receiving increasing attention, consistent with its expanding global incidence. An estimated 22% of U.S. adults have this syndrome.² Until recently, metabolic syndrome had been considered largely a clinical diagnosis,¹ with various indices used for research purposes but not found to be very useful in general practice. In 2001, the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) provided a working definition of metabolic syndrome and emphasized the significant threat that this syndrome represents in terms of its contribution to premature onset and severity of coronary heart disease (CHD).³

Individuals with metabolic syndrome need to be identified and treated to lower their risk for cardiovascular events and for developing type 2 diabetes. A growing body of evidence suggests that cardiovascular benefits can be derived from intervening in some, if not all, components of metabolic syndrome. Evidence-based approaches include lifestyle modifications aimed at minimizing or reversing factors that contribute to the development of metabolic syndrome (eg, overweight/obesity, physical inactivity, insulin resistance) and pharmacotherapy targeting the specific clinical components of the syndrome.

Volume 5 of the *Hospital Physician Endocrinology Board Review Manual* will focus on several key components of metabolic syndrome and their contribution to CHD risk. This manual provides an overview of metabolic syndrome and its role in cardiovascular disease and incorporates two clinical cases to illustrate principles of primary and secondary prevention. Future manuals will examine specific cardiovascular risk factors (ie, obesity,

hypertension, atherogenic dyslipidemia) and their management.

METABOLIC SYNDROME AND CARDIOVASCULAR RISK

SYNDROME COMPONENTS

Both atherosclerosis and metabolic syndrome are complex processes involving multiple organ systems and interrelated metabolic abnormalities. These abnormalities include a few well-known risk factors for CHD as well as some recently described or *emerging* risk factors (**Table 1**). Any one of the risk factors included in metabolic syndrome increases the risk for CHD, with potentially compounding effects when such factors are present together, as is often the case.^{4,5}

CAUSES AND CONTRIBUTING FACTORS

Examining the components of metabolic syndrome, many of the risk factors often coexist, suggesting the possibility of common underlying mechanisms.

Insulin Resistance

Substantial evidence indicates that insulin resistance contributes to hyperglycemia in diabetes mellitus and also plays a pathophysiologic role in other components of metabolic syndrome (**Figure**).⁶ Insulin resistance, characterized by reduced responsiveness to normal circulating levels of insulin, can lead to hyperglycemia and hyperinsulinemia. It has been suggested that a fundamental defect in peripheral insulin sensitivity also may lead to dyslipidemia, hypertension, and compensatory hyperinsulinemia, with eventual loss of glycemic control.^{4,7,8}

Despres et al⁹ have shown hyperinsulinemia to be an independent risk factor for ischemic heart disease. In this 5-year prospective case-control study, diabetic patients were excluded, yet fasting insulin levels were 18% higher in cases compared with controls, and the nondiabetic men who developed CHD (as expected given the