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PULMONARY DISEASE BOARD REVIEW MANUAL

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Primary Pulmonary Hypertension

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Table of Contents

Introduction	2
General Considerations	2
Conventional Medical Therapy	4
Epoprostenol Therapy	6
Lung Transplantation	8
Medications Under Investigation	8
Summary Points	9
Board Review Questions	10
Answers	10
References	10

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Primary Pulmonary Hypertension

Vallerie V. McLaughlin, MD

INTRODUCTION

Primary pulmonary hypertension (PPH), the idiopathic form of pulmonary arterial hypertension, is a disease that affects the pulmonary vascular bed. It is characterized by a sustained and substantial increase in pulmonary arterial pressure and pulmonary vascular resistance. The annual incidence of PPH has been estimated at 1 to 2 cases per million in the general population. The incidence of pulmonary arterial hypertension is increased among patients with portal hypertension or HIV infection and among those who use appetite suppressants.¹ Pulmonary arterial hypertension also occurs in association with collagen vascular diseases (eg, scleroderma, systemic lupus erythematosus) and congenital systemic-to-pulmonary shunts.

The diagnostic classification of the various forms of pulmonary hypertension was revised in 1998 at a symposium sponsored by The World Health Organization (Table 1). Over the years, clinical scientists have become aware that all forms of pulmonary arterial hypertension are similar to each other in terms of pathology, clinical manifestations, and response to therapy. This manual discusses characteristics of PPH and uses case-based discussions to delineate important steps in determining an appropriate treatment for a patient with the disease. The manual also discusses therapies for PPH that are currently under investigation.

GENERAL CONSIDERATIONS

PATHOPHYSIOLOGY

The pathophysiology of PPH involves 3 key features: vasoconstriction, vascular-wall remodeling, and thrombosis *in situ*. Approximately 20% of patients with PPH have a particularly prominent component of vasoconstriction, which has implications for therapy. Altered function of the pulmonary vascular endothelium has been shown, with an imbalance in the ratio of metabolites of prostacyclin to those of thromboxane. Impaired synthesis of the endothelium-derived vasorelaxant nitric oxide and an

enhanced production of the endothelium-derived vasoconstrictor endothelin-1 have also been shown in PPH.

COMMON SYMPTOMS AND CLASSIFICATION

The symptoms of PPH are nonspecific. The National Institutes of Health (NIH) registry for patients with PPH found dyspnea the most common initial presenting symptom,² and it was reported by nearly all patients at some point in the disease process. Fatigue was another common early symptom. The disease is also characterized by angina, syncope, and edema. PPH is usually classified according to the functional classification system developed by the New York Heart Association for heart failure. There are 4 categories (classes I, II, III, and IV). The following clinical vignette describes a patient manifesting typical symptoms of PPH and common physical examination findings related to this disorder.

CASE I PRESENTATION

A 38-year-old woman presents with a 2-year history of dyspnea. Initially, the dyspnea occurred only with substantial exertion. However, over the past 6 months, the dyspnea has worsened and has occurred with less and less exertion. Currently, the patient becomes dyspneic after approximately 1 block of walking or with having walked up less than 1 flight of stairs. She has also experienced light-headedness and near syncopal episodes with exertion. She reports atypical chest pain and mild lower extremity edema. She denies paroxysmal nocturnal dyspnea and orthopnea. She had 2 children without difficulty, 4 and 6 years ago. Her medical and surgical history is otherwise unremarkable, as is her family and social history.

On physical examination, her blood pressure is 104/78 mm Hg; she has a heart rate of 94 bpm. Her lungs are clear to auscultation. Her jugular venous pressure is approximately 12 cm of water. Her carotid upstrokes are reduced. She has a prominent right ventricular impulse. On cardiac auscultation, she has a regular rate and rhythm with a normal S₁, a loud pulmonic component to her S₂, a right-sided S₄, and a grade II murmur of tricuspid regurgitation. Her abdomen is soft and nontender without hepatosplenomegaly. There is 1+ lower extremity edema.