

HOSPITAL PHYSICIAN®

GASTROENTEROLOGY BOARD REVIEW MANUAL

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

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Genetics of Familial Gastrointestinal Malignancy

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Genetics of Familial Gastrointestinal Malignancy

Randall E. Brand, MD, and Michael J. Goldberg, MD

INTRODUCTION

Gastrointestinal malignancies represent a significant proportion of the cancer burden in the United States. It is estimated that colon cancer will be the second most common cause of cancer death in the United States in 2007, with an estimated 52,180 deaths, while pancreatic cancer will be fourth, with an estimated 33,370 deaths (Table 1).¹ Esophageal and stomach cancers will be responsible for 13,940 and 11,210 deaths, respectively, in 2007.¹ Although most cases of gastrointestinal cancer are sporadic (nonhereditary), with hereditary syndromes accounting for only 5% to 10% of cancer cases, it is important for gastroenterologists to understand the many recent advances in our knowledge of the genetics of gastrointestinal malignancies. In the decades ahead, gastroenterologists will increasingly be able to recognize the underlying molecular events that lead to gastrointestinal malignancy, allowing for the development of improved approaches to prevention, diagnosis, and treatment. This manual reviews the genetic basis of hereditary syndromes that have been linked with colon cancer, pancreatic cancer, gastric cancer, and esophageal cancer and discusses approaches to recognizing these syndromes and performing surveillance testing for cancers associated with them.

FAMILY HISTORY

Obtaining a detailed family history of cancer is the most important initial step in the diagnosis of a hereditary cancer syndrome.² Ideally, this history should consist of all cases of cancer at all anatomic sites and include age of onset. Questions should include: Did your mother/father die of cancer? If so, what type? Was there cancer history on your mother's or father's side of the family (ie, aunts or uncles, maternal and paternal grandparents, any other relatives)? Although individual patients may not be able to provide all this information, there is often a family member who knows the family history and may serve as a resource for obtaining an adequate history. When-

ever possible, one should obtain a family history through 3 generations (first-degree and second-degree relatives).

Physicians must appreciate that a hereditary cancer syndrome diagnosis in a family can impact greatly upon their lifetime cancer destiny and influence the use of preventive and surveillance interventions that may contribute to their survival. When the family is sufficiently educated about this matter, in concert with genetic counseling, they often will appreciate the need to participate actively in the best available cancer screening and management strategies. Thus, it is essential to be aware of the different gastrointestinal syndromes and their management as this will allow for appropriate referral for genetic counseling and implementation of surveillance strategies. Important syndromes associated with these cancers are summarized in Table 2.³⁻¹⁷

COLON CANCER

CASE PRESENTATION I

A 60-year-old man is referred to a gastroenterologist by his primary care physician for a screening colonoscopy. The patient is completely asymptomatic and has a past medical history of hypertension, which is controlled by atenolol. The patient's father died of colon cancer at age 65 years. Colonoscopy reveals a 2-cm sessile right-sided colon polyp, a 1-cm left-sided polyp, and 10 diminutive polyps ranging in size from 3 mm to 8 mm. All polyps are resected and are determined to be adenomatous. The patient is contacted with the results, and an attempt is made to obtain further family history. He knows other family members have had polyps and that some have had colon cancer as well as other types of cancer, but he does not recall exactly who had what or when they had it. The patient is referred for genetic counseling and is asked to gather information regarding his family history and attempt to obtain pathologic documentation of any reported cancers to verify histology.