

HOSPITAL PHYSICIAN®

ONCOLOGY BOARD REVIEW MANUAL

STATEMENT OF EDITORIAL PURPOSE

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

PUBLISHING STAFF

PRESIDENT, GROUP PUBLISHER

Bruce M. White

EDITORIAL DIRECTOR

Debra Dreger

SENIOR EDITOR

Bobbie Lewis

ASSISTANT EDITOR

Rita E. Gould

EXECUTIVE VICE PRESIDENT

Barbara T. White

EXECUTIVE DIRECTOR OF OPERATIONS

Jean M. Gaul

PRODUCTION DIRECTOR

Suzanne S. Banish

PRODUCTION ASSOCIATE

Mary Beth Cunney

ADVERTISING/PROJECT MANAGER

Patricia Payne Castle

SALES & MARKETING MANAGER

Deborah D. Chavis

NOTE FROM THE PUBLISHER:

This publication has been developed without involvement of or review by the American Board of Internal Medicine.



Endorsed by the
Association for Hospital
Medical Education

Cancer of Unknown Primary

Series Editor: Arthur T. Skarin, MD, FACP, FCCP

Medical Director, Thoracic Oncology Program, Department of Medical Oncology, Dana-Farber Cancer Institute and Brigham and Women's Hospital, Associate Professor of Medicine, Harvard Medical School, Boston, MA

Contributor: Wolfram Goessling, MD, PhD

Fellow in Hematology/Oncology, Department of Medical Oncology, Dana-Farber Cancer Institute, Department of Medicine, Brigham and Women's Hospital, Fellow in Gastroenterology, Gastrointestinal Unit, Massachusetts General Hospital, Harvard Medical School, Boston, MA

Table of Contents

Introduction	2
Diagnostic Evaluation	2
Pathology	5
Treatment	7
Summary	9
Board Review Questions.	9
Answers	10
References	11

Cover Illustration by Christie Grams

Copyright 2004, Turner White Communications, Inc., 125 Strafford Avenue, Suite 220, Wayne, PA 19087-3391, www.turner-white.com. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, mechanical, electronic, photocopying, recording, or otherwise, without the prior written permission of Turner White Communications, Inc. The editors are solely responsible for selecting content. Although the editors take great care to ensure accuracy, Turner White Communications, Inc., will not be liable for any errors of omission or inaccuracies in this publication. Opinions expressed are those of the authors and do not necessarily reflect those of Turner White Communications, Inc.

Cancer of Unknown Primary

Wolfram Goessling, MD, PhD

I. INTRODUCTION

Modern imaging techniques and pathologic methods have improved the ability to diagnose and classify malignancies. Despite these advances, metastatic cancer of unknown primary (CUP) remains a common diagnosis and poses a special challenge to both the patient and physician. While the disease has an overall poor prognosis, it is important to identify the subset of patients likely to benefit from therapeutic intervention. This review discusses the different types of metastatic malignancies from an unknown site, appropriate diagnostic evaluation, and treatment.

- A. **Definition.** CUP also is referred to as unknown primary tumor (UPT) or occult primary malignancy. Although no definition is universally accepted, CUP is generally considered to be a histologically confirmed cancer with no apparent primary site revealed by an appropriate clinical evaluation of specific signs and symptoms, a thorough history and physical examination, limited blood studies, chest radiograph, as well as computed tomography (CT) of the abdomen and pelvis.
- B. **Epidemiology**
1. The exact incidence of CUP is unknown due to the variable definition of the disease entity and tendency to under-report cases. Recent Surveillance, Epidemiology and End Results (SEER) data suggest a frequency of 2.3% among all cancers in the United States from 1973 to 1987.¹ Other authors estimate the frequency at up to 6%, yielding about 80,000 to 90,000 cases annually in the United States.^{2,3}
 2. CUP is one of the 10 most common cancer diagnoses in developed countries (it is more common than ovarian cancer, non-Hodgkin's lymphoma, or rectal cancer) and ranks fourth among all cancers as a cause of death. It is very rare in the pediatric population, where CUP represents less than 1% of all cancers. The mean age at the time of diagnosis is 59 years with an age range of 17 to 89 years in a recent study.⁴ Men and women are general-

ly equally affected, although some studies suggest a slight male predominance.^{4,5}

- C. **Prognosis.** Overall, patients presenting with CUP have an extremely poor prognosis with a median survival of 6 to 9 months; less than 25% of patients survive the first year and less than 10% are alive after 5 years. However, several studies have recently identified clinical and histologic features that may be used as indicators of favorable or poor outcome⁶ (**Table 1**).
- D. **Etiology.** As CUP occurs in many different pathologic groups (see section III, Pathology), no unifying risk factors or etiologic agents can be determined. However, a smoking history is found in 50% of patients, which may correlate with the high proportion of occult lung cancers in this group.
- E. **Clinical presentation.** Patients with CUP typically present with a brief history of rapidly progressing symptoms that occur over a few weeks to months. These are generally systemic symptoms and symptoms related to the localization of disease:
1. Systemic symptoms include weight loss, anorexia, malaise, fatigue, and fever.
 2. Local symptoms include lymphadenopathy, pain, swelling, deep venous thrombosis, neurologic deficits (with brain or spine metastases), cough, dyspnea (with pulmonary or pleural involvement), and dysphagia.
 3. Localization of disease. The site of metastasis may often be obvious on physical examination. Multiple sites of metastasis are detected in approximately 30% to 50% of patients at presentation. The common sites of metastatic tumor involvement at presentation are listed in **Table 2**.⁴

II. DIAGNOSTIC EVALUATION

- A. **Patient and physician concerns.** The extent of the diagnostic workup has been controversial for a long time, and only recently have comprehensive management guidelines begun to evolve.⁸ The diagnosis of CUP evokes uncertainty and anxiety