

HOSPITAL PHYSICIAN®

NEPHROLOGY BOARD REVIEW MANUAL

PUBLISHING STAFF

PRESIDENT, GROUP PUBLISHER

Bruce M. White

EDITORIAL DIRECTOR

Debra Dreger

EDITOR

Robert Litchkofski

ASSISTANT EDITOR

Tricia Carbone

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

The Association for Hospital Medical Education endorses HOSPITAL PHYSICIAN for the purpose of presenting the latest developments in medical education as they affect residency programs and clinical hospital practice.

Anemia of Chronic Kidney Disease

Series Editor: Stanley Goldfarb, MD, FACP

*Associate Dean for Clinical Education
University of Pennsylvania School of Medicine
Philadelphia, PA*

Contributor: Alden M. Doyle, MD, MPH

*Assistant Professor of Medicine
Renal, Electrolyte, and Hypertension Division
University of Pennsylvania School of Medicine
Philadelphia, PA*

Table of Contents

Introduction	2
Etiology of the Anemia of CKD	2
Clinical Management of Anemia	3
Management of Resistance to Erythropoietic Therapy	6
Hemoglobin Targets	7
Anemia of CKD and Cardiovascular Disease	7
References	10

Cover Illustration by Andrew Grivas

Copyright 2004, Turner White Communications, Inc., 125 Stafford 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.

Anemia of Chronic Kidney Disease

Alden M. Doyle, MD, MPH

INTRODUCTION

Anemia is an almost universal feature of advancing chronic kidney disease (CKD). This anemia is principally caused by the failing kidney's inability to produce sufficient quantities of erythropoietin, the glycoprotein growth factor that regulates erythropoiesis, but other factors frequently are involved, such as iron deficiency and decreased red blood cell survival. The constellation of factors in CKD that lead to low hemoglobin levels (< 12 mg/dL) causes what has become known as the *anemia of chronic kidney disease*. In the United States, an estimated 1.6 million individuals have this type of anemia,¹ and it is present in more than 75% of patients starting dialysis.²

Before the clinical introduction of recombinant human erythropoietin (rHuEPO) for dialysis patients in 1989, many of the clinical features believed to be part of the *uremic syndrome* were actually a result of profound anemia and some of the approaches used for its treatment, such as frequent transfusions of packed red blood cells. When CKD patients' hemoglobin levels were raised with rHuEPO therapy, these patients experienced an improved sense of well-being when directly assessed by Karnofsky scores.³ In addition, patients reported better energy levels, diminished sleep disturbances (with less daytime sleepiness),⁴ improved cognitive function,⁵ and increased ability to take on the tasks of daily living.^{6,7} Higher hemoglobin levels in CKD patients have been found to correlate with better cardiovascular outcomes such as improved left ventricular hypertrophy (LVH),⁸ improved exercise capacity,⁹ and reduced cardiac ischemia during times of stress.¹⁰ Globally, patients who achieved higher hemoglobin values had lower mortality than those who did not.¹¹⁻¹³ The ability to manage anemia has revolutionized the care of CKD patients.

In the wake of these changes in anemia management, questions have emerged concerning how to set hemoglobin targets for erythropoietic therapy. Part of this debate has centered on the reimbursement system for administration of erythropoietic agents, especially as it has become clear that reimbursement strategies have a profound impact on clinical outcomes.^{14,15} The debate over hemoglobin targets, and by extension, reim-

bursement, has hinged in part on the impact of different levels of hemoglobin on cardiovascular mortality in CKD patients. Cardiovascular events are the leading cause of mortality in both CKD and renal transplant patients, and thus cardiovascular outcomes have become a principal endpoint in interpreting studies in these patients. As this debate continues, recommended hemoglobin targets continue to be updated to reflect new research findings.

A working knowledge of the basic tenets of anemia management is essential to the modern practice of nephrology. This manual reviews the factors that lead to anemia in CKD, strategies to treat anemia in different populations of patients with kidney disease, the data connecting cardiovascular outcomes in CKD with different anemia targets, and the controversies surrounding appropriate hemoglobin targets.

ETIOLOGY OF THE ANEMIA OF CKD

CASE PATIENT I

Initial Presentation

A 62-year-old woman with an 18-year history of type 2 diabetes, longstanding hypertension, and hyperlipidemia is referred to a nephrology clinic for evaluation of an "abnormal creatinine" level on routine testing.

History and Physical Examination

The patient has been followed by her family physician for many years and admits that she has not been very diligent in attending to her health. She does not report nausea and vomiting, change in appetite, or metallic taste but does admit to frequent urination and generally feeling tired. She says she "just can't get up and go" like she used to and hopes that this can be addressed with some pills.

Her medications include a calcium channel blocker (nifedipine), a diuretic (hydrochlorothiazide), and the oral hypoglycemic agent glyburide. She states that her primary physician had suggested starting her on insulin some time ago, but she has resisted because she wants to avoid injections. More recently, her diabetes