

HOSPITAL PHYSICIAN®

ENDOCRINOLOGY BOARD REVIEW MANUAL

PUBLISHING STAFF

PRESIDENT, PUBLISHER

Bruce M. White

EXECUTIVE EDITOR

Debra Dreger

ASSOCIATE EDITOR

Daryl A. Kovalich

ASSISTANT EDITOR

Laurie Garrison

SPECIAL PROGRAMS DIRECTOR

Barbara T. White, MBA

PRODUCTION DIRECTOR

Suzanne S. Banish

PRODUCTION ASSOCIATES

Tish Berchtold Klus
Christie Grams

PRODUCTION ASSISTANT

Mary Beth Cunney

ADVERTISING/PROJECT MANAGER

Patricia Payne Castle

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.

Paget's Disease

Series Editor:

Bart L. Clarke, MD, FACP

Assistant Professor of Medicine

Mayo Medical School

Senior Associate Consultant

Mayo Clinic

Rochester, MN

Contributing Author:

Robert D. Tiegs, MD

Associate Professor of Medicine

Mayo Medical School

Consultant

Mayo Clinic

Rochester, MN

Table of Contents

Introduction	2
Definition, Etiology, and Pathophysiology	2
Presenting Features, Diagnosis, and Clinical Course	3
Therapy and Monitoring	6
References	11

Cover Illustration by Andrew Grivas, MA, CMI

Copyright 2000, 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.

Paget's Disease

Series Editor:

Bart L. Clarke, MD, FACP

*Assistant Professor of Medicine
Mayo Medical School
Senior Associate Consultant
Mayo Clinic
Rochester, MN*

Contributing Author:

Robert D. Tiegs, MD

*Associate Professor of Medicine
Mayo Medical School
Consultant
Mayo Clinic
Rochester, MN*

INTRODUCTION

Paget's disease is a chronic, focal disorder of bone remodeling. Bone affected by Paget's disease is architecturally disorganized and mechanically compromised. As a consequence, pain, skeletal deformity, and fracture may develop. The goals of treatment are to control symptoms and reduce disease activity in an attempt to prevent complications.

DEFINITION, ETIOLOGY, AND PATHOPHYSIOLOGY

- **How is normal bone remodeling affected by Paget's disease?**

EFFECT OF PAGET'S DISEASE ON BONE

Normal Bone

In adults, bone continuously undergoes remodeling, providing a mechanism for repair and adaptation to stress. The bone remodeling sequence in cancellous bone involves the following steps: activation of osteoclasts, osteoclast-mediated resorption of bone, differentiation of osteoblasts, deposition of bone matrix (osteoid) by osteoblasts in an organized lamellar pattern, and mineralization of the matrix. Bundles of uniform-size collagen deposited in a parallel fashion produce the lamellar pattern of normal bone.

Pagetic Bone

Paget's disease is a focal disorder of bone characterized by increased metabolic activity and disorganized remodeling.¹ The primary defect is an increase in osteoclast-mediated bone resorption. Osteoclasts are increased in size and number; each enlarged osteoclast contains up to 100 nuclei, compared with 5 to 10 nuclei in a normal osteoclast.² Since bone resorption and formation remain

coupled in Paget's disease, bone formation is increased secondarily. In patients with active disease, the rate of bone turnover may be increased by as much as 10-fold. In Paget's disease, bone collagen is deposited in a random, disorganized fashion, producing bone that has a woven appearance. Woven bone is structurally inferior and mechanically weaker than lamellar bone and may contribute to fracture and deformity that develop in affected patients. Accelerated bone turnover also is associated with an increase in marrow fibrosis and vascularity. The clinical features depend on the degree of disease activity as well as the distribution and duration of the disease.

Histology

The histologic findings in Paget's disease are typical of a high turnover state. Pagetic bone is characterized by an increase in osteoclast and osteoblast number, increased osteoid volume, marrow fibrosis, and an abundance of vascular spaces within the marrow. Trabeculae are thickened and irregular, cancellous bone volume is increased, and the cortex is thickened due to an increase in periosteal bone formation.

Skeletal Distribution

The disease may involve only one bone (monostotic) or multiple skeletal sites (polyostotic), typically in an asymmetric distribution. The pelvis, lumbar spine, and/or femur is involved in more than 75% of patients.³⁻⁵ Other commonly involved sites are the skull, tibia, scapula, sternum, and humerus.

- **What are the theories of causation of Paget's disease?**

ETIOLOGY

Current epidemiologic data support the concept that Paget's disease results from exposure to paramyxovirus, genetic susceptibility, and the interaction of environmental factors.