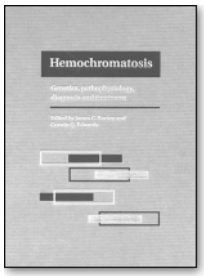
Book Reviews

Hemochromatosis: Genetics, Pathophysiology, Diagnosis, and Treatment

by James C Barton, Corwin Q Edwards, editors.

Book Review by Vincent J Felitti, MD



Medical futurists have predicted that hemochromatosis will be the cholesterol of the 21st century in terms of public notice. Discovery of the HFE gene has now shown that one in 250 Americans has the homozygous genotype for hemochromatosis—the most common genetic disease in the country despite what most physicians currently believe. The patient panel of most Permanente primary care physicians includes about ten cases of hemochromatosis.

Almost no current cases of hemochromatosis are diagnosed. Of course, many affected patients are presymptomatic because they are young enough still to be in the process of accumulating toxic levels of iron. In other patients (for reasons not yet understood), complete penetrance never manifests. But many patients with hemochromatosis are symptomatic, manifesting the myriad signs and symptoms that most physicians still do not appreciate. Cardiomegaly, fatigue, arthralgias, episodic diarrhea, hypothyroidism, arrhythmias, impotence, diabetes, and joint replacement are among the numerous presentations of iron overload. Each of these conditions has other, more common explanations; these multiple signs and symptoms perpetuate the traditional belief that hemochromatosis can be considered—indeed, dismissed—as a rare disease.

Hemochromatosis is important—and is an ideal subject for preventive medicine—because of its prevalence, its easy early diagnosis, and the probability that early diagnosis and treatment will totally prevent every manifestation. Largely because of these factors, the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC) have selected hemochromatosis as the prototype disease to be featured in a nationwide program to help practitioners move into the era of genetic disorders.

James Barton and Corwin Edwards are two American physicians with enormous clinical experience in hemochromatosis who have brought together 100 of the world's experts on iron overload to create a major monograph about hemochromatosis that will dominate the field for years to come. Their book, *Hemochromatosis*, is clearly written, evenly edited, and well made. It is also timely because it is the only monograph available in a field that is rapidly expanding; the other two books on this disorder were published in 1935[1] and 1964,[2] respectively.

The first section of *Hemochromatosis* discusses the history of this common hereditary disorder, which is the most common cause of all diseases of iron overload. The discussion of the genetics of hemochromatosis makes the important point that iron overload is the essence of the disease; and that the mechanism by which that iron overload is accomplished—genetic or not—is not the essential issue for patients. We learn that normal genetic analysis is therefore not at all reassuring when evidence shows the presence or likely development of iron overload.

Subsequent chapters discuss available diagnostic techniques, which range from serum iron saturation through tissue biopsy to magnetic resonance imaging (MRI); the limits of genetic analysis are also made clear. The chapters on clinical presentations remind us that Sir William Osler's dictum "Know syphilis and you know all of medicine" could easily be rewritten as "Know hemochromatosis and you know much of medicine." This view is quite different from what many of us vaguely recall about "bronze diabetes with cirrhosis," that end-stage triad in which delayed diagnosis causes the benefits of therapy to be lost.

The book describes various aspects of treatment, ranging from the standard of phlebotomy through the occasional need for the infused chelating agent, deferoxamine mesylate (Desferal, Ciba-Geneva Pharmaceuticals, Summit, NJ), to the need (which we hope is rare) for liver transplantation. The book also discusses ways in which infection and malignancy are caused by diseases of iron overload (in particular, unusual types of septicemia and hepatoma). Subsequent chapters discuss screening, the combination of hemochromatosis with other disorders (eg, thalassemia trait, alcoholism), and hemochromatosis in animals. Screening is of particular importance because it provides the greatest opportunity for therapy. Closing chapters discuss general problems associated with screening for genetic diseases and transfusing blood from hemochromatosis patients. Changes in blood bank regulations may soon allow this blood to be used within Kaiser Permanente (KP).

This skillful organization of knowledge into a highly readable monograph is a pleasure to use. All KP medical libraries will want this book. I suspect that many Permanente physicians will refer to *Hemochromatosis* as they start recognizing the possibility—perhaps even the likelihood—that some of their patients have hemochromatosis that is undiagnosed. To the degree that this diagnosis is facilitated, patients gain the opportunity for effective treatment of this disease. ❖

$215 ISBN 0521593808 Cambridge: Cambridge University Press, 2000.

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It's Never Easy: The Terminal Diagnosis

Review by Vincent J Felitti, MD

This teaching videotape opens with a line that will resonate with most of us: "Medical school only prepared me for about half of what I experience daily."[1] The words are spoken by a young physician who has just diagnosed a friend with a fatal illness.

This story line is the basis of this continuing medical education (CME) videotape, which is so well made that we can be proud it is produced in-house at Kaiser Permanente (KP). Moreover, the actors are our own in-house CareActors troupe, which supports educational training for SCPMG and TPMG via live theatrical productions as well as video. How many medical groups have an actors' troupe on staff? And what is the role of the arts in treating illness (as opposed to treating disease)? Although the original version of this program about coping with fatal illness was created by the KP Ohio Region, the current, revised version was developed by a nationwide KP committee. I hope they extend their work into other problem areas of clinical practice.

The videotape is divided into three segments, each depicting a major problem in practice: 1) delivering bad news, 2) coping with difficult emotions, and 3) end-of-life care and follow-up. The accompanying *Facilitator's Guide* is designed to stimulate meaningful group discussion among caregivers who view the tape. Of course, the tape can be viewed individually, but the questions posed at the three nodal points make it clear that we all would benefit from hearing the opinions of others on these difficult and conflictual matters.

It's Never Easy is an excellent prototype for thinking about the way we deal with life-threatening illness or with the complexities of disagreement within a patient's family. The tape realistically shows disagreement, passivity, anger, and agitation in family members and shows physicians not anticipating having to treat a whole family; physicians being kind; physicians being socially inept; and physicians facing hostility. The questions provided in the *Facilitators' Guide* help us explore our own emotions, the emotions of patients and their families, and the difficult problem of conveying information when denial fills the air. The tape closes by discussing the task of helping a patient live as well as possible when faced with the actuality of dying.

At a purchase price of six dollars, this videotape has got to be the best medical education buy of the year! After all, who was taught about this most-important topic in medical school? We can all be proud that this program originated as part of the Kaiser Permanente Endowed Lectureship in Bioethics at Case Western Reserve School of Medicine, where the tape was used to advance bioethical discussion among health professionals in the community. ❖

Videocassette. Producer: JoAnn Lesser. Los Angeles: KP MultiMedia Communications; 1999. $6 with instruction guides.

Showdown with Diabetes

By Deb Butterfield.

Review by Alberto Hayek, MD

"It is just diabetes. Don't worry, just take your insulin shots, follow a diet, and you will be just like everybody else." Words like these were commonly heard when I was a pediatrics house officer. In those days, children with diabetes were seen in the general pediatrics clinic. Then, with great reluctance, the pediatric endocrine clinic began to see diabetic children. It was in this medical era that Deb Butterfield was first diagnosed with childhood diabetes. This book is a vigorous statement about her own fight with Type 1 diabetes and about how a person who is motivated to change the status quo may be energized to do so by her own personal experience and by the sincere motivation to help others.

In the decades of the 1960s and 1970s, very little research in diabetes was being done in areas critical to clinical care. Current standards such as daily, multiple, home-based glucose measurements were not easy to implement. Unfortunately, we doctors played a major role in slowing the changes that allowed patients and their families to become more involved with their treatment and its outcome. Because the medical community widely accepted the intensive insulin therapy supported by the Diabetes Control and Complications Trial (DCCT)[1-3] around 1990, we might well assume that more definitive procedures to treat Type 1 diabetes would have been pursued more vigorously in the late 1990s. However, this has not been the case, and procedures such as pancreas transplantation are still not widely available to patients with Type 1 diabetes.

Out of the "health consumer" field now comes the voice of Deb Butterfield, Executive Director of the Insulin-free World Foundation. Her book, *Showdown with Diabetes*, tells the story of a dramatic treatment advance—and who better than a diabetic patient can authoritatively tell the diabetic community that great strides are being taken in the battle to actually cure Type 1 diabetes? The author's description of her improved quality of life after receiving two pancreas transplantations—the first ending in rejection—is so well described that this description serves as the subjective counterpoint to the scientific data presented later in the book. This counterpoint technique shows that in diabetic patients monitored for ten years after pancreas transplantation, complications of diabetes were reversed. Indeed, conventional views of diabetes undoubtedly limit our understanding of the full benefits of pancreas transplantation.

In the author's instance, pancreas transplantation resulted in an unexpected but clinically significant reversal of diabetic neuropathy.

Because of advocates like Deb Butterfield, we can be honest with our patients and agree that conventional treatment of insulin-dependent diabetes with multiple daily doses of insulin (whether by syringe or pump) is time-consuming, demanding, and creates constant worry about hypoglycemic coma. In the daily lives of diabetic persons, insulin allows no breaks from treatment. The great success of pancreas transplantation (today equal to that of kidney transplantation) and the more recent success of islet-cell transplantation (invigorated by results obtained in Edmonton, Alberta, Canada[4]) are the best indication that a new era in the treatment of insulin-dependent diabetes is beginning at several progressive transplantation centers. In its July 27 lead article, *The New England Journal of Medicine* published the best results ever reported for diabetic transplantation recipients: after islet-cell transplantation, all seven patients in one series became independent of the need for insulin injections.[4,5] A procedure with a former success rate under 8% has suddenly become the most promising approach to curing diabetes.[4,5] Because a major requisite step—immunosuppression—will already be in place, pancreas transplantation must now be given serious consideration for all patients with Type 1 diabetes who undergo renal transplantation.[6] We are approaching the point where stopping short of cure will seem unreasonable.

This book enlightens, provides an intimate account of the daily tribulations of living with diabetes, and allows the reader to participate in a real-life story in which a determined person makes the world a better place for people affected with chronic disease. The author is a champion of hope based on her personal knowledge of diabetes. If her book carries but one message—that perseverance, knowledge, and a passion to help others can advance medical practice—then this book can be considered an overwhelming success. ❖

New York, London: WW Norton; 1999. 264 pages. ISBN: 0393047539

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Encouragement

... encouragement increases the chance that people will actually achieve higher levels of performance.

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