

ADVANCES *in* INTERNAL MEDICINE®

VOLUME 28 • 1983

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1985年3月12日

VOLUME 28 • 1983

YEAR BOOK MEDICAL PUBLISHERS • INC.

CHICAGO • LONDON

ADVANCES in
INTERNAL MEDICINE

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Library of Congress Catalog Card Number: 42-20729

International Standard Serial Number: 0065-2822

International Standard Book Number: 0-8151-8298-8

VOLUME 28 • 1983
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Editors' Preface

The publication of this volume, the 28th in the series of *Advances in Internal Medicine*, marks the retirement from the editorial board of Dr. John S. Fordtran and his replacement by Dr. J. Thomas LaMont. To Dr. Fordtran we are most grateful for his characteristic insistence that the highest standards of clinical science dictate the selection of topics, authors and content of *Advances* articles without sacrificing their pragmatic application to clinical practice. The tenure of his editorship, although brief, was most valuable and much appreciated. To Dr. LaMont we extend a warm welcome. He has already ably taken up the baton from Dr. Fordtran for gastroenterologic topics and has brought to Volume 28 a variety of timely and fascinating reviews.

As in past volumes, we have tried to select topics that have medical breadth and depth and that are useful to all internists, both general and subspecialized. A new kind of review is introduced with this volume, one that deals comprehensively with the *total management* of a major, common condition that must be handled competently by all internists. The first of these is an article that describes the management of myocardial infarction. In subsequent volumes we hope to include a "total management" article on other conditions of similar importance.

The following outline of this volume's contents may serve to introduce each of the reviews with a brief statement of the reasons for its selection.

Circulatory Diseases

Dr. David Mirvis lays out a rational and reasonable plan for the management of the patient suspected of acute myocardial infarction; the scope of Dr. Mirvis' treatment covers from the time of entry into the emergency room until discharge from the hospital. This is not a cookbook recipe but rather a discussion of management based on known facts and explained in terms

of the basic pathophysiology of the ischemic syndrome. The management discussion is based on known risk-benefit ratios that are the consequence of various options. Proper distinctions are made between interventions of proved value and those that hold promise but are still in the research phase.

It is now generally recognized that coronary spasm occurs and may be responsible for partial or complete obstruction of a coronary vessel, particularly distal to areas of atherosclerotic disease. Studies in laboratory animals show that platelets aggregate distal to areas of minor obstruction of the coronary arteries. Such platelet thrombi dramatically increase the obstruction to flow along these vessels. Dislodgement or dissolution of such thrombi results in such obstruction being reversible. Drs. Friesinger and Robertson place the role of spasm and platelet thrombi in perspective in terms of their clinical implications. In addition, they speculate on the role of varying coronary "tone," which is under the influence of neural effectors such as the autonomic nervous system, as well as humoral factors such as prostaglandins.

Ventricular premature beats (VPBs) are frequently detected in normal subjects, as well as in patients with coronary artery disease and mitral valve prolapse. The incidence of observed VPBs varies directly with the intensity of the study to detect their presence. The prognostic implications of the presence of VPBs is related to the clinical setting in which they occur. In otherwise normal patients, they usually require no therapy other than reassurance. In the presence of coronary artery disease, the incidence and complexity of VPB is associated with a further increased risk of sudden death. In spite of this fact, there is no good data to support the prediction that decreasing the number of VPBs would favorably alter this risk. Dr. Kastor discusses in detail the presence and risks of VPBs in various subsets of patients and includes a rational approach to the treatment of each group.

Dr. Bonow and his colleagues have shown that many patients with aortic regurgitation manifest severe ventricular systolic dysfunction before the appearance of cardiac symptoms. It is these patients who frequently continue to deteriorate postoperatively. In view of these findings, Dr. Bonow presents a logical approach to the asymptomatic patient with aortic regurgitation that includes close observation with serial

noninvasive cardiovascular evaluation. If echocardiographic evidence of progressive ventricular deterioration is observed, further invasive studies are carried out and surgery may be indicated on the basis of ventricular dysfunction—even in the absence of significant clinical symptoms.

Every summer, cases of heatstroke result in considerable morbidity and mortality. The victims are often the ill-housed, elderly, and debilitated rather than the hyperactive, young athletes, although it is also common enough in the latter. Drs. Anderson, Reed, and Knochel present an informative review of thermoregulation and acclimatization, the clinical spectrum of heat illness, and its pathophysiology, epidemiology, treatment, and prevention. It is an ancient medical subject that demands constant updating. Considering its frequency and severity, it deserves the attention of all those responsible for medical care.

Infection and Immunology

Standard approaches to the management of women with urinary tract infection (UTI) need to be reevaluated and Drs. Stamm and Turck do so quite comprehensively in their timely review. Properly made urine cultures growing less than 10^5 coliforms/ml should no longer be disregarded as a contaminant in acutely symptomatic women with pyuria. Nor can we any longer ignore in urine cultures the presence of coagulase-negative staphylococci that will often be *S. saprophyticus* rather than the skin contaminant, *S. epidermidis*. In sexually active women, another ubiquitous cause of dysuria is chlamydial infections. These organisms are not yet cultured routinely by most clinical laboratories. Single-dose therapy has become a very useful and effective approach to treatment of lower, UTI although its role in deeper UTIs requires more study.

Drs. Culpepper and Andreoli point out that the majority of the glomerulonephropathies are now considered to be the result of injury due to immune-mediated events. Their classification of the glomerulonephropathies calls attention to the distinction between injury to the glomerular structure from the precipitation of circulating immune complexes (CICs) as opposed to immune complexes formed in situ at the glomerulus. The authors describe the pathophysiology of such lesions and offer possible explanations regarding the disease mechanism, including so-

dium retention and albumin wastage based on immune-mediated injury to the glomerular apparatus and secondary changes in tubular function.

Extreme sensitivity of the airways to physical, chemical, and pharmacologic stimuli is a characteristic feature of asthma and of some patients with chronic bronchitis. Various stimuli cause bronchoconstriction to a greater extent and at lower stimuli concentrations in these individuals than in normal individuals. Dr. Jay Nadel's review of this abnormal response of asthmatics provides a lucid explanation of the diagnosis and management of bronchial hyperreactivity and an appreciation of its multiple causes, both genetic and acquired.

Models of immune-induced inflammation show histamine to be an important hormone in influencing the migration of cells to a site of reaction, inhibiting the release from neutrophils of lysosomal contents and their superoxide production, inhibiting the release of histamine from mast cells/basophiles, and effecting a variety of T and B cell functions, including stimulation of suppressor lymphocytes. Drs. Rocklin and Beer present an avant garde clinical view of these newly perceived roles of histamine as a physiologic modulator of inflammation and immune processes. New modes of pharmacologic manipulation of these processes may prove highly effective in many clinical situations.

Oncology and Hematology

The production of monoclonal antibodies has resulted in an explosion of immunologic approaches to the solution of a great variety of medical problems. The diagnosis and treatment of cancer is one of these. The objective of identifying surface antigens associated with and specific for malignant cells may be achieved with the use of this brilliant new research tool. Drs. Ng, Giacomini, and Ferrone bring us up to date with the progress, as well as the frustrations, of the pursuit of this tantalizing objective, which could lead not only to remarkably accurate and early diagnosis but also to exquisitely specific therapy if the selective antibody can be hooked to a cytotoxic agent.

One of the greatest triumphs in modern medicine is the cure of Hodgkin's Disease. New insights into its mode of spread and improved techniques of radiotherapy have resulted in relapse-free survival in approximately 75% of patients. Dr. DeVita and his colleagues have provided the leadership in design of drug

regimens with a similar cure rate, an achievement described in their authoritative article.

Cure of acute leukemia is now attainable in 50% of children with acute lymphoblastic leukemia and, perhaps, in as many adults. In contrast, the majority of patients with acute nonlymphoblastic leukemia die of their disease. But the number of long-term survivors and presumed cures is increasing especially in patients under 40 years of age, a development that provides reason for optimism. Drs. Arlin and Clarkson have provided a restrained but encouraging review of the treatment of this most aggressive disease.

Gastroenterology

The radiologic evaluation of gallbladder and bile duct diseases is a rapidly changing field, as pointed out by Drs. Berk, Leopold, and Fordtran in their timely review. Ultrasound examination of the gallbladder has replaced oral cholecystography as the primary diagnostic procedure for gallstones, while the HIDA scan has become the test of choice for acute cholecystitis. Percutaneous ("skinny needle") cholangiography and ERCP are superior to the older technique of intravenous cholangiography in visualizing the extrahepatic bile ducts. This review places the indications and limitations of these newer X-ray and nuclear medicine techniques in clear perspective.

"Cytoprotection" is the newly discovered property of prostaglandins by which to protect the stomach and intestines from various types of injury. Dr. Robert, who originally described this phenomenon, summarizes the clinical results obtained with prostaglandins in protecting the gastrointestinal tract from ethanol, aspirin and other noxious agents, and discusses the possible future clinical uses of prostaglandins. Prostaglandins have a protective effect on the gastric mucosal barrier as opposed to traditional antiulcer agents which reduce acid secretion or neutralize acid in the lumen.

Drs. Bengoa and Rosenberg review the clinical indications for total parenteral nutrition therapy in patients with gastrointestinal diseases. The greatest potential application of this new technique is in chronic inflammatory bowel disease and short bowel syndrome. Parenteral nutrition has added a new therapeutic option to the management of these difficult problems. The review outlines the nutritional assessment of these pa-

tients, cost-benefit considerations, nutritional requirements and hazards of parenteral nutrition.

Patients with anorexia nervosa might be evaluated initially by the generalist, adolescent specialist, gastroenterologist, endocrinologist, or gynecologist. Dr. Drossman focuses on the protean signs and symptoms of this fascinating disorder of adolescent girls, as well as the premorbid personality. Management and prognosis of this serious condition (6% mortality) are critically reviewed, with special emphasis on the importance of combined medical-psychiatric care and careful follow-up.

Endocrinology and Metabolism

The development of computed tomography (CT) has not only led to a Nobel Prize, but has virtually revolutionized the approach to diagnosing disease in every field of medicine, and endocrinology is no exception. Drs. Genant, Turski, and Moss have reported on the ability of the CT scan to quantify bone density and thereby accurately to diagnose and determine the extent of osteoporosis. Furthermore, they have provided some of the first convincing data that with the information provided by this technique, adequate estrogen therapy may lead to the prevention and perhaps reversal of postmenopausal osteoporosis, a finding that correlates with the extensive review of this subject by Carr and MacDonald in this volume. The ability of the CT scan to detect even microadenomas of the pituitary has made this procedure the standard approach to diagnosing this increasingly recognized tumor. CT scan of the adrenal gland carries, remarkably, a 90% accuracy in diagnosing Cushing's disease, hyperaldosteronism and pheochromocytoma.

Few advances in the treatment of diabetes have excited so much interest as the recent introduction of portable devices for the continuous infusion of insulin. The published literature, however, is sparse, and the average internist remains uncertain as to the role of the "insulin pump" in the management of the diabetic. Dr. Kitabchi has anticipated the literature by contacting each of the major investigative groups studying this technique, and through preprints and personal discussions, has produced a very up-to-date and balanced review of the status of this important advance in diabetic therapy. With improvement of the technology in this field, there appears to be no question that, even recognizing the occasional dangers of hy-

per- and serious hypoglycemia, the insulin infusion pump offers a means of obtaining superior control of blood glucose. Perhaps most important, this technique may provide a means of determining whether such improved control of blood glucose will prevent or delay the devastating microvascular manifestations of both Type I and Type II diabetes.

If and when postmenopausal women should receive estrogen treatment remains an important and, unfortunately, an unanswered clinical question. In reviewing the pros and cons of this frequent problem, Drs. Carr and MacDonald have provided a balanced presentation, emphasizing the possible prevention of osteoporosis, vasomotor (hot) "flushing," and tissue atrophy that represent the potential benefits of estrogen therapy. On the other hand, the risks of estrogen therapy remain unresolved, and the possibility of increased hypertension, thromboembolic disease, and endometrial cancer must be evaluated before initiating treatment of postmenopausal symptoms. The careful, in-depth discussion of these issues by Carr and MacDonald will be of great assistance to the internist who is regularly faced with the request, if not demand, for estrogen therapy of the menopausal and postmenopausal woman.

Hypomagnesemia is a not uncommon and frequently overlooked complication of such disorders as alcoholism, malnutrition, short bowel syndrome, and diabetic ketoacidosis. In their extensive review of this increasingly recognized clinical problem, Drs. Cronin and Knochel discuss not only the pathophysiology of hypomagnesemia, but also the serious clinical consequences of low-body magnesium on a number of the more widely recognized electrolyte disorders. In particular, the relationships of hypomagnesemia to hypokalemia, hypocalcemia, and hypophosphatemia are very well covered. Similarly, the complex but clinically important relationship of magnesium to parathormone secretion and activity makes the recognition and treatment of hypomagnesemia important in any patient in whom the signs of hypocalcemia suggest diagnosis of hypoparathyroidism.

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