# ADVANCES IN INTERNAL MEDICINE

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Volume 30

# ADVANCES *in* INTERNAL MEDICINE®


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ADVANCES IN INTERNAL MEDICINE®

VOLUME 30

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# Editors' Preface

With a two-year lead time from commissioning a review article to its appearance in print, the editors of ADVANCES engage frequently in a game of crystal ball gazing. We can recall some spectacular successes. A few of our authors published their reviews on the eve of their award of the Nobel prize and several others, less publicized, appeared with equally gratifying timing when one considers the narrow zone between scientific discovery and clinical application within which we try to work. Moreover, timing has to be achieved within the additional constraints of topical interest to internists and pragmatic value to practioners.

This year, we are pleased to note, Volume 30 begins with a "bulls-eye." Two sagas in the field of oncology, infection, and immunology were evolving rapidly and were becoming intertwined. One was the story of T-cell lymphoma viruses and the other, the ominous spread of the AIDS epidemic. We knew that commissioning Dr. Gallo and his colleagues to review their spectacular studies on the T-cell retrovirus lymphomas could hardly miss. *That* story could have stopped short of AIDS and still have been a "must" for review. When the T-cell virus story spilled over to AIDS, however, and the Pasteur Institute team isolated apparently the same new T-cell retrovirus from a homosexual man with lymphadenopathy (LAV), while at the same time, Dr. David Durack was summarizing the epidemiologic and clinical picture of AIDS, we had to "stop the presses." We now begin Volume 30 with a two-chapter review of where we stand on both subjects without the benefit of a pause to collect more nuggets for our readers from the avalanche of invaluable articles appearing weekly and "still in press."

No doubt we shall need a "chapter three" very soon but, meanwhile, Volume 30 of ADVANCES carries as much as it can hold. Herewith is a summary of its contents with a brief statement about the topics and reasons for their selection.

## ONCOLOGY, INFECTION, AND IMMUNOLOGY

The above comments about T-cell lymphoma viruses and AIDS need no further expansion here. The most recent immunologic studies at this writing (July 1984) leave little doubt that the AIDS virus has been discovered, although how many variants or closely related agents there are is not yet clear. A specific ELISA test, made with total LAV proteins as antigen detects antibodies in almost all AIDS patients, should soon be available to tell who is "AIDS-positive" and who is "AIDS-negative." This could well become the Wassermann test of the 1980s.

On another subject, we call your attention to the review by Drs. Levitz and Diamond of the range of diseases produced by the ubiquitous aspergillus fungus. An agent that we once dismissed as commensal, actually as a kind of "organic dust" producing allergic or hypersensitivity pulmonary reactions, or, at most, one that grows superficially in some heavily inoculated bronchi or in a moist aerobic cavity in the lungs, we now find produces a whopping invasive fatal pneumonia in immunologically devastated hosts. In particular, the patient with myelogenous leukemia treated with marrow-blasting doses of combination chemotherapy is highly susceptible to the "new" aspergillis pneumonia, which, like mucormycosis, thrombose large pulmonary vessels and necrose the lung.

Five years ago, Dr. Edwin Beachey introduced our readers to the broadening clinical concept of bacterial adherence, the specific lectin (adhesin)-receptor interaction between bacterial surfaces and the surfaces of cell membranes that accounts for the localization of bacteria to specific host sites. In this volume, Drs. Christensen and Beachey catch up with the burgeoning literature on the modern concept of colonization and describe the molecular basis for the localization of bacterial infections. It would appear that in the future, receptor therapy, adhesin therapy, and anti-adherence drugs may become important approaches to the treatment and prevention of bacterial infections.

Infections of the genitourinary tract in women are finally receiving the attention from general internists that they deserve. The overlapping symptoms of infections of the lower genital and the lower urinary tracts cause confusion unless (as usual!) the history is carefully taken, the patient is carefully examined, specimens are appropriately examined, and cultures are

properly interpreted. As in the case of cystitis and urethritis, only complete clinical data and the response to therapy will provide correct diagnosis and management of vaginitis, cervicitis, and pelvic inflammatory disease. Vaginitis, like other "orificial" infections, presents a challenge to accurate but economical management because of its high incidence and multiple causes. Drs. Rice and Dale present a carefully documented and scholarly review that we hope internists will find useful in the primary care of their patients.

This volume's review article on a major problem of medical management is devoted to pneumonia. For the internist its management is one of the hallmarks of his skills. A wide variety of factors have made the topic of pneumonia increasingly complex. Within the hospital, pneumonia no longer seems to be Osler's "old man's friend," but rather the intensive care unit's constant enemy. The compromised host is all too often the *model* for the treatment of pneumonia in the general population, and community-acquired infections may no longer be the old-fashioned "wild" ones, but, as in hospitalized patients, suprainfections in a population that is overtreated with antibiotics. The selective advantage of this setting to antibiotic-resistant bacteria encourages their survival beyond hospital walls when respiratory infections in the community are treated promiscuously and in "shotgun" fashion, particularly with broad-spectrum antibiotics, such as cephalosporins. Drs. Parrino and Stollerman offer a review of the systematic approach to management that puts a large premium upon basic clinical skills and judgment and the clinician's emphasis upon individualized management in which clinical epidemiology and assessment of the host prevail in decision-making.

One of the most important developments in the understanding of inflammation since the discovery of prostaglandin physiology is the discovery of the leukotrienes. Only recently have we perceived this "other pathway" of arachidonic acid metabolism. The cyclooxygenase enzyme that converts arachidonic acid in membranes to prostaglandins, thromboxanes, and prostacyclines has dominated the attention of those absorbed with understanding and controlling blood clotting and tissue inflammation. It has become clear, however, that our antiprostaglandins and antihistamines are not controlling a major pathway of inflammation that is now clearly defined—the 5-lipoxygenase-mediated conversion of arachidonic acid to the 5-HETE leukotrienes. Several of these ($LTC_4$ and $LTD_4$) are potent constric-

tors of pulmonary and vascular smooth muscle and $LTB_4$ is a potent chemotactic agent and mediator of neutrophile activation. Drs. Stenson and Parker update us on what has been discovered so far about the biology of these newly recognized hormones of inflammation and their roles in immediate hypersensitivity reactions. We had better tool up on the basic science background of these substances because we are sure to see soon a barrage of pharmacologic substances designed to control their powerful biologic actions.

## CARDIOVASCULAR DISEASES

Since the introduction of beta-adrenergic receptor blocking agents 20 years ago, the number of these agents available has steadily increased as has their range of application. Doctors Hager, Messineo, and Katz clearly delineate the specific mechanism of action, metabolism and excretion of the various members of this family of drugs and relate these characteristics to their intelligent use in patients, especially in those with symptomatic coronary artery disease or hypertension.

Toxic nephropathy occurs more frequently from medications than from noxious environmental agents. With the exception of analgesic abuse, most nephrotoxins represent drugs prescribed by physicians; therefore, prevention as well as early recognition of this type of renal disease is a serious physician responsibility. Dr. Maher reviews the various drugs as well as the clinical settings that place patients at high risk for this increasingly common form of renal disease.

Cardiomyopathies are diffuse or multifocal diseases of the heart muscle capable of producing cardiovascular dysfunction, including heart failure. The usual classification divides the cardiomyopathies into the congestive (dilated), restrictive (nondilated), and hypertrophic types. Doctors Johnson and Palacios address the subject of the nondilated cardiomyopathies. This is the least common of the three groups but is fascinating to clinicians for a number of reasons. The prototype of this disease, which is amyloid heart disease, may mimic constrictive pericarditis or primary valvular heart disease. The authors draw on their rich clinical experience to describe the pathophysiology and clinical picture of this type of cardiomyopathy, which in turn will alert the clinician to the proper diagnosis.

Dr. Satler and colleagues point out that emergency cardiac catheterization with angiocardiography in patients suffering

acute myocardial infarction has shown that most infarcts are accompanied by partial or complete thrombotic occlusion of a major coronary vessel. Both intracoronary and intravenous streptokinase can result in thrombolysis in such vessels. In addition, such therapy is frequently accompanied by improvement of left ventricular function as confirmed by invasive and noninvasive studies. There are also preliminary reports of decreased mortality in treated patients. The authors evaluate the present status of this rapidly moving field of endeavor, including the importance of subsequent anticoagulation and the possibility of percutaneous transluminal coronary angioplasty in selected patients.

Although primary tumors of the heart are rare, cardiac involvement as part of metastatic disease is not uncommon. Most cardiac involvement is usually an incidental finding at autopsy. Nevertheless, in a small percentage of cases, cardiac metastases become a clinically important part of the patient's disease. Such cardiac involvement is usually in the form of malignant pericardial effusions, which may cause cardiac embarrassment in the form of tamponade or constriction. Doctors Lancaster and Ewy point out clearly that the clinical appearance of such symptoms is more common now that patients live longer with solid tumors or with diseases such as lymphoma and leukemia. In addition, treatment modalities, such as mediastinal radiation and cardiotoxic drugs, represent an added risk of serious myocardial or pericardial complications in patients being treated for malignancy.

## GASTROENTEROLOGY

One of the most important applications of endoscopy has been in the management of GI bleeding. Nearly all patients with acute upper intestinal bleeding undergo endoscopy. Dr. Gregory L. Eastwood has prepared a comprehensive review of the yield and cost-effectiveness of emergent endoscopy, with particular emphasis on the use of thermal and alsar coagulation in controlling acute upper gastrointestinal hemorrhage. Dr. Eastwood's review should help clarify a number of controversial issues surrounding this new and rapidly expanding technology.

The number of choices available for medical treatment of peptic ulcer has grown considerably since the introduction of cimetidine. Several new agents including muscarinic-receptor

antagonists, prostaglandins, sucralfate, and third generation $H_2$ blockers will soon be available in this country. Dr. Levine reviews the mechanisms of action and effectiveness of these new agents in treating peptic ulcer disease. It is a timely review, as there is little doubt that cimetidine will lose some of its market share to these newer agents.

The overall mortality of colorectal cancer has changed little in the past two or three decades. A number of studies from this country and Europe suggest that early diagnosis of asymptomatic colon cancer allows curative resection, and markedly improved 5-year survival. Drs. Winawer, Miller and Sherlock critically review the literature on screening protocols, and offer practical guidelines for the practicing physician who wishes to institute colon cancer screening in their practice or community. The key procedure is use of the Hemoccult protocol to screen for asymptomatic bleeding. Colonoscopic detection and polypectomy has assumed an important place in the subsequent management of occult blood-positive patients. The authors have provided a comprehensive and critical review based in part on their personal experiences at Sloan-Kettering Cancer Center in New York City.

## ENDOCRINOLOGY AND METABOLISM

With the increasing interest in nutrition in clinical medicine, there is a growing realization that a number of rather esoteric metals actually play essential roles in human metabolism. Iron, of course, is needed for hemoglobin synthesis, cobalt for vitamin $B_{12}$, and iodine for thyroxin; however, although not so well appreciated, the essential roles of zinc, molybdenum, selenium, and chromium are now well-established. In their review, Drs. Fitzgerald and Tierney critically discuss the nine trace metals that are known to be required in human nutrition and survey the clinical problems that result from deficiencies of each of these metals. In addition, there is at least some evidence that such metals as vanadium, silicon, tin, and even arsenic have specific metabolic functions in higher animals. It is clear that we shall continue to hear a great deal more about trace metals in human disease.

Major strides have been made in the last few years in our understanding of the pathogenesis of the bone diseases that accompany renal failure. This problem is becoming of increasing clinical importance as medical technology has prolonged the

lifespan of patients in renal failure through hemodialysis, peritoneal dialysis, and renal transplant. As Drs. Coburn and Henry emphasize in their review, the term "renal osteodystrophy," in fact, encompasses bone destruction from osteomalacia, secondary hyperparathyroidism, and osteoporosis. Effective therapeutic approaches to each of these aspects of renal osteodystrophy are available and, perhaps most intriguing, the recently recognized role of aluminum in renal osteodystrophy offers new insights into the pathogenesis and prevention of the bone disease of renal failure.

Hypokalemia is one of the most common, yet frequently unrecognized, electrolyte disorders in clinical medicine. In his review of this important problem, Dr. Knochel points out the role of diuretics as the major cause of hypokalemia and emphasizes both the predisposing factors and the means by which this electrolyte disorder can be avoided. The effects of hypokalemia on carbohydrate and protein metabolism, as well as on the function of skeletal and cardiac muscles are systematically reviewed. Dr. Knochel then addresses the question that has concerned all clinicians: should mild hypokalemia be considered a benign disorder or does it deserve vigorous therapy? As one of the leading investigators in this field, Dr. Knochel's review of the causes, manifestations, and prevention of hypokalemia will prove valuable to clinicians, regardless of specialty.

While hardly among the life-threatening diseases, impotence remains a disconcerting and, in many individuals, a serious threat to well-being. Dr. Silber has extensively reviewed the anatomy and physiology of erection and the causes of impotence. His discussion, moreover, addresses the very real problem of the emotional basis for impotence, extensively reviewing what is known about the hormonal control of libido and erection, and evaluates the therapeutic role of hormonal treatment of impotence. Finally, Dr. Silber assesses the current status of penile implants in correcting organic impotence. This is a broad, yet practical, review of a problem that is still ignored by many internists and adequately treated by even fewer.

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