ADVANCES *in* INTERNAL MEDICINE®

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Editors' Preface

IN THE PREFACES of recent issues, we have sounded the recurrent theme of *Advances in Internal Medicine*—that of updating internal medicine subspecialists as well as generalists on major conceptual scientific advances that constitute the cutting edge of state-of-the-art practice of internal medicine. Our aims for Volume 31 have not changed, but the challenge of fulfilling such ambitions has become more difficult. Some of the reasons for this difficulty are not confined to the accelerating pace of bioscience. They are also related to the broadening scope of clinical investigation. Society requires that the physician's competence extend into formal knowledge of the behavioral, economic, social, and ethical-legal aspects of medical practice. Managerial competence of medical practice includes more than biotechnical know-how. It demands that practice be of proven efficiency, effectiveness, and acceptability to individual patients and to the public at large.

In this issue, we serve our usual smorgasbord of subjects to try to gratify the sophisticated appetites of our gourmet readership. The galloping pace of immunology and immunogenetics is featured in the first few articles along with the chemotherapy of bacterial, viral, and other invasive diseases, including homografting. Specific technology such as magnetic nuclear resonance scintigraphy, sonography, and computer science is faithfully reviewed. Newly perceived diseases such as Lyme disease and polyglandular failure, and newer wrinkles in the old problems such as hyperkalemia, pulmonary embolus, and sarcoidosis, are also reviewed. The oldest clinical skill, interpreting the subjective symptoms of pain and disability, is featured as a precise instrument of modern behavioral science: the highly researched questionnaire for arthritis called "Arthritis Impact Measurement Scales" (AIMS). We wind up with our regular annual clinical management feature. This year it is one with which we are all increasingly concerned—postmyocardial management decisions.

The editors hope you will enjoy this wide range of subjects as much as we have enjoyed soliciting them from the talented authors whose specific efforts we hereby introduce.

Immunology, Oncology, and Infection

T lymphocytes play a central role in the immune response, extending from immunodeficiencies to autoimmune disorders to lymphopro-

liferative malignancies. Included in the spectrum of relevance are AIDS and the resistance or susceptibility of individuals to cancers of all kinds. Dr. Stuart F. Schlossman has long been in the forefront of research on the T cell circuit. The development of anti T cell monoclonal antibodies, much of it accomplished in the laboratory of Dr. Schlossman and his associates, has been essential to the rapid progress realized in this field. This is an outstanding review of a topic of extraordinary importance.

The frontiers of tissue transplantation seem to be limited only by our ingenuity. For example, in the forthcoming year it is estimated that as many as 3,500 heart transplants will be carried out. Bone marrow transplantation has become a common and reasonably safe procedure not only in the treatment of malignant diseases but also in the management of genetic disorders. Drs. Paul A. Keown and Calvin R. Stiller provide us with a timely review of the present state of knowledge of mechanisms of rejection of transplanted organs and the state of the art with respect to their control. This subject now touches the lives of each of us and our patients, and is addressed authoritatively by two experts.

For the well-read physician, the term oncogenes has appeared throughout the medical literature during the past few years, but for clinicians to understand the role of oncogenes in the pathogenesis of cancer has not been easy, inasmuch as most of us are not molecular biologists. Drs. Mark Colb and Theodore G. Krontiris lead the reader through the intricacies of this subject in a scholarly fashion highlighted by its clarity. The article is recommended to all who would keep abreast of this fast moving, important field.

The promise of chemotherapy for viral infections is beginning to be fulfilled, albeit progress is not as dramatic as that of the treatment of those parasites whose life is not as inextricably tied up with the host's cellular metabolism as are viruses. Drs. Vernon Knight and Brian Gilbert consider the antiviral properties of ribavirin, amantadine, rimantadine, acyclovir, interferon, enviroxime, and vidarabine and how they relate to the treatment of viral respiratory infections. The authors come up with a surprisingly diverse armamentarium and remind us that for at least influenza viruses we have surprisingly safe and effective primary practice agents.

For bacterial infections, the picture is almost more dazzling than we can afford, both financially and biologically. Manipulation of the beta-lactam ring antibiotics has resulted in an array of agents that appear to penetrate and destroy all bacteria that have some cell wall proteins capable of binding penicillin-like chemotherapeutic agents. The advantages, limitations, and side effects of this overwhelming array of penams and cephems are comprehensively reviewed by Dr. Robert Moellering, Jr., and his associates Drs. J. D. Allan and G. M. Eliopoulos.

Of the rheumatic diseases, none gives me greater pleasure to in-

clude this year than so-called Lyme disease. The story of its discovery and the elucidation of its etiology, epidemiology, treatment, and management read like a major saga of modern medicine that has been condensed into only a few years. Its presentation by those most responsible for revealing the scope and importance of this infectious-rheumatic-immunologic disease, Drs. Stephen Malawista and Allen C. Steere, is highly appropriate and most rewarding to one who has been cheering them on from the sidelines for some time.

It is not inappropriate to include Dr. Robert F. Meenan's paper on the use of the AIMS questionnaire for arthritis in this section because the major consequences of chronic arthritis are pain and disability. Furthermore, it is appropriate for rheumatologists to show us all how such subjective complaints can be measured accurately and used scientifically to evaluate treatment and management. We can expect this article to be seminal for future clinical investigation that can and should be extended into the subjective but quantifiable realm of patient's complaints. After all, from our patient interviews alone we usually know when we are or are not succeeding in our management of their illnesses.

Cardio-Pulmonary-Renal

Patients who have sustained an acute myocardial infarction have a highly variable clinical course and prognosis. This variability is the result of the basic pathophysiology of the disease process including the size and type of infarct, the extent and distribution of the underlying coronary disease and the electrical stability of the heart. Drs. David E. Bush and Bernadine Healy present a rational stepwise approach to accurate risk assessment through the targeted use of specific diagnostic procedures. The "decision tree" approach permits the reader to think through with the authors the management of these patients based on an understanding of the disease process and its inherent risks.

John S. Gottdiener critically analyzes the value of 2D echo in identifying and localizing cardiac masses. He evaluates the technique in terms of its sensitivity, specificity, and predictive validity in the setting of a given pretest probability. It is obvious that the number of false positives (too much) and false negatives (too little) can be minimized by the echocardiographer himself who must be careful and knowledgeable. Dr. Gottdiener also discusses the clinical and therapeutic implications of echo findings such as left ventricular thrombus and valvular vegetations.

Pulmonary embolism continues to be a vexing diagnostic and therapeutic dilemma for the clinician. Particularly distressing is the poor correlation between clinical signs and symptoms and the actual presence or absence of the condition. Drs. Heim and Des Prez outline the scope of the problem including the causes and risk factors at play.

They then guide the reader carefully through the proper use and interpretation of lung scans pointing out the pitfalls of over and under diagnosis of the disease in groups at varying risk. As part of the clinical problem, the authors review the diagnosis of deep vein thrombosis and the clinical correlation between this latter diagnosis and the risk of pulmonary embolism as well as the use of the diagnosis of deep vein thrombosis of the thigh as a sufficient criteria for anticoagulant therapy with or without evidence of pulmonary embolism. Therapy with heparin in various dosages and schedules as well as warfarin, thrombolytic therapy, and surgery is reviewed. The authors alert the reader to the syndrome of pulmonary hypertension secondary to chronic pulmonary thromboembolic disease. The point is made that the risks of anticoagulant therapy are frequent enough and serious enough to demand that the diagnosis of pulmonary embolism be clearly established before therapy is initiated.

The natural history and management of sarcoidosis is outlined in detail by Drs. Rebecca Bascom and Carol Johns. Using as guidelines the recommendations of the 1984 International Congress on Sarcoidosis, these authors reiterate the fact that since the etiology of the disease remains unknown, the diagnosis is a clinical one based on the compatible clinical history, biopsy evidence of noncaseating granuloma, and the exclusion of other causes of granulomatous diseases. The authors, fully recognizing the variability of the clinical course of the disease, nevertheless recommend the judicious use of steroids to resolve inflammatory lesions that severely interfere with organ function. The new diagnostic and staging procedures have proven disappointing. Bronchoalveolar lavage, gallium scanning, and angiotensin converting enzyme levels are stated to have no role in directing the clinical management of the disease. Rather, the course of the disease is best monitored with serial clinical observations, chest radiographs, and vital capacity.

Drs. Vincent W. Dennis and Roscoe R. Robinson review the physiology as well as the pathophysiology of the glomerular and tubular factors that determine the presence or absence of clinical proteinuria. They discuss the relative importance of size, shape, and electrical charge as well as preferential binding and immune complexing in enhancing or hindering transglomerular passage of plasma proteins. With this as background they then call on their clinical experience derived from following subjects with isolated proteinuria for more than 20–25 years to inform the reader of the clinical course of such patients. They classify proteinuria as persistent, intermittent, fixed, transient, orthostatic, or constant in type, recognizing that the patients may have one type at one time and another type later. Although many of these patients have underlying structural disease, the prognosis for the immediate and intermediate follow-up period remains favorable. Their recommendations for management are based on these considerations.

In this era when virtually all aspects of life have been touched and changed by computer technology the development of applications to clinical diagnosis and treatment has lagged, but a small group of pioneers has not been deterred. Among these pioneers is Dr. Robert H. Friedman who takes us on a voyage through seas he has helped chart using a cancer data management system developed by the Medical Information System Unit at Boston University School of Medicine. With conviction, he projects that computer applications in clinical medicine will be commonplace by the end of this decade.

Endocrinology and Metabolism

The increasing recognition and the probable rising incidence of hyperkalemia is making the clinician far more aware of the dangers that result from elevated serum potassium levels. In their extensive review of the causes, consequences, and treatment of hyperkalemia, Drs. Mark E. Williams, Robert M. Rosa, and Franklin H. Epstein have presented a very thorough and practical approach to this important clinical problem. Physicians may not yet be adequately aware that such commonly used agents as propranolol, heparin, the many anti-inflammatory agents, as well as triamterene and spironolactone can readily produce hyperkalemia especially in the patient with impaired renal function. Further, as Addison's disease becomes rare as a cause of hyperkalemia, the syndrome of hyporeninemic hypoaldosteronism has become the single most common disease leading to elevations of serum potassium. Dr. Williams et al. address each of these iatrogenic and clinical causes of hyperkalemia and emphasize that, if recognized, the treatment of this potentially dangerous condition is in most cases both relatively simple and effective.

Vascular disease is now the most common cause of morbidity and death in patients with diabetes mellitus, of either the insulin dependent or insulin independent types. Microangiopathy may lead to renal failure and blindness in the younger, insulin dependent diabetic while large vessel disease (especially coronary atherosclerosis) represents the major cause of death in the older diabetic. Further, atherosclerosis in the large vessels of the lower extremities is a major cause of amputation in the older diabetic. Drs. Kenneth R. Feingold and Marvin D. Siperstein present a current review of the factors thought to cause and to influence the progression of both micro and macroangiopathy. While the underlying cause of diabetic microangiopathy remains controversial, at least four factors (diabetes itself, smoking, hypercholesterolemia, and hypertension) are each independently responsible for producing the premature atherosclerosis of diabetes. In fact, in the absence of smoking, hypercholesterolemia, and hypertension, the incidence of coronary disease in the diabetic patient can be reduced almost to nondiabetic levels. This review therefore, provides the physician treating the diabetic with practical guidelines for the

management and prevention of the major causes of death in the adult diabetic.

It is increasingly recognized that autoimmune diseases play a major role in various endocrine deficiency states. Circulating antibodies against pancreatic islet cells are present in at least 80% of insulin dependent diabetics, and recent evidence indicates that these autoantibodies may actually precede the earliest clinical evidence of the insulin deficiency and resulting hyperglycemia of diabetes. It is also now realized that in addition to diabetes, antibodies against the respective endocrine organs can lead to Addison's disease, hypothyroidism, and hypoparathyroidism as well as to gonadal failure and even to pernicious anemia. These disorders, however, tend to cluster into relatively discrete clinical syndromes, the recognition of which can provide the physician with powerful predictive tools by which to anticipate further endocrinopathies in specific disorders. Drs. S. L. Rabinowe and G. S. Eisenbarth have provided a complete review of the current concepts of autoimmune endocrinopathies and have carefully classified the major types of endocrine disorders caused by autoantibodies. With the rapid advances in our knowledge of immunogenic mechanisms and their control, there is increasing anticipation that specific treatment of the autoimmune endocrinopathies may be soon forthcoming.

For the past 30 years nuclear magnetic resonance (NMR) has been an essential tool of analytic and organic chemists. Over the last decade it has been introduced into clinical medicine and is now used at many medical centers. NMR is based on the fact that certain atomic nuclei have an inherent spin, influenced in a small but measurable way by the chemical environment surrounding them, permitting the obtainment of localized chemical information. Drs. Thomas J. Brady and Jason A. Koutcher review the techniques of in vivo NMR spectroscopy and chemical shift imaging. These complementary techniques are potentially of great clinical significance. While the fundamental aspects may initially bewilder the uninitiated, the essentials of these new technologies should be comprehended by the modern clinician. Not only are they here to stay but they will become an increasingly necessary part of our practice.

Gastroenterology

Spectacular progress has been made in endoscopic management of common duct gallstones. As outlined by Dr. David S. Zimmon, the finding of an impacted stone in the ampulla of Vater is no longer an iron-clad indication for common duct surgery. It is now possible to remove common duct stones via the endoscope, thus decompressing the biliary tree. In high-risk patients endoscopic papillotomy and simple cholecystectomy may be as effective as the more traditional cho-

lecystectomy, exploration of the common duct, and prolonged T-tube drainage.

Nuclear medicine scans are being used increasingly as noninvasive techniques to study the motor function of the esophagus, stomach, and biliary tree. Drs. Robert S. Fisher and Leon S. Malmud point out that nuclear medicine studies can now be quantitated using newer computerized scanners. These tests are very useful in assessing patients with achalasia, scleroderma, diabetic gastropathy, and gallbladder disorders. The authors draw on their vast clinical experience to place scintigraphic studies of the gastrointestinal tract in proper perspective.

Drug therapy of portal hypertension in patients with cirrhosis and other liver disorders is a rapidly growing and potentially important area of investigation. Effective nonsurgical control of portal hypertension would benefit thousands of patients, and reduce the severity of variceal hemorrhage, the commonest cause of death in cirrhotics. Drs. Roberto J. Groszmann and Colin E. Atterbury review the hemodynamics of the portal circulation and the clinical effectiveness of several vasoconstrictors and vasodilators on portal hypertension and variceal bleeding. It is clear from their critical review that effective, safe drug therapy for portal hypertension will be available in the not-too-distant future.

A related complication of cirrhosis and portal hypertension is ascites. This condition is often mismanaged by internists because of unfamiliarity with the pathophysiologic mechanisms causing fluid accumulation. Drug and dietary therapy for this condition is aimed at the several disturbances of salt and water excretion that characterize end-stage cirrhotics. Drs. Thomas D. Boyer and Ira S. Goldman in their comprehensive review stress the overall management of ascites, including the place of peritoneovenous shunt.

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