

Inflammation and Diseases of Connective Tissue

A Hahnemann Symposium

Edited by

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To
the memory of

JOHN G. BILL

whose devotion to the
health of mankind
nurtured this symposium

*"The measure of a man is not solely what
he contributes to the world, but what
he inspires others to contribute."*

———ROBERTSON

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PREFACE

In the not too distant past, the connective tissues of the body received little more than passing interest from investigators in the basic sciences and from clinicians alike; they were regarded merely as supportive tissues of the body and of little relative importance to the function of other apparently more important structures and organs. However in recent years the recognition and study of the so-called "collagen" diseases has stimulated interest in these tissues, and indeed it has been shown that these tissues are of major importance in the normal body physiology. In addition, the isolation of cortisone and the subsequent synthesis of this compound as well as other chemical substances having a closely related structure have led to intensive investigation of the biochemical alterations in diseases of connective tissues and have provided effective pharmacologic agents for their therapy. However, because the understanding of these processes is still in its infancy, it seemed particularly appropriate to arrange a symposium devoted to a discussion of current aspects of the biochemistry and functions of connective tissues and to the pathogenesis and therapy of the diseases of these tissues. Investigators from the United States and abroad, whose interests ranged from basic biochemistry to clinical management of patients, from immunology and bacteriology to pathology and pharmacology, were invited to contribute to the symposium, which was held in Philadelphia in December 1960. Each investigator presented one or more papers and participated in the panel discussions which followed each series of papers on a given subject. The discussions were transcribed from tape recordings and were edited by the editors of this volume. It was hoped that through this type of program the clinicians might obtain a better understanding of the fundamental abnormalities of these diseases and the basic scientists a greater appreciation of their clinical implications. The biochemical, pathological and immunological abnormalities were discussed at the beginning of the symposium, and it is apparent that much has been learned about these mechanisms. It is also apparent that these mechanisms are extremely complex and that further intensive investigation will be necessary to clarify them. In addition, it appears that many of the immunological phenomena observed in the collagen diseases are not causative factors but rather results of the diseases. It is yet to be determined

whether certain of these diseases are actually due to antigen-antibody reactions, although at the present time this is the favored theory.

Subsequently, the participants discussed the pharmacology and metabolic actions of anti-inflammatory steroids. An exciting development was the report that in addition to separation of the sodium and water retaining effects from the anti-inflammatory effect, it may be possible to abolish certain other undesirable properties of the synthetic anti-inflammatory steroids. Of course we must await further confirmatory trials in humans, but the reported data suggest that indeed it may be possible to synthesize an anti-inflammatory steroid which will have minimal effects on other biochemical processes. The development of such a compound would have extremely widespread basic and clinical implications and applications.

In the last two days of the symposium, the use of various anti-inflammatory agents in the therapy of the collagen diseases was discussed. Anti-inflammatory steroids are usually effective in abolishing the acute manifestations in many of these disease processes, but it was disappointing to hear reports of unrelenting progression of joint damage in patients with rheumatoid arthritis and of valvular disease in patients with rheumatic fever. Such reports were counterbalanced at least to some extent by others of the effectiveness of these agents in the treatment of lupus nephropathy, a process thought until recently to be unaffected by steroid therapy. Although there was not complete agreement among the participants about the effectiveness of the steroids, the favorable studies were well controlled and apparently valid. In these studies, the principal determinants of positive response were the high dosage and long duration of steroid therapy; this observation offers hope that more satisfactory results can be obtained in patients with rheumatoid arthritis and rheumatic fever, since in these two diseases therapy usually has been given at minimal dose levels or for only relatively short periods of time.

In addition, the so-called antimalarial compounds appear to offer considerable promise as effective therapeutic agents for certain connective tissue diseases, and the reports on such compounds should stimulate research into the as yet unstudied biochemical abnormalities underlying these conditions. These data also suggest that it may be possible to synthesize other nonsteroidal compounds which may in the end prove to be the agents of choice in the therapy of the collagen diseases.

Finally, some of the undesirable effects of steroid therapy were discussed. Infection, activation of peptic ulcer disease and the development of mental aberrations, as well as many other effects, must always be kept in mind, but it is also apparent that with careful and intelligent use of these compounds and institution of appropriate prophylactic therapy as indicated, the frequency and seriousness of these effects will be greatly reduced.

Even from this brief résumé of a few of the major areas discussed by the participants, it must be apparent that there is still much to be learned. In fact, in many areas only the outward manifestations of a process are presently known; in others we are beginning to understand some of the internal mechanisms, and the excellent presentations of the participants in this symposium are powerful aids to our understanding.

Many other investigators and clinicians are concerned with the problems represented here. We hope that the papers and discussions in this volume will be of interest to them and will serve to stimulate further investigation. We hope that this symposium will also be of value, because of its large number of references to related areas, as a summarizing source of information about connective tissues and their diseases.

LEWIS C. MILLS, M.D. and JOHN H. MOYER, M.D.

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