Book Reviews


The Archives have had the good fortune to publish a number of original papers from the Pharmacological Institute of the University of Freiburg im Br. during the last few years. Dr. Schmutzler was co-author of many of them. In the present monograph he summarizes the experimental results concerning histaminase-liberation.

The discovery which initiated the investigations discussed in the present monograph, was that the histaminase activity of guinea pig plasma is strongly increased during anaphylactic shock. This finding invalidated the earlier results of histamine determinations in guinea-pig blood during anaphylaxis. The true histamine concentration cannot be determined unless a suitable histaminase inhibitor is applied to the animal shortly before challenge or to the blood immediately following withdrawal.

Schmutzler could show that histaminase activity in anaphylaxis is dependent on the kind of the antigen, ovalbumin eliciting the highest, bacterial antigens the slightest increase. In anaphylatoxin shock in the guinea pig there is a slight increase only. The histaminase level in Forssman shock remains unchanged. Anaphylatoxin is a potent histamine liberator, therefore, this result shows that the increase in histaminase activity cannot be caused by histamine. This could be corroborated by giving histamine directly, there was no increase of the histaminase level in histamine shock. In passive anaphylaxis, the increase of histaminase level is dependent on the relation of antibody to antigen dose. It is interesting to note that Schmutzler found certain dose relations which, suitable timing presumed, produced a significant histaminase increase without plasma histamine increase and shock. Addition of the antigen to the blood of sensitized guinea pigs in vitro does not lead to increased histaminase activity. The author concludes that histaminase in anaphylactic shock is liberated from an organ. In ingenious experiments he proved that the source of histaminase is the liver. Furthermore, he demonstrated that intravenously injected heparin produces an increase of the plasma histaminase activity in guinea pigs (and so do certain other polyanions), similar to that seen in anaphylactic shock. The effect of these substances is dose dependent and they act solely on the liver. A large dose of heparin (500 IU/kg) exhausts the histaminase store of the liver within 2 min. During anaphylaxis only about 10% of the liver histaminase is liberated.

The localization of histaminase in the liver cells and its enzymatic properties were also thoroughly investigated.

These thorough investigations, which are clearly described, open promising avenues for future research. P. Kallós, Helsingborg

According to the publisher’s advertisement, this book is aimed to ‘cover all existing knowledge concerning lupus erythematosus (both in the discoid and systemic forms) and its relationship to other closely allied disorders such as rheumatoid arthritis’. E. Dubois has been particularly qualified to conduct such an ambitious program, being the director of the Collagen Diseases Clinic, Los Angeles County General Hospital, and having ‘personally observed 520 cases of this illness (systemic lupus erythematosus, SLE) and approximately half that number of cases of discoid lupus (DLE) and the intermediate forms’. Thirteen co-writers have assisted him in producing ‘the most authoritative text available on this ailment’.

The volume is introduced by a chapter on the history of DLE and SLE, written by J. H. Talbott. It arises interest not least through the generous quotations of earlier investigators who have given essential contribution to our knowledge about these syndromes. B. Cruickshank then gives a thorough descriptions of the basic pattern of tissue damage and pathology of SLE. He pays particular attention to the hematoxylin-stained bodies, being a less widely known lesion than fibrinoid but present in almost any affected tissue and much more specific than the latter change. The text contains many valuable differential diagnostic remarks. The pathology of the kidney in SLE has been devoted a separate chapter by V. E. Pollak and C L. Pirani, known for their careful biopsy studies and their high-dosage corticosteroid regimen in the treatment of SLE nephritis. E. Dubois and J. D. Arterberry discuss the etiology of DLE and SLE. They accept a background of hereditary dysproteinemia in both syndromes. It may be objected that the presence of hereditary factors in discoid LE has not yet been sufficiently explored. The authors suggest that the basic hereditary dysproteinemia might be superimposed by a chronic infection (virus?) or by a metabolic defect, because only a limited number of individuals from a similar genetic background eventually develop SLE or related disorders. External influences such as sun exposure, drugs, and infections have been widely accepted as triggering factors. I. R. Mackay extends the autoimmune aspects of SLE and outlines the classic forbidden-clone hypothesis of Burnet. P. A. Miescher, Naomi Rothfield and Annatina Miescher give a review of the immunologic phenomena seen in patients with SLE. Unlike Mackay, these and several other contributors to the volume are sceptical of the direct pathogenetic significance of antinuclear factors and other autoantibodies. McGehee Harvey and L. Shulman present their experience of the chronic biologic false-positive test for syphilis and SLE – demonstrating that the manifestations of SLE often pile up successively during years in predisposed individuals. The description of the clinical picture and pathology of DLE has been entrusted to two dermatologists, J. H. Epstein and D. L. Tuffanelli. E. Dubois himself is responsible for a most comprehensive chapter on the clinical picture of SLE. All symptoms and signs encountered in this multi-facetted syndrome are described in detail and in a critical way. The author calls attention to the extreme variability of the skin lesions and to the joint affection, being found in more than 90% of the patients and often being indistinguishable from ‘definite rheumatoid deformity’ (26% in Dubois’ series). He points out the significance of widespread arteritis giving rise to so different manifestations as gross psychosis, ulcers of the legs, and aseptic bone necrosis. This latter finding was first described in SLE by Dubois and Cozen (1960) and was observed in 26 patients of the total series of 520, the commonest localization being the femoral head. The chapter is concluded with a section on marriage and pregnancy in SLE, in which the author shows a judicious approach to the difficulties in the life of female patients with SLE.
In the following chapters, Dubois discusses the relationship between DLE and SLE, and between SLE and rheumatoid arthritis, respectively. He vigorously defends the standpoint that these syndromes are closely related, both clinically and etiologically. Dubois is reluctant to accept the concept of lupoid hepatitis as an autoimmune syndrome in between active chronic hepatitis and SLE (Mackay, 1956). He believes that such cases are essentially patients with SLE who contract virus hepatitis because of their general susceptibility to infections. Whatever the primary cause of hepatitis, however, a pre-

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disposition to autoimmunity is, in the opinion of the reviewer, a prerequisite for the self-
perpetuating liver destruction in all these variants of chronic hepatitis.

The LE-cell phenomenon is described in detail in a special chapter. Dubois points out, with right, that the unspecificity of the LE-cell phenomenon claimed by some workers might partly be due to the false interpretation of pseudo-LE-cells as true LE-cells, the latter being characterized by the homogenous hematoxylin-staining inclusion bodies. On the other hand, the LE-cell test may be repeatedly negative also in otherwise classical cases of SLE.

The significance of the LE-cell phenomenon as a diagnostic criterion of SLE is further settled in a chapter on differential diagnosis, criteria for diagnosis, and classification of SLE. Dubois states that ‘all patients with unequivocal LE cells on two or more occasions have definite SLE except for those classified as ‘Variants of SLE’ (rheumatoid arthritis, lupoid hepatitis, and drug-associated SLE)’. Patients with a negative LE-cell test (126 of 520 cases in Dubois’ series) were classified as definite, probable and possible SLE depending on the amount of specified major and minor criteria. Dubois’ approach is of interest in view of the need of internationally accepted criteria for the diagnosis of SLE. However, the reviewer doubts that the majority of clinicians and investigators would accept the diagnosis of definite SLE merely on the basis of two positive LE-cell tests. It could also be discussed why two other major plus two or more minor criteria would be necessary to classify a case as definite SLE, when typical ‘wire-loop’ lesions are found in the kidneys on biopsy or on post mortem. Finally it could be seriously questioned why ‘fractured short frontal hair’ should be enumerated as a major criterion side by side with the characteristic histological lesions – the specificity of this sign having obviously not yet been the subject of systematic investigation.

In a following chapter, Dubois gives an exhaustive account of his method of management of DLE and SLE. Dubois has been an early spokesman for individual corticosteroid dosage, not hesitating for enormous amounts of cortisone or its equivalents in critical situations. The inclusion of phenylbutazone in the therapeutic armamentarium, however, appears hazardous to the reviewer, who has seen severe flare-ups of the disease process in several patients with SLE treated with this drug; also the trial of a new drug in fashion, indomethacin, would seem an unnecessary experiment. There are both theoretical and empirical reasons to avoid drugs not urgently needed for suppressing disease activity (preferably corticosteroids) and for combatting complications (antibiotics against infections) – as Dubois himself stresses in other passages. According to Dubois, the overall prognosis of SLE has improved, partly because of the introduction of corticosteroids in the therapy, partly because many milder cases are now being recognized. The patients nowadays less often succumb to acute exacerbations but live for a sufficiently long time to develop progressive renal damage – uremia ranking the list of primary causes of death.
It remains for the reviewer to acknowledge that the goal of the editor’s ambition has been reached with a good deal of perfection. Dubois has through his own contributions and by assembling a competent group of specialists on various aspects of discoid and systemic lupus erythematosus created a standard work which will be consulted by most investigators in the field of autoimmune disorders and one would hope, also by all clinicians who have to attend patients with these syndromes.

T. Leonhardt, Vänersborg