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Systemic Lupus Erythematosus [*Abridged*]

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Classification Criteria for Systemic Lupus Erythematosus, with Particular Reference to Lupus-like Syndromes

Diagnostic criteria define the mode but exclude the fringe, the fruste and the früh; they are useful practical weapons for the purpose in hand. Just as history books tell one more about the author's prejudices than about history, diagnostic criteria tell one more about widespread beliefs than about the disease; the most reliable mouthpiece of the disease is the individual patient, since there are as many diseases as patients. It is convenient, however, for scientific and sometimes for therapeutic purposes, to group these similar cases together. Thus we make diagnostic pigeon-holes for two purposes:

(1) Scientific grouping for detailed analysis; this may be grossly impractical, but valuable scientifically: examples include criteria for population surveys and criteria for comparison of serological, pathological and radiological data.

(2) Practical reasons—prognosis and treatment. There is little reason to separate two similar types of disease if prognosis and treatment are the same. We need to differentiate if there is more than a qualitative difference in prognosis or treatment between two groups of patients.

The process of making such criteria involves a series of steps: (*a*) Proposals by experienced clinicians. (*b*) Discussion of sensitivity and specificity. (*c*) Testing of criteria against, for instance, SLE patients and 'not-SLE' patients. (*d*) Revision of criteria. (*e*) Validation of criteria and follow up of patients to confirm prognosis and exclude other diagnoses.

Systemic lupus erythematosus has always needed such criteria. The Medical Research Council Survey published in 1961 used a comparatively simple set for a therapeutic review demanding disease activity. Dubois (1966) has recommended a more complicated set drawn up at Johns Hopkins University School of Medicine. The World Health Organization recently convened a group to discuss criteria in the connective tissue diseases, chaired by Dr L E Shulman of Johns Hopkins University School of Medicine in Baltimore.

This group, building on previous work by the American Rheumatism Association Subcommittee, by Professor Sitaj of Piestany and others, have put forward proposals to the WHO which will doubtless soon be published. These involve combinations of major and minor criteria defining 'systemic lupus erythematosus' as well as other combinations defining a category of 'probable SLE'. In the application of such criteria it is necessary to exclude other diseases and other causes of individual signs such as drug rash or pyrexia due to intermittent infection. Adequate definition of each criterion must be made and adequate witness or attestation must be demanded. Even then proposals such as these are only provisional and need validation on a world-wide scale; it is hoped that arrangements for this can be made in the near future.

Standardization is also needed for biological tests. There are many different antinuclear factors, and their methods of detection vary considerably in sensitivity. The standard method described by Holborow in 1957 (Holborow *et al.* 1957) and

since employed by him at Taplow used calf thyroid substrate. Other methods, for instance using rat liver imprints, may show a sizeable incidence of positive individuals even in population controls.

Lupoid-like Syndromes

I will briefly deal with two of these (omitting discoid lupus) and mention our experience of rheumatoid-like arthritis and SLE.

Drug-induced SLE-like syndromes appear in association with a mere handful out of the thousands of drugs used; only in a very small proportion of the people who take these do they cause the production of antinuclear factor with or without certain clinical manifestations of this protean disease. In some instances we may be dealing with unrecognized genuine lupus patients who by chance have been given one of these drugs, but in general most patients on such drugs who develop antinuclear factor have few other manifestations of SLE and when the drug is discontinued these manifestations and the antinuclear factor disappear.

Lupoid hepatitis: Most people are now beginning to feel that this is essentially hepatitis with abnormal serological reactions rather than systemic lupus with hepatitis and the prognosis is that of the hepatitis rather than determined by any of the lupoid manifestations. Some help with this group may be given by the demonstration of smooth muscle antibody described recently by my colleagues at Taplow (Johnson *et al.* 1965) and confirmed elsewhere. Antibody to bile canaliculi and to certain glomerular components are often associated. As Johnson *et al.* (1966) have shown, if patients with hepatitis are divided into those with probable lupoid hepatitis, possible lupoid hepatitis and those without, there is close correlation with this smooth muscle factor. This antibody was not found in cases of systemic lupus erythematosus or in the small series of controls using the calf thyroid method. This serum factor may prove to be of considerable use in the detection and definition of lupoid hepatitis.

Rheumatoid-like syndrome associated with SLE: While classical and definite rheumatoid arthritis patients show antinuclear factor in 22% of cases (Ward *et al.* 1964), this does not seem to be particularly associated with systemic disease or more serious outcome, which is that of rheumatoid arthritis and not of SLE. Cases of SLE, however, sometimes present with or develop rheumatoid-like features. Usually these are mild and transient without erosions. Any rheumatoid-like arthritis which remains free of erosions for two years or more should be regarded as doubtful and more likely not to be rheumatoid arthritis. Occasionally, however, in bona fide SLE, chronic changes ensue, as illustrated by a patient showing the development of ulnar deviation, associated, like ulnar deviation in Jaccoud's syndrome, with hook erosions and subluxation; at post-mortem there was certainly some synovitis and cartilage erosion but histologically this was unlike that seen in typical rheumatoid disease even on steroid medication. The typical synovitis as seen in pre-steroid days was a benign mild lesion with few infiltrating cells and a surface layer of fibrin. My feeling is that such patients do not have rheumatoid arthritis, but may develop a chronic type of fibrosing synovitis leading to a condition somewhat like that of Jaccoud's syndrome, following repeated attacks of rheumatic fever (Bywaters 1950), but in this case stemming from lupus synovitis. This does not seem to be adequately recognized. It is another example of the close similarities between these diseases of connective tissue and the necessity for agreed criteria.

In summary, I have tried to stress the importance of agreed and validated criteria in the definition of this group of diseases, which will help both with comparisons between centres and in defining serological and other manifestations.

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Experimental Aspects of Systemic Lupus Erythematosus

Systemic lupus erythematosus is a disease remarkable for the variety of serological abnormalities with which it is associated. Of these the most constant and perhaps the most characteristic are the autoantibodies found reacting with cell nuclei. Experimental interest in these serological abnormalities – and in the antinuclear antibodies as a typical case in point – centres on two main