EDITORIAL

Bone Marrow Examinations and the "L. E." Cell

CAREFUL examination of bone marrow aspiration material has recently uncovered some developments of unusual interest. One may mention the finding by Sundberg and Spink\textsuperscript{1} of granulomatous lesions in brucellosis and the more recent finding of somewhat similar lesions by Hovde and Sundberg\textsuperscript{2} and by Schleicher\textsuperscript{3} in infectious mononucleosis. These lesions were discovered by employing heparinized material and sectioning the fixed material in Zenker's solution.

Another "ten-strike" from Minnesota is the finding by Hargraves and co-workers\textsuperscript{4} at the Mayo Clinic of what appears to be a specific cellular abnormality (the "L. E.") cell) in the marrow of patients with disseminated lupus erythematosus. Marrow preparations are heparinized routinely at the Rochester clinic and the failure of other observers to note the abnormal cells previously is undoubtedly due—at least in part—to the common practice of making smears directly from unmodified marrow aspirates.

In 50 cases of disseminated lupus, Hargraves found a highly unusual picture involving the marrow granulocytes. Within the cytoplasm of these cells, a very large mass of amorphous material was present. This caused an extreme degree of distortion of the nucleus, giving the cell a highly bizarre appearance. The lobes were thinned out and pushed to one end of the cell by the apparently ingested material. This striking phenomenon inevitably invites speculation.

Acute lupus erythematosus has been variously described as a generalized vascular disease, a disorder of the collagen system or a "system" disease. It may be related, although this is by no means certain, to dermatomyositis, periarteritis nodosa, and to rheumatoid arthritis. These conditions have the common denominator of an unknown etiology, a more or less generalized character and progressive disability. Until this work from the Mayo Clinic, no specific laboratory test for disseminated lupus was present and one had to make a reasonably good deduction by adding up a combination of such factors as debility, fever, joint pains, heart murmur, splenomegaly, leukopenia and rapid sedimentation rate, in the absence of any evidence of subacute bacterial endocarditis. The finding of "L. E." cells in heparinized, oxalated, or citrated marrow seems to represent the answer, until newer developments appear, for a specific test.

Hargraves found two types of previously undescribed cells in marrow material. The "tart" cell, a histiocyte with a large "secondary" nucleus, was present in a variety of conditions but was found chiefly in severe debilitating diseases of various types. Except for its finding in one case of multiple myeloma,\textsuperscript{7} the "L. E." cell was seen only in disseminated lupus. Various stages in the development of the cellular abnormality could be visualized, particularly in supravital spreads. Of greatest interest was the clustering of several polymorphonuclear cells (chemotaxis?) about a mass of material, apparently ready to engulf it. These findings have been confirmed by Hasenick and Sundberg\textsuperscript{5} and Sundberg and Lick.\textsuperscript{6}

The nature of the large, round amorphous mass engulfed by the granulocytes
has thus far eluded investigation. It is purplish in color and fairly homogeneous. Morton showed that it gave a positive Feulgen reaction, thus suggesting a nuclear origin. Other histochemical studies in our laboratory reveal that ribonucleoprotein of cytoplasmic origin may also be present. Glycogen, lipids, acid and alkaline phosphatases appear to be lacking. These features may indicate, as Haserick and Sundberg have already pointed out, that the ingested material is lymphocytic in nature.

Sundberg and Lick also found "L. E." cells in the blood of 3 of 4 cases of the disease. The anticoagulants were added to venous blood; this was centrifuged and buffy coat smears prepared. In his more recent studies, Hargraves exposed normal marrow material to the plasma from a patient with disseminated lupus and characteristic cells were observed after short periods of incubation. This indicates that an abnormal substance is present in the circulating blood of patients with disseminated lupus.

That the observed phenomenon is an artifact somehow induced by an anticoagulant seems hardly likely. It is reminiscent of the development of toxic granulation and vacuolization in granulocytes when exposed to antigen and antibody or when already sensitized granulocytes are exposed to antigen. Hargraves speculates upon a possible hypersensitivity phenomenon. In any event it is clear from these developments that not only has a new diagnostic test been evolved but an entirely new avenue of investigation opened up for the study of the etiology and pathologic physiology of disseminated lupus.

WILLIAM DAMESHEK
MARVIN L. BLOOM

REFERENCES

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WILLIAM DAMESHEK and MARVIN L. BLOOM