EDITORIAL

ACTH and Its Hematologic Impact

ALTHOUGH new therapeutic methods follow one another in bewildering succession these days, it is probably safe to say that nothing more startling than ACTH will enter the medical horizon for a long time to come. From the time of Hench's announcement[1] in April 1949 of the almost miraculous effects of cortisone in rheumatoid arthritis, wonder has piled on wonder as one disease after another has been strikingly affected.[2] Although the mechanisms underlying the therapeutic improvement in such nonhematologic conditions as rheumatoid arthritis and disseminated lupus are by no means clear, there is at least a degree of rationale for the results seen in certain hematologic conditions. Some of these are reported briefly in the abstracts of the recent (April 30, 1950) meeting of the Blood Club in Atlantic City and appear in this issue (pp. 785–792).

The results noted in the leukocytic proliferative diseases, notably in lymphocytic leukemia and lymphosarcoma,[3, 4] and in acquired hemolytic anemia associated with abnormal antibodies in the blood serum,[5, 6] had already been foreshadowed in the publications of Dougherty and White.[7] These investigators demonstrated lympholysis in rats following the use of pituitary and adrenal cortical extracts and hypothecated a reciprocal relationship between the adrenal cortex and the lymphoid system. They showed further the close relationships of the lymphoid tissue to serum protein, more particularly globulin, and to antibody formation. Simultaneously, Selye's[8] often revolutionary concepts regarding the effects of stress indicated such relationships further, and emphasized the reciprocal relationships, during the "alarm" reaction, between the granulocytes on the one hand, and the lymphocytes and eosinophiles on the other. These relationships had often been noted by clinicians in acute pyogenic infections and in such nonspecific reactions as those induced by milk, turpentine and the like. The standard response was always a rise in polymorphonuclears, a simultaneous reduction in lymphocytes and a disappearance of eosinophiles. These various studies indicated that the use of pituitary and adrenal cortical extracts might conceivably produce some effect in the proliferative white cell disorders. That such is actually the case is evident from the results already obtained, which show that definite, although temporary, beneficial effects often follow the use of ACTH and cortisone in acute leukemia.

Multiple myeloma (aleukemic plasmacytic leukemia) may also be suitable for ACTH therapy since the plasma cells are perhaps peculiar lymphocytes and produce an abnormal protein. Preliminary results in some cases already indicate a striking effect on these abnormalities.[2, 9]

Of perhaps even greater interest are the results in acquired hemolytic anemia with circulating abnormal antibodies. Dougherty and White noted an increase in antibody titer with single doses of hormone, and postulated from this that antibody was produced in lymphoid tissue. Other investigators[10, 11] failed to confirm these early studies and, indeed, the striking reduction in antibodies taking place

with continued ACTH therapy seemed to negate Dougherty and White's results.[5, 6] However, it is possible that the "chronic" or continued use of ACTH might lead to a depletion of antibody-forming tissue after an initial stimulation. These results are of particular interest and of potentially great value in the hemolytic anemia of lymphocytic leukemia and lymphosarcoma, where a "double target" is present for ACTH, i.e., the lymphoid hyperplasia and the abnormal antibody. The usual therapeutic methods in such cases are as a rule very unsatisfactory, but the results thus far obtained with ACTH indicate that striking temporary remissions may occur, with the added possibility that antibody formation may be controlled by continued maintenance therapy.[6]

The reticulocytosis and thrombocytosis which often develop with the use of ACTH,[4] even in the presence of apparently complete displacement of the marrow by leukemic cells, might indicate that the adrenal cortical hormones had a stimulatory effect on the marrow, while at the same time depressing lymphocytic tissue. This is again indicative of a possible reciprocal effect upon bone marrow and lymphoid tissue, and brings to mind the erythrocytosis of Cushing's syndrome and the anemia of Addison's disease, as well as the sex differences in red cell counts. It is indeed possible that in ACTH and cortisone we have actual marrow *stimulants* which thus far have unfortunately been lacking. This suggests that the hormones might be given a trial in hypoplastic anemia.

In any event there can now be no question that the hematologist has been thrust, willy-nilly, into the turbulent waters of endocrinology. Conversely the endocrinologist must perforce learn something about hematologic problems—or are most of the unsolved problems in medicine simply variations on the broad theme of the general adaptation syndrome of Selye,[8] to be mediated through hormonal means?

Truly, we live in a hectic era in which the eternal verities themselves seem to be toppling.

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