ACTH and Adrenalcorticosteroids in the Treatment of Ulcerative Colitis

LOUIS ZETZEL, M.D., and HARVEY L. ATIN, M.D.

The use of ACTH and cortisone in the treatment of patients with ulcerative colitis, though originally based on theoretical considerations, has come to rest on the practical needs and results obtained. The evaluation of the effectiveness of any therapeutic agent in such a disease is made difficult by the variability of its natural course and the heterogeneity of statistical data available for comparison.

In an effort to provide a baseline for the natural history of ulcerative colitis as seen within the relatively stable confines of a single medical institution, the clinical course of 244 out of 245 patients with ulcerative colitis observed at the Beth Israel Hospital between 1930 and 1950 has recently been reviewed and reported after an average follow-up of approximately 12 years. The introduction of antibiotics and sulfonamides in the 1940s produced only a slightly better control of the disease than was possible in the previous decade. At the end of this period of observation, the following conclusions could be made—20 per cent were well, 20 per cent were having mild recurrences, 20 per cent were experiencing serious exacerbations, 17 per cent were relatively asymptomatic after definitive surgery, 3 per cent had a malfunctioning ileostomy, and 20 per cent were dead.

It is against this background of a well-documented past experience that we have attempted to assay the role of corticotropin and corticosteroids, first introduced in 1950, not only in securing a remission but in altering, if possible, the natural course of the disease.

METHODS

ACTH was the preparation most commonly employed initially,
with 20-80 units in aqueous form given daily in an intravenous drip over 8-12 hours, or 80-120 units intramuscularly in aqueous or gel form divided into two equal doses. When first introduced into clinical practice, the continued intramuscular use of ACTH often resulted in a progressive loss of effectiveness, at times as much as 50 per cent, when compared with the intravenous approach.\(^5\) With the development of more purified preparations this discrepancy between the two methods of administration has diminished.

When cortisone was first made available, some of its low effectiveness in relation to ACTH was justifiably attributed to inadequate dosage. In this series, cortisone was given initially in daily doses of 200-300 mg; with gradual reduction, as remission was obtained, to the usual maintenance level of 25-75 mg.

Prednisone or prednisolone was given orally in a dosage of 45-60 mg, and was thus presumed to be four or five times more effective by unit weight than cortisone. The lessened tendency of these synthetic analogues to produce disturbances in electrolyte equilibrium made it unnecessary to add the unattractiveness of a low-sodium diet to the formidable problem of a low-residue regimen in patients with anorexia and malnutrition.

Not included in the series are 3 patients with localized ulcerative proctitis who received 50 mg. of hydrocortisone hemisuccinate dissolved in 30-60 cc. of saline and given as a daily retention enema over 2-3 weeks. The results were locally favorable, without any undesirable constitutional reactions. However, in all 3, relapses occurred within three weeks of stopping treatment.

RESULTS

These drugs were employed in all instances in addition to the generally accepted components of a comprehensive medical program, such as diet, rest, sedation, transfusions, antibiotics, and superficial psychotherapy. In spite of the associated therapy, the results obtained could in most instances properly be attributed to the use of ACTH and corticosteroids, in view of the dramatic and reproducible nature of the response and its direct relationship to the preparation and dosage as the only variables introduced.

The use of these drugs was limited to patients who were considered to be in need of adjuvant therapy. This was most urgent in individuals with the acute fulminating form of the disease, as well as in those with severe chronically active colitis who had