York State, and the eastern United States in general, emerging from the aforementioned researches, has very recently been given a sounder chronological perspective through the radioactive carbon studies of Libby and Arnold, of the University of Chicago. The dates they have derived from charcoal samples, taken from hearths on archaic period sites in New York during the course of our excavations, indicate an antiquity for the earliest occupation of more than 5,000 years of elapsed time. Other equally startling dates have been obtained.

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Technical Papers

Effectiveness of Cortisone Administered Orally[1]

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Since the report by Hench and his associates (*1*) that cortisone (Kendall's Compound E) has great antirheumatic properties, much research has been conducted to learn (1) how this hormone effects its results, and (2) how cortisone might be used with the greatest practical value as a therapeutic agent. In the latter category there have been studies to determine whether cortisone is effective when administered in ways other than intramuscularly, as it was used originally. Scarcity of the hormone has limited research but recently, through the kindness of its medical director, James Carlisle, Merck & Co., Inc., has supplied us with a small quantity of tablets (each 100 mg) of cortisone for clinical trial.

This preparation of cortisone has been tested in 4 patients with rheumatoid arthritis. The dose commonly employed for intramuscular injection was used orally, namely, 300 mg the first day, 200 mg the second, and 100 mg daily thereafter. In 2 patients the dose was increased to 200 mg daily, following a few days of 100-mg dosage.

In all patients cortisone taken in tablet form effected impovement in the rheumatic disease. In 2 patients cortisone tablets were given for only 10 days; the patients improved significantly from the 2nd day of treatment and relapsed promptly after cessation of the drug. The 3rd and 4th patients received tablets of cortisone for longer periods, 20 and 19 days, respectively. In each of these patients there was excellent clinical effect; the arthritic condition improved promptly and progressively, erythrocyte sedimentation rate was reduced to nearly normal, and general systemic improvement was gratifying. The 3rd patient previously had received cortisone intramuscularly during 2 periods of 23 and 20 days, and ACTH for 1 period of 14 days. In all respects the clinical effects of orally administered cortisone were comparable to those of this hormone given parenterally, and to ACTH. The 4th patient had prompt improvement during the first 3 days that cortisone was administered orally, then worsened somewhat. Consequently, the dose was increased to 100 mg twice daily and was continued at this level for the last 11 days it was administered. With the larger dose, improvement again progressed until there was nearly complete clinical arrestment of the arthritis. Subsequently, when this patient received cortisone intramuscularly in dosage similar to that employed orally, clinical response was comparable to that effected by cortisone taken orally. Both the 3rd and 4th patients volunteered preference for the tablets, because they considered the effects to be smoother than when the hormone was injected.

These observations clearly indicate that cortisone is effective when administered orally. This knowledge is indeed gratifying, especially in anticipation of practical therapy, for in patients with a chronic illness, such as rheumatoid arthritis, prolonged use of any drug should be facilitated by an effective oral preparation. At the same time *abuse* of tablets of such a potent hormone must be avoided.

Further studies of oral use of cortisone will be conducted as soon as supplies will allow.

[1] These studies were made possible by generous grants from the Masonic Foundation for Medical Research and Human Welfare, and the Fund for Research in Rheumatic Diseases. Hospital for Special Surgery.

Reference

1. Hench, P. S., *et al.* *Proc. Staff Meet. Mayo Clinic,* 1949, **24**, 181.

Cytological Changes in Human Hypophyses after Cortisone and ACTH Treatment

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Following injections of cortisone in patients with various diseases, microscopical changes have been noted in the anterior hypophyses at post-mortem examination. The relevant data concerning age, principal disease, total