Cleveland Clinic Quarterly

Volume 24 APRIL 1957 No. 2

A RATIONAL APPROACH TO THE TREATMENT OF RHEUMATOID ARTHRITIS: INTRODUCTION

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RHEUMATOID ARTHRITIS is a highly complex systemic disorder of unknown etiology. It is characterized by great variations in disease activity and therapeutic response which make it difficult to evaluate the results of treatment. As yet no treatment has proved to be consistently effective. The favorable results that have been achieved with various therapeutic agents often are only temporary and, when relapse occurs, unfortunately an increased dosage of the therapeutic agent does little more than produce toxic reactions.

We have investigated during the past six years the effects of drugs on rheumatoid arthritis of varying severity. The effects of intravenous *nitrogen mustard** have been studied for six years (part I), intraarticular *nitrogen mustard** for two years (part II), the hydrazides *isoniazid* and *iproniazid*** for five years (part III), and the antimalarial agents *hydroxychloroquine sulfate*† and *chloroquine phosphate*†† for two years (part IV). The drugs were administered singly and

**Mustargen hydrochloride, Merck Sharp & Dohme, Division of Merck & Co., Inc.*

***Marsilid phosphate, Hoffmann-La Roche, Inc.*

†Plaquenil sulfate, Winthrop Laboratories.

††Aralen phosphate, Winthrop Laboratories.

also in combination with *corticotropin* (*ACTH*) and various corticosteroids[a-g]—*cortisone acetate*,[a] *hydrocortisone*,[b] *prednisone*,[c] *prednisolone*,[d] *hydrocortisone acetate*,[e] *hydrocortisone tertiary-butylacetate*,[f] and *prednisolone tertiary-butylacetate*.[g] In combination, each drug usually was administered in a dose that alone had little suppressing effect on disease activity. The effects of each drug were observed for one year or longer, during which time the desirable and undesirable actions were evaluated. Combinations of drugs, dosages, and routes of administration were determined which would most effectively suppress disease activity and cause the least number of toxic reactions. Corticotropin and corticosteroid were used sparingly and temporarily in an attempt to avoid undesirable side effects. The combinations of drugs were altered in accordance with the individually fluctuating state of the disease in each patient. The entire program of chemotherapy as now conducted for patients with active rheumatoid arthritis of varying severity is discussed in part V.

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[a]*Cortone acetate, Merck Sharp & Dohme, Division of Merck & Co., Inc.*

[b]*Hydrocortone, Merck Sharp & Dohme, Division of Merck & Co., Inc.*

[c]*Meticorten, Schering Corporation.*

[d]*Meticortelone, Schering Corporation; Stearane, Pfizer Laboratories, Division of Chas. Pfizer & Co., Inc.*

[e]*Hydrocortone acetate, Merck Sharp & Dohme, Division of Merck & Co., Inc.*

[f]*Hydrocortone-T.B.A., Merck Sharp & Dohme, Division of Merck & Co., Inc.*

[g]*Hydeltra-T.B.A., Merck Sharp & Dohme, Division of Merck & Co., Inc.*