

nize that my comments dealing with the effect of oral contraceptive agents on patients with several forms of arthritis should not be construed as being generally appropriate to the population at large. Precise data on potential or proven adverse effects from any drug are justified only after rigorous biostatistical evaluations have been accomplished.

It would be premature to conclude from our data that we can generalize on the biological effects of oral contraceptives. We do feel, however, that there are a small number, perhaps 5 percent, of young women with early rheumatic disease in whom these agents should be employed with caution.

The general term "arthritis" is commonly used to describe a large number of rheumatic diseases. Currently, there are approximately 80 different forms of rheumatic disease. In general, I will speak about two of the most important forms of inflammatory joint disease, rheumatoid arthritis and a much rarer disorder, systemic lupus erythematosus. These conditions are generally chronic. Clinical course in most patients is highly variable and in many instances, it is difficult to establish a precise diagnosis during the early phase of the illness. These factors are of particular importance when one attempts to evaluate the effect of any therapeutic agent on one or more of these diseases. We are more confident that alterations in certain of the laboratory tests useful in differential diagnosis of these diseases have been produced during treatment with oral contraceptive drugs.

First it is appropriate to point out that there have been suggestions going back many years that there is an association between female hormones and variation in the clinical status of patients with rheumatoid arthritis and the less common condition of systemic lupus erythematosus. It has been found that natural pregnancy has an ameliorating effect upon rheumatoid arthritis. The biological basis for this change has eluded adequate scientific explanation to the present time. By contrast, patients afflicted with systemic lupus erythematosus may in some instances have worsening of their disease during pregnancy. In these two disorders we observe a paradoxical influence of female hormones on the clinical course of two of the major forms of rheumatic disease. These long-established clinical observations are of theoretical and practical significance if one is concerned with the factors that affect inflammatory conditions in man.

When the synthetic estrogen-progestogen combinations were marketed as oral contraceptive drugs, two investigative groups attempted to evaluate the therapeutic effect of these agents on rheumatoid arthritis. In 1962 two preliminary reports were published—Balis and Demers: *Arth. & Rheum.* 5:284, 1962; Rotstein, J., Gilbert, M., Cunningham, C., Estrin, I., and Pincus, G.: *Arth. & Rheum.* 5:655, 1962. Beneficial effect from use of these agents in treating patients with rheumatoid arthritis were equivocal, as judged by the authors themselves.

The first report of a potential adverse effect of oral contraceptive agents on patients with rheumatic disease appeared in 1966. Since that time, at least five preliminary studies have been recorded in the medical literature. These reports appear to be in conflict. On close examination,