Mr. DUFFY. Thank you.

Senator MCINTYRE. Thank you, Mr. Duffy.

Mr. Gordon, do you desire any further questions?

Mr. GORDON. No, sir.

Senator MCINTYRE. Thank you very much, Dr. Bole, for your very careful testimony. We appreciate your coming here.

(The complete prepared statement and supplemental information submitted by Dr. Bole follows:)

STATEMENT OF DR. GILES G. BOLE, JR., ASSOCIATE PROFESSOR OF INTERNAL MEDICINE, UNIVERSITY OF MICHIGAN MEDICAL SCHOOL

Mr. Chairman: I am Giles G. Bole, Jr., Associate Professor of Internal Medicine, University of Michigan Medical School, Ann Arbor, Michigan; and Acting Physician in Charge, Rackham Arthritis Research Unit at the University of Michigan.

Your Committee has invited me to discuss the effect of oral contraceptive agents on patients with arthritis. My colleagues and I have published certain preliminary observations dealing with this problem (J. Lab. Clin. Med. 72:873, 1969; Lancet i:323, 1969; Arth. Rheum. 12:306, 1969; Bull. Path. 10:358, 1969). Several other investigative groups have also reported preliminary observations bearing upon the effect of oral contraceptive agents on patients with rheumatic disease. Our studies were initiated in the spring of 1968 and include observations on three groups of women seen and evaluated in the Arthritis Clinics at the University of Michigan Medical Center during the years 1967–69. We are currently completing a study of 450 presumably healthy young women seen at a local Planned Parenthood Clinic in Ann Arbor, Michigan. We are all aware of the increased interest in potential adverse biological effects of oral contraceptive agents. It is important to recognize 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 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 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 or 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 effect inflammatory conditions in man.

When the synthetic estrogen-progestogen combinations were marketed as oral contraceptive drugs, two investigative groups attempted to evaluate the thera-