the second batch of aureomycin. Under the experimental conditions, aureomycin inactivated by heat, and penicillin were non-toxic. The LD50 of the least toxic lot of aureomycin for the chick embryo was 20 mg/kg. The *in vitro* effect of aureomycin on the herpes simplex virus is shown in Table I. The drug apparently has no *in vitro* action on the virus, under the conditions of the present experiments. The *in vivo* effect of aureomycin on the herpes simplex virus is shown in Table II. Because of the difference in toxicity and a possible difference in activity in the two lots of aureomycin, the results with each lot are recorded separately. There seems to be little difference in the effectiveness of the two lots of drug. Although in some of the dilutions small differences occurred between the controls and the drug treated embryos, at the critical dilutions with moderately large doses of drug and small amounts of virus there is no significant increased survival of aureomycin treated eggs. Analysis of the data also failed to show any significant delay in time of death of treated infected eggs.

Conclusions. (1) Aureomycin appears to be more toxic for the chick embryo than for most other laboratory animals. (2) There seemed to be a significant difference in toxicity between the 2 lots of aureomycin used. Incubation of aureomycin at 56°C for five days destroys the embryo-toxic principle as well as its antibiotic activity. (3) Aureomycin has no *in vitro* activity against herpes simplex virus. (4) As compared with its activity against the larger viruses, no similar *in vivo* effect against herpes simplex virus could be demonstrated.

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Remission of Disseminated Lupus Erythematosus Induced by Adrenocorticotropin.* (17499)

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This report describes the effect of pituitary adrenocorticotropic hormone (ACTH) in inducing 3 temporary dramatic remissions in 2 patients with classic disseminated lupus erythematosus. There was a virtually complete clinical remission while the ACTH was being administered. A description of this phenomenon has not been previously published.

Case I: A.F., a 36-year-old white housewife was admitted complaining of fever, weakness, weight loss, and arthralgia of 9 months' duration. She appeared acutely ill, with a daily temperature of 101°F. There were erythematous, scaly plaques on both cheeks which also showed telangiectatic vessels and areas of atrophy. The eruption, in addition, involved the forehead, chin, ears, scalp, arms and legs. Scalp and pubic hair were sparse. There was a soft, blowing, systolic murmur over the 4th left intercostal space. The spleen was not palpable. Examination of the blood showed anemia, leukopenia, thrombocytopenia and an elevation of the sedimentation rate; protein and microscopic collections of red blood cells were constantly present in the urine. A section of the involved skin of the face showed changes usually seen in disseminated lupus erythematosus.

Beginning May 24, 1949, 150 mg of ACTH was injected intramuscularly in 6 divided doses daily for 5 days when they had to be stopped because further supplies of this scarce hormone were unavailable.

A remarkable change in the patient's condition was apparent within 12 hours after the injections were started. She appeared more

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alert, sat up in bed and expressed a desire for food for the first time in months. The arthralgia and myalgia disappeared. Within 24 hours, the temperature returned to normal and remained so as long as the hormone was given. The skin lesions began to fade and had almost disappeared by the 7th day after ACTH was started. The improvement in the appearance of the skin lesions continued for several days after the hormone was stopped, although the temperature was elevated on the day after ACTH was discontinued; thereafter the patient gradually relapsed into the clinical condition described before treatment was instituted. During the period of administration of ACTH, the eosinophils disappeared from the peripheral blood, the leukocyte count increased from 6,000 to 11,000, and the lymphocytes dropped from 48% to 23%. There was no appreciable change in the sedimentation rate or urinary findings. The urinary 17-ketosteroids increased from 5.2 mg to 27 mg. By June 11th the patient was irrational and appeared moribund. On the following day 150 mg of ACTH was again given daily and maintained for 3 days during which the skin lesions began to fade, she became rational, fever was partly controlled and appetite returned. On June 15th, when the supply of ACTH was exhausted, she again became irrational and died 4 days later.

Case II: S.P., a 30-year-old white housewife was admitted complaining of swollen joints and an eruption on the face of 6 months duration. The eruption was made worse by exposure to sunlight. The classical erythematous lesions were present upon the face; warm, painful swellings existed over the wrists and metacarpophalangeal joints of both hands and there was a daily rise of temperature to 101°F. The spleen was moderately enlarged. Marked weakness of the upper and lower extremities was regarded by a neurological consultant as the result of peripheral neuritis. Examination of the blood showed anemia, leukopenia and an elevation of the sedimentation rate. There was only an occasional trace of protein in the urine from which porphyrin was also absent. The histopathologic picture of the erythematous skin was that usually seen in disseminated lupus erythematosus.

Beginning June 5, 1949, 100 mg of ACTH was injected intramuscularly in 4 divided doses daily for 5 days. Striking improvement followed and was manifested by disappearance of the swelling and pain in the wrists and joints of the hands, the fading of the skin lesions, diminution in size of the spleen, increase in muscular strength of the upper and lower extremities, return of temperature and appetite to normal; in addition, the eosinophils disappeared from the peripheral blood, the leukocyte count rose from 5,600 to 12,400 and the sedimentation rate returned to normal. Within 2 days after ACTH was discontinued the temperature began to rise, and 5 days later, there was a clinical relapse.

Discussion. After the first published demonstrations(1,2) that adrenal cortical activity induced either by administration of ACTH or the synthetic adrenal cortical steroid, 17-hydroxy-11-dehydrocorticosterone (Compound E of Kendall) was effective in alleviating acute nonbacterial arthritis, it appeared desirable to test these hormones in other members of the group of so-called "collagen diseases"(3) that also exhibit arthritis as part of the clinical picture. The effectiveness of Compound E in acute rheumatic fever has already been reported.(4) In addition, not only the arthritis, but cutaneous lesions of psoriasis disappear after the administration of ACTH(5) and return upon its discontinuance.

The temporary remissions induced by 5 days administration of ACTH represent an unequivocal, dramatic improvement in the course of a progressive, usually fatal disease. There is reason to expect that the continued administration of ACTH or Compound E would prolong the remission. It appears

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likely that the hormones only inhibit or mask the peripheral manifestations of rheumatoid arthritis, rheumatic fever, lupus erythematosus and psoriasis and do not affect the underlying causative disease mechanism, since a clinical relapse usually occurs promptly after cessation of hormone treatment.(2,4) In acute gouty arthritis, on the contrary, ACTH apparently completely aborts the acute attack.(1)

There are none of the usual signs or symptoms of adrenal insufficiency in the diseases benefitted by ACTH or Compound E and it is unlikely that the hormones act as substitution therapy for a deficiency. The expected change in the ketosteroids, eosinophils, lymphocytes, and total white count is evidence for adequate adrenal cortical function.(6) A "pharmacologic" extension of the usual physiologic properties of the hormones may be responsible for their action. In this connection, it is interesting to note the similarities between the effects produced by the salicylates and the adrenal hormone. Both groups of compounds lower fever and sedimentation rate, inhibit hyaluronidase,(7,8) cause hyperglycemia,(6,8) increase uric acid excretion(9,10) and are local anesthetics.(8,11) In addition, the salicylates and the adrenal hormones are both effective in rheumatoid arthritis and lupus erythematosus.(8)

Summary. Two patients with classical disseminated lupus erythematosus were given three separate courses of injections of adrenocorticotropic hormone (ACTH). In each case, there was temporary, striking clinical improvement and fading of the skin lesions, accompanied by the expected signs of increased adrenal cortical activity. These results suggest that continued administration of ACTH or Compound E may be of benefit in lupus erythematosus.

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A Test of Triazolopyrimidines on Mouse Sarcoma 180.* (17500)

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For nearly two years the major portion of a cancer chemotherapy program(1) has been devoted to a study of compounds that might serve as anti-metabolites to nucleic acid components. The studies were stimulated by the development of knowledge concerning the effects of anti-metabolites in bacteria and

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