Summary. 1. Rat skin incubated anaerobically accumulated labeled squalene from acetate and only negligible amounts of labeled sterols. Incorporation of acetate into squalene was enhanced markedly by the presence of glucose in the medium. 2. Insulin, ferricyanide and methylene blue enhanced squalene synthesis *in vitro* in presence of glucose. Increasing amounts of insulin or ferricyanide produced regular increases in squalene synthesis until a plateau was reached; methylene blue on the other hand showed a sharp maximum at 10^{-3}M, with a decline at higher concentrations. 3. Skin containing labeled squalene accumulated labeled sterol on subsequent incubation under oxygen.

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Received January 4, 1961. P.S.E.B.M., 1961, v106.

Activity of Pituitary-Adrenal Cortex Axis During Acute and Chronic Reserpine Treatment.* (26408)

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It has been demonstrated that reserpine treatment affects endocrine systems(1,2,3). It was reported that reserpine interferes with the estrous cycle in mice and rats(1,4), ovulation and menstruation in monkeys(5), prolactin production and secretion in rats, rabbits and women(6,7,8), and normal function of the pituitary-gonadal axis(9). Reserpine was found also to effect recession of exophthalmus(10), thyroid inhibition(11), and to have antithyroid activity(12).

It has been suggested that adrenal hypertrophy and ACTH hypersecretion occur during reserpine administration(1,13,14,15,16). On the other hand, inhibition of pituitary ACTH release after administration of reserpine(17,18), and suppression of adrenal hypertrophy in male mice(19) have been reported.

* This paper has been aided by a generous grant from Keren Nechuth, administered by Dr. S. Kott.

In view of these conflicting reports we have studied the mode of action of reserpine treatment on the pituitary-adrenal cortex axis.

Materials and Methods. Reserpine stock solution was prepared according to the method described in Martindale's Extrapharmacopoea(1959), and diluted to the required concentration. Studies were carried out on adult male guinea pigs, adult male rats, and on human patients.

Exp. 1. Five adult guinea pigs (600± 30 g) were injected subcutaneously with 0.2 mg/kg reserpine daily for 7 days. The animals were then sacrificed, the adrenals weighed and histological sections prepared and studied.

Exp. 2. Ten adult male rats (200 ± 20 g) were injected subcutaneously with 0.01 mg/kg reserpine daily for 10 and 40 days respectively while 5 animals served as controls.

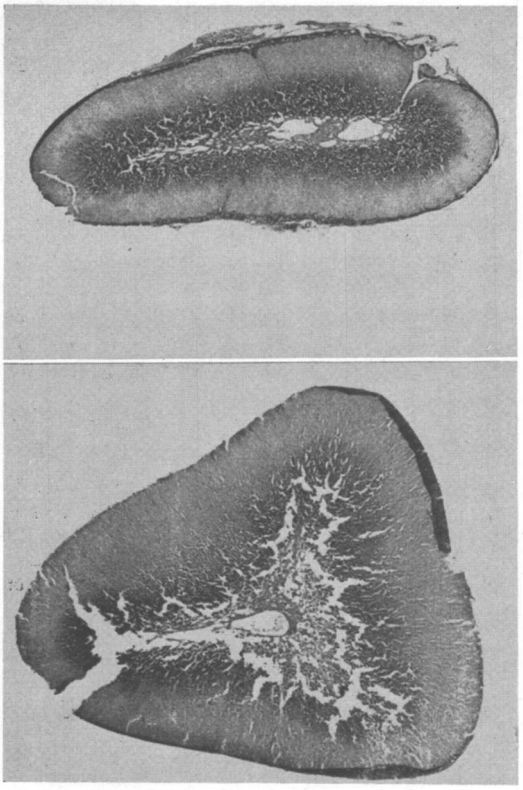

FIG. 1. Histological sections of left side adrenals of guinea pigs (10 ×). Top: control, 165 mg. Bottom: reserpine treated, 255 mg.

The animals were sacrificed and the adrenals dissected and weighed.

Exp. 3. Ascorbic acid depletion was determined by the method of Roe(20) on adrenals of 15 adult male rats (250 ± 25 g) treated with 0.2 mg/kg reserpine daily for 1, 2 and 7 days respectively, one hour after last administration.

Exp. 4. 17-KS and 17-OHCS were determined periodically by the method of Sulman (21,22) on 24 hr urines of 7 human patients receiving 1 mg reserpine daily for 30-40 days.

Results. Administration of reserpine to guinea pigs (Exp. 1) for 7 days caused adrenal hypertrophy of 60-80% by weight. The histological sections showed an enlarged adrenal cortex, especially in the *zona fasciculata* (Fig. 1). Adult male rats treated with reserpine (Exp. 2) were found to have significantly hypertrophied adrenals on the 10th day of treatment, ranging between 30-50%. Forty days' treatment resulted in almost no hypertrophy (Table I). A higher adrenal ascorbic acid depletion (Exp. 3) was found after the first injection than in chronic treatment at the same dose level (Table II). The 17-KS content in 24 hr urines of 7 human patients (Exp. 4) showed higher titers during the first 7-10 days (average 17 mg/d), then tended to return to normal (average 12 mg/d) by the 30-40th day. Corresponding average values for 17-OHCS excretion were 5.5 mg/d at the beginning, declining to 3 mg/d with continued treatment.

Discussion. Hertting *et al.*(13) found that adrenal hypertrophy in rats treated with reserpine could be inhibited by simultaneous administration of cortisone, and suggested that the hypersecretion of ACTH caused by reserpine had been inhibited by cortisone. Tindal (14) reported thymus atrophy in rabbits, indicating pituitary-adrenal cortex hyperactivity during reserpine administration. Higher 17-OHCS blood levels in monkeys were reported after i.v. injection of 1 mg/kg reserpine(15), estimated to be equivalent to the elevation caused by 16 mg/kg exogenous ACTH. Similar results were noted in man(16).

While our results showed that reserpine has a stimulating effect on the pituitary-adrenal cortex through acute treatment, as revealed by adrenal hypertrophy, adrenal ascorbic acid depletion and increased 17-KS

TABLE I. Adrenal Weight of Reserpine Treated Adult Male Rats at a Dose Level of .01 mg/kg.

No. of rats	Days of treatment	Wt of adrenal, mg
5	0 (control)	27 ± 1.5*
5	10	35 ± 2.1
5	40	28 ± 3.2

* ± stand. errors.

TABLE II. Ascorbic Acid Depletion in Adrenals of Adult Male Rats Treated with .20 mg/kg Reserpine Daily.

No. of rats	Days of treatment	Ascorbic acid contents, mg/100 g adrenal
5	0 (control)	310 ± 21*
5	1	170 ± 17
5	2	210 ± 15
5	7	260 ± 24

* ± stand. errors.

and 17-OHCS levels, they indicate that this effect is transitory. These findings suggest that reserpine is not a specific stimulant of the hypophysis which causes hypersecretion of ACTH, but that the acute ACTH hypersecretion following reserpine administration may be due to the non-specific transitory stress reaction brought about by the drug.

Summary. Acute reserpine treatment of guinea pigs, rats and human patients resulted in activation of the pituitary-adrenal cortex axis demonstrated by hypertrophy of adrenals, adrenal ascorbic acid depletion and higher 17-KS and 17-OHCS levels. These changes disappeared during chronic treatment. It is hence suggested that reserpine through its transistory stimulating effect on the pituitary-adrenal cortex axis acts as a non-specific stimulus, which loses its effect on chronic administration.

Our thanks are due to Mr. E. Zawojski for devoted technical assistance.

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Received January 6, 1961. P.S.E.B.M., 1961, v106.

Propagation of Measles Virus in Suspensions of Human and Monkey Leucocytes.* (26409)

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Many viral diseases are associated with a reduction of circulating leucocytes which as a rule is most conspicuous when patients manifest clinical and laboratory evidence of diffuse viral dissemination. The leucopenia accompanying measles is characterized by an absolute reduction of both lymphocytes and polymorphonuclear leucocytes. In attempting to elucidate factors responsible for leucopenia in this disease experiments were designed to determine whether *in vitro* leucocytes of several animal species including man were capable of supporting the growth of measles virus.

* Supported in part by research grant from U. S. Public Health Service, Dept of HEW.

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Materials and Methods. Preparation and