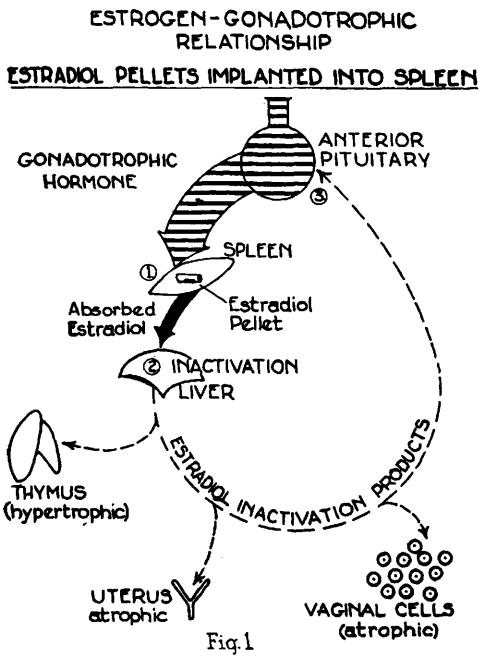

Fig. 1

dose necessary to maintain constant estrus in the intact animal. This large dose of α-estradiol was completely inactivated, as demonstrated by the atrophic uteri and vaginal smears, and the large thymus. Therefore, many times the physiological amount of inactivation products were present in the circulation. However, the pituitary gonadotrophic content rose to castrate levels.

The castrated rats with pellets implanted in the spleen which developed vascular adhesions from the spleen to the systemic circulation absorbed essentially the same amount of α-estradiol daily as the rats without adhesions (19.7 μg vs. 21.9 μg). The rats with estradiol pellets implanted subcutaneously absorbed 74.0 μg daily. In both the adhesion group and in the rats with pellets implanted subcutaneously, constant estrus was observed along with atrophy of the thymus and suppression of pituitary gonadotrophic content. These changes are noted only with unphysiologically large doses of estrogen,[1] thus indicating that larger than normal amounts of estrogen were being absorbed.

Conclusions. 1. The inactivation products of α-estradiol produced by passage of estradiol through the liver do not exert a significant inhibiting influence on anterior pituitary gonadotrophic secretion.

2. The absence of this effect supports the thesis that pituitary gonadotrophic content and secretion are controlled principally by ovarian inactivation of circulating gonadotrophins.

16779

Effect of Adrenal Cortical Extract on Recovery from Severe Pneumococcic Infection in Mice.*

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Many observations suggest that the increased adrenal cortical secretion during stress provides an increase in nonspecific resistance.[1] In patients or animals moribund from infections, it was thought that administration of large doses of adrenal cortical extract might temporarily increase resistance and thus gain time for antibacterial agents such as penicillin to effect recovery. To test this possibility two similar experiments were performed.

Methods. Albino Swiss mice were inoculated intraperitoneally with large numbers of Type I pneumococci. After a certain percentage of the inoculated mice had died, the survivors were placed at random into 3 dif-

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[1] Selye, H., *J. Clin. Endocrinol.*, 1946, **6**, 117.

TABLE I.
Effect of Adrenal Cortical Extract and Penicillin on Survival of Mice Infected with Pneumococci.
Treatment begun 22 hours after inoculation when 5% of mice were dead.

Hr after pneumococcus inoculation	Group I Penicillin G + adrenal cortical extr.		Group II Penicillin G + corn oil		Group III Saline + corn oil	
	No. living	% living	No. living	% living	No. living	% living
22	34	100	34	100	25	100
24	18	53	23	68	15	60
26	15	44	16	47	4	16
28	13	38	13	38	1	4
30	12	35	10	29	0	0
34	10	29	9	26	0	0
38	9	26	8	24	0	0
42	8	24	8	24	0	0
46	8	24	8	24	0	0
50	7	21	8	24	0	0

TABLE II.
Effect of Adrenal Cortical Extract and Penicillin on Survival of Mice Infected with Pneumococci.
Treatment begun 22 hours after inoculation when 10% of mice were dead.

Hr after pneumococcus inoculation	Group I Penicillin G + adrenal cortical extr.		Group II Penicillin G + corn oil		Group III Saline + corn oil	
	No. living	% living	No. living	% living	No. living	% living
22	37	100	39	100	14	100
24	30	81	35	90	14	100
26	26	70	31	80	13	93
28	22	59	30	77	11	79
30	22	59	30	77	8	57
34	21	57	29	74	3	21
38	21	57	28	72	3	21
42	20	54	28	72	0	0
46	20	54	28	72	0	0
50	19	51	25	64	0	0

ferent therapy groups.

Group I received 250 units of crystalline sodium penicillin G dissolved in 0.5 cc saline intraperitoneally every 2 hours. These mice were also injected subcutaneously with 0.2 cc of adrenal cortical extract (Upjohn's "Lipo-Adrenal Cortex") immediately after the first penicillin injection. Subsequently, at 4 and 8 hours after this injection they received an additional subcutaneous injection of 0.1 cc of adrenal cortical extract.

Group II was treated on the same dosage schedule of penicillin as Group I. However, subcutaneous injections of corn oil (Mazola) were administered instead of adrenal cortical extract.

Group III was a control group. Mice in this group received 0.5 cc of saline instead of the penicillin solution every 2 hours, as well as the same type of corn oil injections received by Group II. In both experiments the therapeutic program was carried out for 28 hours.

First experiment. Ninety-eight mice averaging 14 g in weight were inoculated intraperitoneally with 25,000 pneumococci per mouse. Treatment was delayed until 22 hours after inoculation when 5% of the mice were dead. The 93 survivors were divided at random into 3 groups and treated according to the plan described above.

Second experiment. One hundred mice averaging 20 g each were inoculated intraperitoneally with 75,000 pneumococci per

mouse. Treatment was withheld until 22 hours after inoculation when 10% of the animals had died. The 90 survivors were divided at random into 3 treatment groups as outlined above.

In addition, control experiments were performed which showed that adrenal cortical extract, corn oil, penicillin and saline injections in the dosages and schedules used in the experiments had no noticeably harmful effects on uninfected mice.

Results and comments. The mortality in the 3 treatment groups is indicated in Table I for the first experiment and in Table II for the second experiment. As would be expected, the groups treated with penicillin showed a much lower mortality than the controls receiving no penicillin. No further improvement in mortality was effected by additional treatment with large doses of potent adrenal cortical extract. If these experiments are applicable to clinical situations, the results do not lend encouragement to the use of adrenal cortical extracts in the treatment of patients moribund from bacterial infections.

Summary. Mice of varying weights were inoculated intraperitoneally with large numbers of Type I pneumococci and the infections allowed to proceed until from 5 to 10% of the animals had succumbed. The survivors were divided into groups at random and treated with penicillin and penicillin plus potent adrenal cortical extract. No improvement was obtained in the therapeutic results achieved with penicillin by the additional treatment with adrenal cortical extract.

We wish to thank Dr. E. Gifford Upjohn of the Upjohn Pharmaceutical Company for generously supplying us with Lipo-Adrenal Cortex (Upjohn).

16780

Reproduction of Human Ulcerative Pulmonary Tuberculosis in Rabbits by Quantitative Natural Airborne Contagion.*

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The purpose of this report is to outline a study in which the acquisition and development of human ulcerative pulmonary tuberculosis was closely simulated in rabbits by exposing them to the inhalation of known numbers of tubercle bacilli while breathing naturally in an experimental apparatus.

Materials and methods. An apparatus for airborne infection of rabbits, constructed at the Cornell University Medical School, was placed at our disposal by Dr. Eugene L. Opie. This was modified in accordance with the principles elaborated by Wells[1] and further adjusted by certain appliances directed toward improving its quantitative aspects.

Fig. 1 gives a schematic drawing of the instrument. Briefly, a fine suspension of largely isolated, virulent bovine type tubercle bacilli, freed from clumps larger than a red blood cell by filtration through Whatman number 5 filter paper, is atomized with a known volume of compressed air in unit time through a specially designed nozzle. The large droplets settle out quickly in the spraying flask. A uniform flow of droplet nuclei, containing tubercle bacilli, is delivered into a mixing device where it is diluted with room air. Thence the contaminated air is drawn through a 16-foot pipe into a chamber where the rabbits are exposed. This chamber is exhausted by the draft action of a hot flame at the bottom of a baffled chimney connected

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† Tuberculosis Control Division, Public Health Service, Federal Security Agency.

1 Wells, W. F., *Science*, 1940, **91**, 172.