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Changes in Adrenal Function During the Alarm Reaction.

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Previous investigators have shown that during the alarm reaction produced by nocuous stimuli the adrenal cortex hypertrophies[1-3] and that this enlargement is accompanied by a definite hyperfunction.[4] Weil and Browne[5,6] demonstrated that, when the human organism is subjected to stress, the excretion of corticoids in the urine is significantly increased above the normal. Davidson,[7] Howard,[8] and Burrill and Greene[9] demonstrated the production of testoids by the adrenals of young castrate male rats and mice. Recently Forbes[10] has shown that the characteristic reaction of the adrenal to stress results first in an increase (for 12-48 hr) then a decrease in 17-ketosteroid excretion.

It seemed of interest to demonstrate whether the enlarged adrenal produces excessive amounts of testoid or folliculoid compounds during the alarm reaction. The weights of the seminal vesicles and the prostate were used as indicators of testoid activity in the castrate male, while the vaginal smear was used as an indicator of folliculoid activity in the spayed female.

Twelve mature male albino rats were castrated and divided into 2 equal groups; one group received 0.3 cc of a 10% solution of formalin subcutaneously thrice daily for 12 days and the other served as non-injected controls. On the thirteenth day all animals were killed. The adrenal glands, seminal vesicles and prostate were weighed after fixation in Heidenhain's "Susa" mixture. In the non-injected control group the adrenals averaged 36 mg (range: 34-38 mg), the seminal vesicles 93 mg (range: 80-114 mg), the preputial glands 32 mg (range: 23-39 mg) and the prostatic complex 94 mg (range: 68-133 mg). In the formalin-treated animals the adrenals weighed 54 mg (range: 46-63 mg), the seminal vesicles 87 mg (range: 81-94 mg), the preputials 29 mg (range: 20-36 mg) and the prostatic complex 94 mg (range: 83-111 mg).

A similar experiment was performed on spayed mature albino female rats. Four days after gonadectomy injections were started. Daily vaginal smears were taken during the entire experiment to determine whether estrus would reappear. The control adrenals averaged 41 mg (range 38-47 mg) and the preputial glands 45 mg (range: 31-55 mg), while in the formalin-treated animals the adrenal weighed 56 mg (range: 42-64 mg) and the preputials 38 mg (range: 29-48 mg). At no time during the entire experiment did estrus appear in any of the animals.

These experiments demonstrate quite clearly that in rats, during the alarm reaction produced by the injection of a solution of 10% formalin, there is a marked increase in the weight of the adrenal glands, but no significant change in that of the accessory sex organs or of the vaginal smear. We may, therefore, conclude in agreement with Forbes[10] that during exposure to stress the stimulation of adrenal function is such as to give maximum protection against stress, resulting in a specific overproduction of

1 Selye, Hans, *Endocrinology*, 1937, **21**, 169.

2 Selye, Hans, *Can. Med. Assn. J.*, 1936, **34**, 706.

3 Freud, J., Manus, M. B. C., and Mühlbock, O., *Acta brev. Neerl.*, 1938, **8**, 6.

4 Dosne, C., and Dalton, A. J., *Anat. Rec.*, 1941, **80**, 211.

5 Weil, Paul, and Browne, J. S. L., *Science*, 1939, **90**, 445.

6 Weil, Paul, and Browne, J. S. L., *J. Clin. Invest.*, 1940, **19**, 772.

7 Davidson, C. S., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 703.

8 Howard, Evelyn, *Proc. Am. Physiol. Soc.*, 1938, p. 105.

9 Burrill, M. W., and Greene, R. R., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 327.

10 Forbes, A. T., Preliminary report published by the Josiah Macy, Jr., Foundation, 1942.

corticoids without a corresponding increase in either testoids or folliculoids.

Summary. In gonadectomized animals treated with 10% formalin solution there occurred a marked hypertrophy of the adrenal glands, but no significant change in the size of the accessory sex organs (vaginal smear and preputial glands in the female; seminal vesicles and prostate in the male). It is concluded that the adrenal cortical hypertrophy, so characteristic of the alarm reaction, is not accompanied by increased sex hormone production.

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Effects of Anoxia at Birth on Central Nervous System of the Guinea Pig.

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Studies on intrauterine respiration, respiratory changes at birth and tolerance by the newly born of anoxia have been reviewed elsewhere.[1] It has been observed that manifestations or cerebral pathology and impairment of the intellect are frequently associated with histories of cyanosis and apnea at birth.[2,3] Some investigators have cautioned that nerve cells of the young may be even more susceptible to damage by anoxia than those of the adult. These and similar clinical studies have been questioned because they were based on selected cases, and fully adequate controls were not available.[4] In the present experiments in guinea pigs with litter-mate controls, the thesis that asphyxia neonatorum can elicit irreparable destructive changes in the central nervous system has been tested.

The abdomen of the animal at or near term was anesthetized with 1 cc of a 1% solution of procain hydrochloride. No other anesthetic was employed. One fetus was delivered immediately through a midline incision to serve as a control. The uterine vessels were then clamped or the umbilical cords of the remaining fetuses were compressed through small incisions in the uterus.

Varying degrees of anoxia were induced in 103 animals. Fifty-eight of them were delivered just before or just after intrauterine respiratory movements, induced by the anoxia, had ceased. Survivors (38%) were those which suffered no anoxial apnea and required no resuscitation. Forty-five guinea pigs were delivered after 6 to 21 min of anoxia, after the fetal heart had become slow and often after it could no longer be palpated. Resuscitation was accomplished in 71% of them by inflating the lungs with oxygen or oxygen containing 10% carbon dioxide. The gases were administered from small rubber bags attached to hypodermic needles which were inserted into the trachea. Respiration was simulated by compressing and releasing the trachea above the needle. Resuscitation was accomplished in a few minutes to more than an hour; the time required was not consistently related to the duration of anoxia. These animals exhibited characteristic symptoms of asphyxia pallida; namely, apnea, atonia, bradycardia, relaxation of anal sphincters, and cold pale skin.

Results. All experimental animals, including those in which anoxial apnea had not

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1 Windle, W. F., *Ann. Rev. Physiol.*, 1943, **5**, in press.

2 Schreiber, F., *J. A. M. A.*, 1938, **111**, 1263.

3 Clifford, S. H., *J. Pediat.*, 1941, **18**, 567.

4 Galaway, C. E., in discussion of Schreiber's paper.[2]