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Effect of Low Atmospheric Pressures on Reproductive System of the Male Rat.

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Adult male rats (200-280 g) were exposed to pressures of 280-250 mm Hg. (25-28,000 ft) 6 hours daily for 14 to 18 days. The mean testicular, seminal vesicle and ventral prostate gland weights ± the Standard Error are shown in Table I. Body weight losses in the experimental animals averaged only 8.7%.

Examination of sections of testes from low pressure-exposed rats (Group A) showed marked degeneration of the spermatogenic cells. Polychromasia and coalescence of cytoplasm, pyknosis of nuclei, and chromatolysis were observed in these reproductive elements. The tubular lumina were devoid of sperm. The interstitial tissue of the testis and epithelium of the seminal vesicle and prostate gland, however, appeared only slightly atrophied. Pituitary glands of the low pressure-subjected animals displayed increases in the numbers of basophiles. Some of these were enlarged and showed signs of degranulation. Others resembled the vacuolated cells occurring in pituitary glands after castration.

The gonadotropic hormone contents of the pituitary glands from normal and low pressure-subjected rats were determined in 48 immature female rats employing the method of Reece and Weatherly.[1] Three assay experiments were performed using pituitary glands from 3 different sets of animals. In each case, the gonadotropic hormone potency was found to be significantly greater in the glands obtained from the low pressure-exposed rats. The mean ovarian weight in the test animals injected with pituitaries from low pressure-exposed animals was 88.3 ± 6.5 mg as against a mean ovarian weight of 62.8 ± 3.9 mg in rats receiving normal pituitary glands.

In another experiment, 8 rats were subjected to the same low pressure treatment but, in addition, were injected intrascrotally twice daily with 20 I.U. pregnancy urine hormone and 10 R.U. pregnant mare serum extract for 3 days preceding and during the entire period of exposure. As seen from Table I (Group B) the hormone treatment succeeded in elevating the testicular weights but these did not attain normal values. The injections, however, resulted in a marked increase in the weights of the reproductive accessories. Histological studies of the testes from these hormone-treated rats showed no repair of the gametogenic tissue but considerable hypertrophy and hyperplasia of the interstitial cells. The failure of the hormone material to restore spermatogenesis in the low pressure-exposed animals was not due to inadequate quantities of follicle-stimulating hor-

TABLE I.

Group	Treatment	No. of animals	Testes (mg)	Seminal vesicles (mg)	Ventral prostate (mg)
A	Low Pressures	47	1718.5 ±52.9	204.5 ±8.8	201.7 ±11.0
B	Low Pressures + Gonadotropin	8	2110.3 ±115.5	336.4 ±24.6	413.3 ±25.4
C	Controls	44	2443.1 ±46.3	264.3 ±10.8	318.0 ±12.4

[1] Reece, R. P., and Weatherly, E. J., PROC. SOC. EXP. BIOL. AND MED., 1942, **49**, 218.

mone in the injected extracts. Administration of the same hormonal treatment to 3 hypophysectomized non-exposed rats resulted in complete repair of the germinal tissue along with marked development of the interstitial cells of the testis.

It is concluded that the degenerative changes described in the male gonad are due to a direct inhibitory action of the low atmospheric pressures on the germinal tissue of the testis. The histological and gonadotropic hormone content changes in the anterior lobe of the pituitary, for the period of low pressure exposure employed, probably represent a reflection of this inhibition.

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Local Anesthetic Activity of a Number of New Monohydrochlorides of Dialkylaminomethyl Phenyl *p*-Aminobenzoates.*

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The present studies are concerned with an appraisal of the local anesthetic activity of a number of new phenyl *p*-aminobenzoates (Table I) synthesized by Dr. R. L. Shriner† and associates in the Department of Organic Chemistry, University of Illinois. The technic described by Rose[1] was used to detect dermal anesthesia. Aqueous solutions of the compounds were injected in 0.1 cc volumes in guinea pigs shaved free of hair and the presence or absence of anesthesia determined by faradic stimulation of each area injected. Solutions prepared just prior to testing were used because precipitation of all derivatives is apparent shortly after preparation. As shown in Table I the new aminobenzoates produced insensitiveness to electrical stimulation for 79-99 minutes in 1.0% and 31-79 minutes in 0.5% concentration. In both 1.0% and 0.5% solution all compounds produced hyperemia followed in most cases by necrosis at the site of injection.

In order to assess topical activity, freshly prepared aqueous solutions of derivatives (I-IX) were instilled into, and allowed to remain in the conjunctival sac of rabbits for 2 minutes. Anesthetic activity was determined by touching the cornea with the rounded end of a fine glass rod. Absence of the winking reflex was taken as evidence of anesthesia. As shown in Table I, compounds I, II, and III in 1.0% solution were inactive. While definite anesthesia was not observed, a sluggish reflex occasionally was noted for 5-10 minutes after application of these substances. In 1.0% concentrations IV, V, VI, VII, VIII and IX exhibited anesthetic activity for average periods of 21-73 minutes (Table I). The depth of anesthesia after V, VIII and IX was greater than that produced by IV, VI and VII. In the present studies, local application of 1.0% cocaine hydrochloride caused anesthesia for an average duration of 18 minutes. The corneal reflex was abolished for an average of 50 minutes after compound IX in 0.5% solution but in this concentration all of the other derivatives were ineffective.

Since IX appeared to be the most interesting of the new compounds, its acute toxicity after subcutaneous injection in mice was compared with that of cocaine hydrochloride. The MLD of IX was found to be approximately 300 mg/kg and that of cocaine between 100-150 mg/kg (Table II).

Summary. Intradermally in guinea pigs the hydrochlorides of 9 new dialkylaminomethyl phenyl *p*-aminobenzoates were found

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† Samples of these compounds were made available for the present experiments by Dr. R. L. Shriner, Department of Organic Chemistry, University of Indiana.

1 Rose, C. L., *J. Lab. Clin. Med.*, 1929, **15**, 128.