responding matrix layer, as determined by planimetric measurement. Corrections for variations in cell density were made. For further details, see KÄLLÉN's paper.

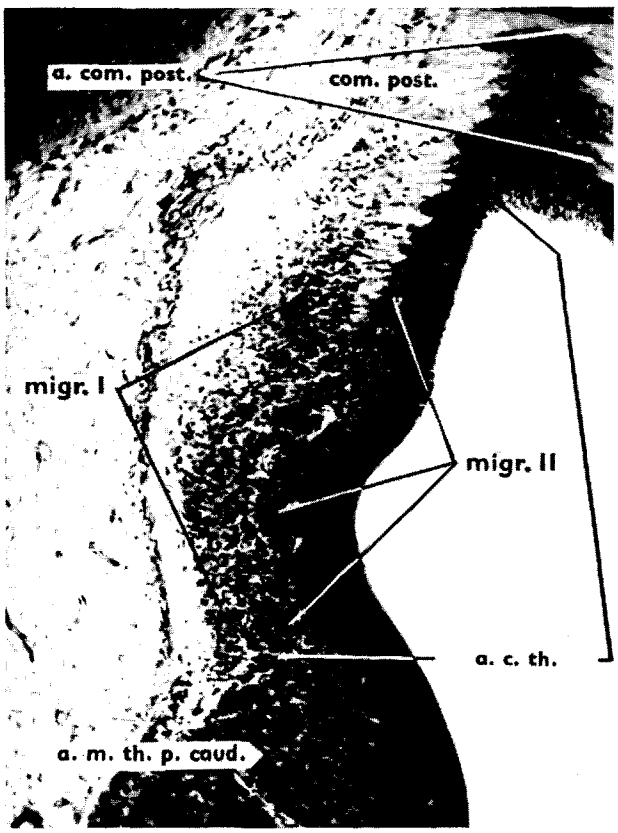


Fig. 3.—Cross section through the diencephalon in chick embryo, stage no. 29, showing the migration layer II (migr. II). Magnification × 33. – a.c.th. – area caudalis thalami; a. com. post. – area commissurae posterioris; a.m.th., p.caud. – area medialis thalami, pars caudalis; comp. post. – commissura posterior (= caudalis); migr. I – migration layer I; migr. II – migration layer II.

Results.—In Figure 1 the different embryonic stages are marked on the abscissa and the relative mitotic rate on the ordinate. The graph shows two maxima at stages 18–20 and 28–29, and a minimum about stage 25; the relative mitotic rate then decreases from stage 30. Corresponding to the first-mentioned maximum, the postneuromeres (= transverse bands) develop in the brain. Immediately after the maximum (stage 19) the first migration layer starts to develop (Fig. 2). Immediately after the second maximum (stage 29) the second migration layer is visible (Fig. 3). At stage 37 and later no mitotic activity occurs at the ventricular wall of the neural tube.

Conclusions.—The mitotic counts thus verify the relation between the proliferation processes and the successive migration, supposed to exist by BERGQUIST and KÄLLÉN[11].

It may be emphasized that the mitotic changes accompanying the successive migration processes are strictly local processes (BERGQUIST[14]). These changes may therefore have a different basis than those related to the formation of neuromeric patterns, which have been further analyzed by KÄLLÉN[15].

[14] H. BERGQUIST, J. Embryol. exp. Morphol. *4*, 152 (1956).
[15] B. KÄLLÉN, Kgl. Fysiogr. Sällsk. Lund Handl. (N.F.) *26* (1956).

The migration layers are not visible until a short time after the maximum of mitotic activity. This condition is explained by the fact that the cells which are formed at the proliferation migrate lateralwards into the periphery and form there a migration layer, which is still later delimited from the ventricular neural epithelium.

H. BERGQUIST

Institute of Anatomy, Medical Faculty University of Gothenburg, Sweden, October 10, 1956.

Zusammenfassung

Mitosezählungen bestätigen das von BERGQUIST und KÄLLÉN[11] angenommene Verhältnis zwischen Proliferation und sukzessiver Migration. Der Rhythmus der Mitoseaktivität, den KÄLLÉN[15] im rhombenzephalen Teil des Neuralrohres während der ungleichen neuromerischen Phasen nachgewiesen hat, entspricht also einer ähnlichen Aktivität bei der sukzessiven Migration in der Area thalami.

Im Unterschied zur Mitoseaktivität in den genannten Proliferationsstadien tritt die sukzessive Migration nur lokal auf (BERGQUIST[14]).

Erst einige Zeit, nachdem die Mitoseaktivität ihr Maximum erreicht hat, erscheint die Migrationsschicht. Dies ist wahrscheinlich dadurch bedingt, dass bei der Proliferation die Zellen im Neuralepithel an der Ventrikeloberfläche entstehen, in der Ventrikelwand in lateraler Richtung wandern und sich zum Schluss in einer zusammenhängenden Migrationsschicht sammeln, die vom weiter innen liegenden Neuralepithel deutlich abgegrenzt ist.

On the Endocrine Basis of Sexual Differences in Hexobarbital Sleeping-Time in Rats

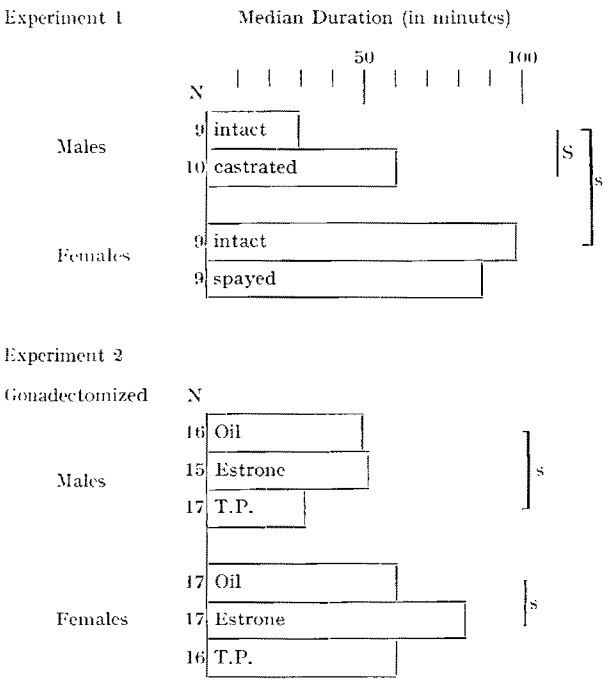
BRODIE[1] has recently demonstrated that in rats there is a distinct sexual difference in the duration of hexobarbital hypnosis, females sleeping longer than males. He also showed that the administration of estradiol to intact males prolonged sleeping-time whereas testosterone shortened it in normal females. We have extended these experiments in an attempt to differentiate between the possible direct action of the hormones and their indirect actions which result from pituitary blockade and peripheral inhibitory interactions.

Experiment 1. 20 male and 20 female rats, 140–160 g body weight, from the Sprague-Dawley colony were employed. Half of the males and half of the females were gonadectomized April 6, 1956, and on May 3 all animals received 100 mg/kg hexobarbital sodium intraperitoneally. Sleeping-time was recorded as the period in min from hexobarbital injection till the return of the righting reflex.

Experiment 2. The intact animals from experiment 1 were gonadectomized May 7, 1956. Prior to evaluation of sleeping-time the animals were treated daily for 4 days with estrone (10 μg) or testosterone propionate (250 μg) subcutaneously; these materials were contained in 0·1 ml of corn oil which also served as a control. 24 h after the final injection the animals received 100 mg/kg hexobarbital sodium. The total number of rats of each sex was divided into three groups of about six rats each,

[1] B. B. BRODIE, J. Pharm. Pharmacol. *8*, 1 (1956).

and the experiment was run on three separate occasions (18 and 25 May and 15 June). Treatment was rotated from week to week so that all animals received both compounds and served as controls.



Effects of castration and gonadal hormones on the duration of hexobarbital hypnosis in rats. N = number of rats in group. S = difference between bracketed groups significant at the 1% level; s = difference between bracketed groups significant at the 5% level; by Wilcoson Rank Sums Method[2].

The results of the two experiments are shown in the Figure. These data confirmed the sexual difference reported by BRODIE, females sleeping significantly longer than males. Castration of the males caused an increase in length of sleeping-time, so that the castrated males did not differ significantly from the normal females ($P > 0{\cdot}10$), although the median duration of sleeping time was much shorter for the castrated males. Hypnosis was shorter for spayed than for intact females, but this difference was not significant ($P > 0{\cdot}10$). This experiment was repeated on another group of rats on August 28, 2 weeks after gonadectomy. Results were essentially similar, except that the spayed females slept longer than the normal females. Median sleeping times for the four groups were: normal males 22 min, castrate males 64 min; normal females 105 min, spayed females 120 min.

In the second experiment control males and females showed essentially similar responses.

Of particular interest was the fact that testosterone propionate shortened the sleeping period of the males while estrone had no effect. In the females estrone produced a lengthening of hypnosis whereas testosterone propionate had no effect.

These data suggested that both male and female sex steroids affected hexobarbital hypnosis, but that the responses of the animals to the steroid depended upon the pre-castration state of the animal. BRODIE has shown that hexobarbital metabolism resulted from enzyme concentrations in the liver which markedly differed from males to females, the latter showing a much smaller concentration. The data from the present experiments suggested that removal of the primary sources of sex steroid production resulted in an intermediate rate of hexobarbital destruction, which in normal animals is delayed by female estrogens and increased by male androgens, and that replacement therapy normalized the responses in the appropriate sex. The failure of testosterone propionate to shorten sleeping time of spayed females and of estrone to increase it in castrated males suggested that pre-castration sexual development had affected liver enzyme systems in such a way that they were capable of responding only to the hormone-type which stimulated early development[3]. If these considerations be correct then BRODIE's experiments would appear to have measured pituitary blockade by testosterone in the females and by estradiol in the males or peripheral estrogen-androgen antagonism as suggested by PELLERIN *et al.*[4] for pentobarbital anaesthesia.

CREVIER *et al.*[5], studying pentobarbital anaesthesia, showed that the duration of hypnosis was decreased by testosterone in gonadectomized animals of both sexes whereas estradiol appeared to have little effect in ovariectomized females. PELLERIN *et al.*[4] present data suggesting that progesterone may also lengthen sleeping time.

R. A. EDGREN

Division of Biological Research, G. D. Searle & Co., Chicago 80, Ill., September 4, 1956.

Zusammenfassung

Die Schlafdauer ist nach Hexobarbitalbehandlung bei weiblichen Ratten länger als bei männlichen. Durch Kastrierung wird sie bei männlichen Tieren verlängert, bei weiblichen verkürzt. Bei ovariektomierten Ratten wird sie durch Oestron verlängert. Testosteron-Propionat ist wirkungslos. Bei kastrierten männlichen Ratten wird sie dagegen durch Testosteron-Propionat verkürzt während Oestron keinen Einfluss hat.

[2] F. WILCOXON, Biom. Bull. *1*, 80 (1945).

[3] B. B. BRODIE (Fed. Proc. *11*, 632 [1952]) has shown that hexobarbital localizes in the body fat, from which it is slowly released into the circulation, suggesting that the lipo-tropic effects of the sex steroids may also be involved.

[4] J. PELLERIN, A. D'IORIO, and E. ROBILLARD, Rev. canad. Biol. *13*, 257 (1954).

[5] M. CREVIER, A. D'IORIO, and E. ROBILLARD, Rev. canad. Biol. *9*, 336 (1950).

Action of Reserpine on the 5-Hydroxytryptamine (Enteramine) Biosynthesis and Metabolism in Dogs and Rats

SHORE *et al.*[1] and PLETSCHER *et al.*[2] have shown that reserpine produces a release of 5-hydroxytryptamine (5-HT) from the gastrointestinal mucosa, blood platelets and brain, and the contemporaneous appearance of an increased urinary excretion of 5-hydroxyindoleacetic

[1] P. A. SHORE, S. L. SILVER, and B. B. BRODIE, Science *122*, 284 (1955). – P. A. SHORE, A. PLETSCHER, and B. B. BRODIE, J. Pharmacol. *116*, 51 (1956).

[2] A. PLETSCHER, P. A. SHORE, and B. B. BRODIE, Science *122*, 374 (1955); J. Pharmacol. *116*, 46 (1956).