of epinephrine were completely prevented by comparatively small doses of adrenergic blocking drugs, N-(2-bromoethyl)-N-ethyl-l-naphthalenemethylamine.HBr (SY-28) and N-(2-chloroethyl) - N - ethylbenzhydrylamine.HCl (SY-2).

2. It would appear unlikely that epinephrine toxicity and the pulmonary edema involved are importantly related to histamine release from tissues since the antihistaminics, Pyranisamine (Neoantergan maleate) and Phenergan (3277 RP), failed to prevent edema although large subcutaneous doses of Phenergan reduced mortality.

3. The barbiturates, pentobarbital sodium and phenobarbital sodium did not decrease mortality or edema.

4. The available evidence indicates that epinephrine toxicity is most readily reduced by vasodilator drugs which represent physiological antagonists, and by adrenergic blocking drugs which are pharmacological antagonists of epinephrine.

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17105. Myelination of the Hypothalamus and Its Relation to Thermoregulation in the Hamster.*

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Correlation of the ability to regulate body temperature in a cold environment with progressive myelination of the hypothalamus has been previously demonstrated in albino rats.[1] The ability of rats to maintain body temperature is acquired at ages ranging between 18 and 30 days. The earlier literature indicating that function of fiber tracts in the central nervous system may be dependent upon myelination of their component nerve fibers was briefly reviewed in a previous report.[1]

In the present report the results of an investigation of myelination in the hypothalamus of the hamster and the development of its ability to regulate against cold are presented. The investigation seemed indicated in view of the fact that hamsters are more immature at birth than rats.

Methods and materials. Six litters of Syrian hamsters were used in the present study. Their body temperatures were recorded by means of a Brown electronic continuous recording potentiometer and copper-constantan thermopiles. The thermopiles were inserted into the colons of the animals to a depth of 4-5 cm. Animals varying from 6-71 days of age were subjected to environmental temperatures of 5-8°C for periods varying from 30 minutes to 20 hours. After exposure the hamsters were anesthetized and perfused with 3½% potassium dichromate followed by Regaud's solution. The brains were then removed, divided in the median sagittal plane and placed in 5% potassium dichromate where they remained for 10 days days at a temperature of 37-39°C. After washing, dehydration, embedding, and sectioning at 20 μ they were stained according to the method of Ulett, Dow, and Larsell.[2] Sections were made in the parasagittal plane to permit study of all areas of the hypothalamus (rostral, caudal and middle) in each section. Representative sections from the lateral hypothalami of all members of a given litter were stained en masse and myelin was quantitated by means of a Photovolt electronic photometer as previously described.[1] In only two instances, because of the difficulty in procuring large litters of hamsters, was a litter-mate control sacrificed with the experimental animals.

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1 Buchanan, A. R., and Hill, R. M., PROC. SOC. EXP. BIOL. AND MED., 1947, **66**, 602.

2 Ulett, G., Dow, R. S., and Larsell, O., *J. Comp. Neur.*, 1944, **80**, 1.

Results. The first animal from the first litter of hamsters studied was subjected to cold stress at 6 days of age and the other members were successively stressed on the 13th, 18th, 20th, 25th, and 32nd days. The duration of cold stress was 30 minutes. The fall in body temperature of the first animal was approximately 20°C. The older hamsters gradually improved in ability to regulate until the 32nd day when the temperature of the last animal in the litter fell only 3°C. The concentration of myelin in the dorsolateral areas of the caudal hypothalami, as determined photometrically, increased with age and reached its highest level in the 32-day animal. A parallel increase was evident in the myelin of the medullary pyramids but the concentration was considerably higher than in the hypothalamus at all ages.

The members of the second litter were cold-stressed for 30 minutes at ages ranging from 12-36 days. Regulation was best in the 31-day animal in which hypothalamic myelin was also at its highest level. The same was true of Litter No. 3 which was cold-stressed (30 minutes) at ages ranging from 18-46 days. Deterioration in regulatory ability and some apparent decrease in myelin were observed in the 3 members of this litter over 31 days of age (Fig. 1).

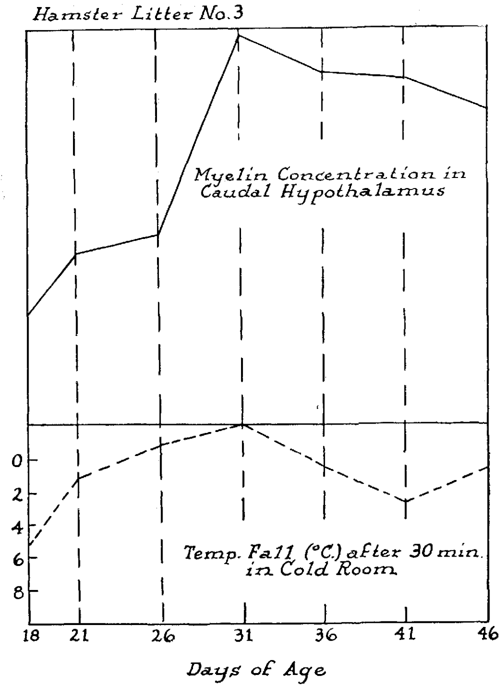

FIG. 1.

Temperature falls after 30 min. at 5-8°C and myelin concentrations in the caudal hypothalami of hamsters in Litter No. 3.

Cold stress was continued for 2 hours in the fourth litter studied (Fig. 2). Body temperatures of these hamsters averaged approximately 1°C lower at the end of 2 hours in the cold room than at 30 minutes. Myelin reached its highest level in the 25- and 30-day animals and regulatory ability was best at 30 days. Myelin appeared to decrease in hamsters over 30 days of age and there was an associated deterioration of regulatory ability which was most evident in the 55-day animal after 2 hours of exposure.

There were 10 hamsters in the fifth litter studied which may account for the fact that attainment of regulatory ability was somewhat delayed. Regulation was best at 42 days with myelin content of the caudal hypothalami increasing rather rapidly from 18-42 days. Regulation in the 50-, 60-, and 71-day animals was only slightly less efficient than in the younger animals and was actually better after 8 hours of exposure to the cold environment than after 2 hours. Myelin concentration in the hypothalami of the 3 oldest members fluctuated between levels slightly above and slightly below that of the 42-day animal.

The sixth and last litter also consisted of 10 hamsters, the first of which (18 days) was not included in Fig. 3 since its temperature, after 2 hours of exposure, had dropped below the range of available recording equipment. Regulation against cold was best at 44 days at which time myelin in the caudal hypothalamus was also at its highest level. Litter-mate controls were sacrificed with the 40- and 59-day stressed animals of this litter and, in both instances, showed higher levels of myelin in their caudal hypothalami than the stressed hamsters (Fig. 3). The 40-, 44-, 59-, and 69-day animals were left in the cold room for 9, 11, 17, and 20 hours respectively; all maintained their body temperatures at levels equal to or higher than those manifested after exposure for 2 hours.

Discussion. The experimental data which

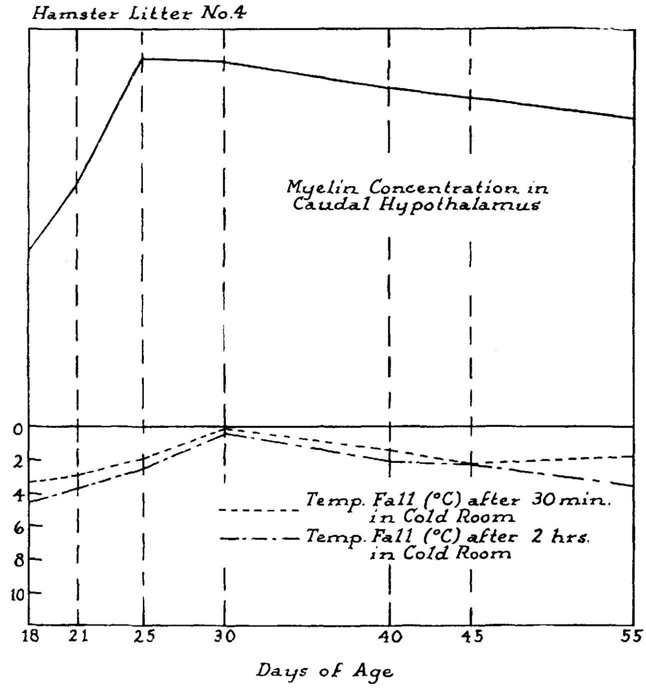

FIG. 2.
Temperature falls after 30 min. and 2 hr in the cold environment and myelin concentrations in the caudal hypothalami of hamsters in Litter No. 4.

have been obtained from subjecting hamsters to an environmental temperature of 5-8°C indicate that their attainment of ability to regulate against cold is considerably more delayed than in albino rats, or 32-44 days of age as compared to 18-30 days. This was to be expected since the gestation period in hamsters is considerably shorter than in rats with the result that hamsters are more immature at birth.

The maintenance of body temperature by reasonably mature hamsters in an environment ranging between 5° and 8°C for periods of 20 hours or more is not surprising. Sexually mature hamsters over three months of age were kept in an environmental temperature of 4° ± 2°C for periods of one or two months by Lyman[3] without appreciable reduction from normal of their body temperatures until they entered hibernation. Most of his hamsters "entered hibernation within a month or two after being brought into the cold room"; during hibernation their temperatures were only about 1°C above that of the environment.

As is the case in rats,[1] myelination, determined photometrically, reaches its highest level in the caudal hypothalamus of the hamster at the age when regulatory function is established. This observation, in an additional rodent, supports the hypothesis previously advanced that the role of the hypothalamus in thermoregulation is facilitated, at least in part, by myelination of the axons of hypothalamic neurons.

The observation that myelin concentration in the hypothalamus is higher, according to our method of measurement, in unstressed than in stressed animals from the same litter and at the same age suggests mobilization or change in chemical composition of myelin as a part of the metabolic reaction to cold stress. This may be a more prominent feature in older animals in which the process of primary myelination is essentially complete and it may account for the apparent tendency for myelin

[3] Lyman, C. P., *J. Exp. Zool.*, 1948, **109**, 55.

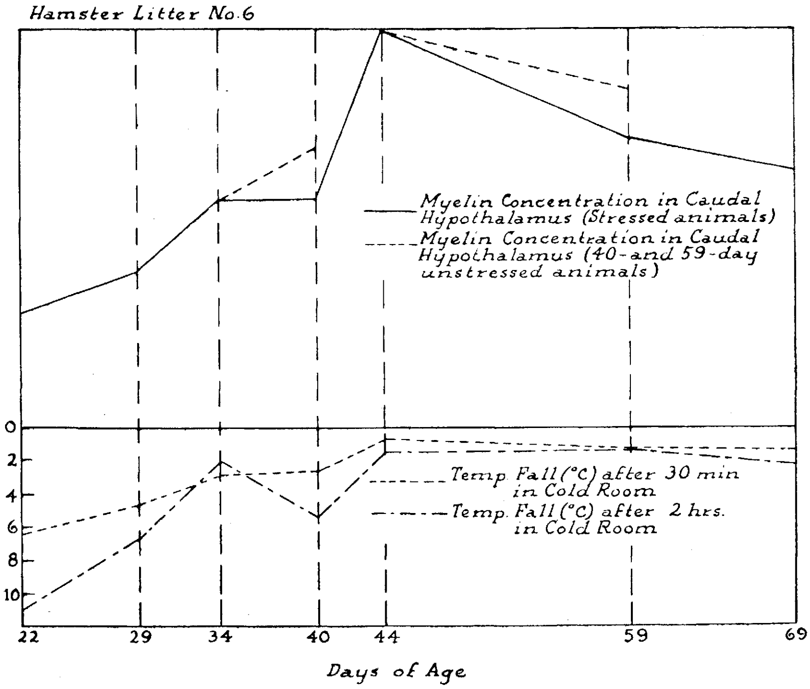

FIG. 3.

Temperature falls after 30 min. and 2 hr in the cold environment and myelin concentrations in the caudal hypothalami of hamsters in Litter No. 6. The differences between myelin concentrations in stressed and unstressed animals at 40 and 59 days of age are also shown.

to decrease after reaching its highest level in hamsters and in the rats previously studied.[1] All the animals heretofore used in plotting myelin curves have been stressed animals, sacrificed immediately after removal from the cold environment. It is unlikely that the mild but consistent deterioration in regulatory ability evident in the older animals (Fig. 2 and 3) is directly related to the decrease in density of stained myelin in the hypothalami, but the possibility cannot be overlooked.

Summary. Hamsters acquire the ability to effectively regulate their body temperatures in a cold environment (5° - 8°C) at ages ranging from 30-44 days. Myelination in the dorsolateral areas of the caudal hypothalamus, as determined photometrically, reaches its height at the time thermoregulation becomes fully developed. It appears therefore that myelination of hypothalamic neurons may be essential to functional maturation of the hypothalamus. The data with respect to hamsters are similar and lend support to those previously reported for albino rats.

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