

These experiments confirm the work of BROWN¹ that acute doses of PTU increase iodide excretion by a mechanism which is independent of its action on the thyroid, and circulating thyroxine levels. Furthermore this work demonstrates that PTU is a chloruretic agent and, as was shown by MCCARTHY, FREGLY and NECHAY² using diuretics, iodide clearance is closely correlated with the

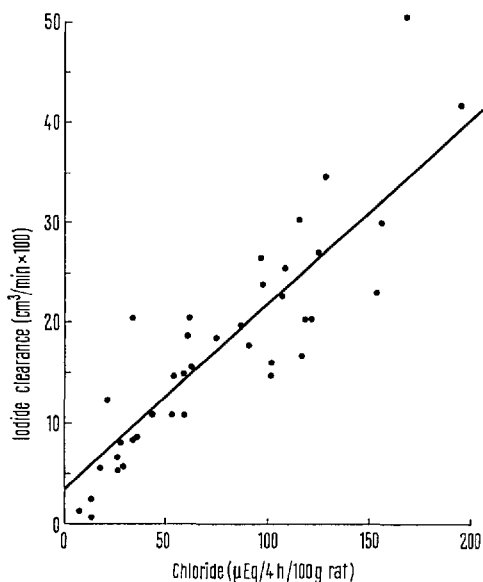
excretion of chloride. One significant difference however between these diuretics and PTU is that we found no increased urine flow with PTU treatment.

It is known that chronic treatment of rats with PTU increases water and electrolyte excretion, an effect which is due to the hypothyroid state of these animals⁴⁻⁸. In the work reported here acute doses of PTU increase urinary electrolyte output in the rat by an extrathyroidal action⁹.

Zusammenfassung. In kurzdauernden Versuchen wird gezeigt, dass Propylthiouracil, das sonst als Thyreostaticum bei Hyperthyreose gebraucht wird, die Jodidausscheidung durch die Niere erhöht. Die Erhöhung der Jodidausscheidung ist mit der ebenfalls auftretenden Steigerung der Ausscheidung von Chlorid, Natrium und Kalium korreliert, ohne dass Wasser in vermehrtem Masse ausgeschieden wird.

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Correlation between renal iodide clearance and chloride excretion. Each point represents 1 rat experiment from data in Table I. The best straight line was calculated by the method of least squares.

⁴ R. E. TAYLOR and M. J. FREGLY, *Endocrinology* 75, 33 (1964).

⁵ M. J. FREGLY and R. E. TAYLOR, *Endocrinology* 75, 27 (1964).

⁶ F. STEPHAN, H. JAHN and B. METZ, *C. r. Séanc. Soc. Biol.* 153, 1262 (1959).

⁷ F. STEPHAN, H. JAHN and B. METZ, *C. r. Séanc. Soc. Biol.* 153, 332 (1959).

⁸ F. STEPHAN, H. JAHN and P. RÉVILLE, *C. r. Séanc. Soc. Biol.* 154, 1082 (1960).

⁹ Acknowledgment: We thank Dr. G. B. BRISCOE for providing radioisotope counting facilities and Miss K. BEYNON for technical assistance.

A Contribution on the Effect of Noradrenaline on Heat Production in Mice

The calorogenic effect of noradrenaline has been studied primarily in the new-born of various mammals¹, to a lesser degree in adult organisms. In laboratory animals, attention has focused mainly on the effect on rats and guinea-pigs. In our experiments we concentrate our interest on the action of i.p. injections of L-noradrenaline on heat production in adult mice.

Our observations were made on 3 groups of mice, males aged 10 weeks. 1 group consisted of normal mice of H strain, kept under laboratory conditions at 23–25 °C, while the second group of animals of the same strain was adapted for 6 weeks to a temperature of 17 °C, and the third group of hairless mice of Biofysikální ústav (BFU) strain² was kept at 23–25 °C. In the mice of each group the oxygen consumption was measured individually with a gas analyser 30 min before the injection of noradrenaline and after the injection for the duration of the effect. L-noradrenaline (SPOFA) was applied in doses of 1.6 and 0.8 mg respectively per kg of body weight i.p. diluted in distilled water. The control animals were given only distilled water or were subjected to the needle prick without injecting any substance. The mice were measured in a small thermostated chamber; just before the injection the animals were taken out of the chamber and put back again after the injection. The temperature in the chamber was in all cases 30 °C.

The results of the effect of noradrenaline are summarized in the Figure, together with the initial values of the individual groups prior to injection. The time behaviour of oxygen consumption after the injection is presented as the mean of 5-min intervals of measurements. The initial values prior to injection are marked as the mean of the intervals with minimum oxygen consumption. In the mice of the first 2 groups, this value corresponds at the chamber temperature of 30 °C approximately to the basal value in the thermoneutral zone. In the hairless animals the oxygen consumption is somewhat higher owing to the fact that their thermoneutral temperature lies in the neighbourhood of 34 °C³. In the region of their thermoneutral temperature, the value of oxygen consumption, established on the basis of actual measurements, amounts to 2.3 ± 0.1 (cm³/h × g).

In all groups of mice a marked increase in oxygen consumption occurs after the injection. In the control groups the increase is caused primarily by the adaptation

¹ R. E. MOORE and M. C. UNDERWOOD, *Lancet* 1277 (1960).

² J. CHLUMECKÝ, *Folia. biol., Praha* 13, 396 (1967).

³ B. HOŠEK, J. MŘUSTOVÁ and J. CHLUMECKÝ, *Pflügers Arch. ges. Physiol.* 296, 248 (1967).

reactions to handling of the animals outside the chamber. This circumstance means that the oxygen consumption after doses lower than approximately 0.8 mg/kg body weight can no longer manifest itself, because it does not exceed the increase caused by the adaptation reaction to the intervention. The limit of maximum oxygen consumption after the injection is distinctly marked only for higher doses in the groups of normal mice, while in the hairless animals the plateau is indistinct. After this higher dose, about 40% mortality of animals in all 3 groups occurs on the second to the third day after the injection. The difference in hairiness manifests itself in the reaction to noradrenaline primarily in the achieved maximum increase in oxygen consumption over the normal animals kept at 24°C and also over the animals adapted to 17°C ($p < 0.05$), where the slight excess over the non-adapted group is only insignificantly indicated. The more marked reaction of the hairless animals corresponds to the findings⁴⁻⁶ that adaptation to cold, accompanied by a simultaneous elevation of the rest values of respiratory metabolism, causes a multifold higher calorogenic effect of nor-

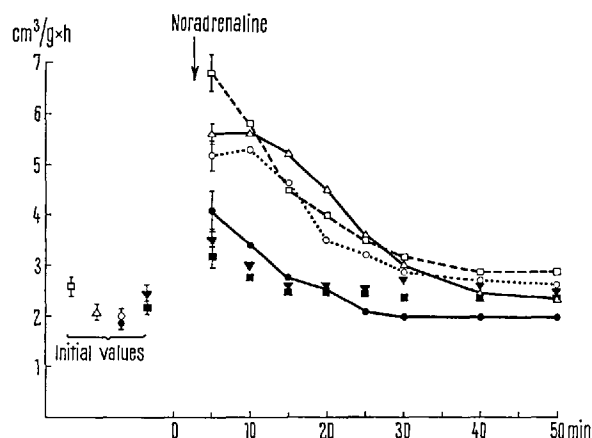
adrenaline. Owing to the rapid fading of the reaction, the question remains how much higher is the dose necessary for producing the maximum effect in mice than in rats or guinea-pigs, where it is 0.2–0.4 mg/kg.

Unlike rats or guinea-pigs it has been found that in mice the calorogenic effect of noradrenaline is very intensive also in adult individuals. In rats kept at 25°C, JÁNSKÝ et al.⁴ report an elevation of 25%, while in adult guinea-pigs kept at 30°C the increase lies about 20% over the value in the thermoneutral zone⁷. In the adult mice measured by us the % excess over the value in the thermoneutral zone after a dose of 1.6 mg/kg for mice of the H strain kept at 24°C makes 155%, for H-strain mice adapted to 17°C 170%, and for hairless animals 195%. The question arises how the method of administering noradrenaline, which had been applied i.m. in the cases cited, influences the overall reaction. It appears that owing to the association between the response to noradrenaline and the extent of non-shivering heat production, demonstrated distinctly in guinea-pigs⁸, the intensity of non-shivering heat production in adult mice reaches markedly higher values compared with other mammals.

Zusammenfassung. Bei ausgewachsenen Mäusen wurde nach i.p. Noradrenalininjektion die Steigerung der O₂-Aufnahme über den Grundumsatz in der Thermoneutralzone verfolgt. Nach einer Dosis von 1,6 mg/kg wurde ein bedeutender Unterschied ($p < 0,05$) der O₂-Aufnahmesteigerung zwischen der Gruppe normaler (155%) und normaler, auf 17°C adaptierter Mäuse (165%) und der Gruppe haarloser Mäuse (195%) festgestellt.

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Oxygen consumption before and after i.p. injection of L-noradrenaline in mice. □—□ Hairless (1.6 mg/kg); △—△ normal adapted to 17°C (1.6 mg/kg); ○—○ normal kept at 24°C (1.6 mg/kg); ●—● normal kept at 24°C (0.8 mg/kg); ■ controls (distilled water); ▼ controls (needle prick only).

⁴ L. JÁNSKÝ, R. BARTUŇKOVÁ and E. ZEISBERGER, *Physiologia bohemoslov.* 16, 336 (1967).

⁵ E. ZEISBERGER and K. BRÜCK, *Pflügers Arch. ges. Physiol.* 296, 263 (1967).

⁶ A. C. L. HSEH and L. D. CARLSON, *Am. J. Physiol.* 190, 243 (1957).

⁷ E. ZEISBERGER, K. BRÜCK, W. WÜNNENBERG and C. WIETASCH, *Pflügers Arch. ges. Physiol.* 296, 276 (1967).

Effect of Cardiac Catecholamine Depletion Through Sympathectomy on Spontaneous Ventricular Fibrillation During Induced Hypothermia in Cats

Much evidence has accumulated to show that the sympathetic nerves are highly involved in the spontaneous development of ventricular fibrillation, a common complication during induced deep hypothermia in homeothermic mammals. Thus, blockade of the adrenergic neurons with bretylium¹, depletion of the neuronal noradrenaline stores with prenylamine^{2,3} or reserpine⁴, and blockade of the adrenergic β -receptors with INPEA⁵ effectively prevents the spontaneous ventricular fibrillation constantly developing in untreated cats subjected to hypothermia to about 21°C body temperature.

In the present series of experiments, an attempt was made to obtain a more limited interference with the adrenergic mechanisms by way of cardiac sympathectomy.

In detailed investigations on the sympathetically innervated nictitating membrane of the cat, it has been demonstrated that the denervation supersensitivity starts to build up during the first 2 days following operation, accompanying the progressive degenerative changes and

¹ K. C. NIELSEN and CH. OWMAN, *Life Sci.* 7, 159 (1968).

² K. C. NIELSEN and CH. OWMAN, *Experientia* 23, 203 (1967).

³ K. C. NIELSEN and CH. OWMAN, *Circulation Res.* 27, 45 (1967).

⁴ K. C. NIELSEN and CH. OWMAN, *Archs int. Pharmacodyn. Théor.*, in press (1968).

⁵ K. C. NIELSEN and CH. OWMAN, *Life Sci.* 5, 1611 (1966).