The Effect of Acute Doses of Propylthiouracil on the Renal Excretion of Iodide and Other Electrolytes in the Rat

BROWN[1] demonstrated that acute doses of propylthiouracil (PTU) increase the renal clearance of injected iodine-131 in the thyroxine-maintained, thyroidectomized rat. He suggested that this was due to inhibition of an active tubular transport mechanism for kidney iodide. It has since been shown that the diuretics which increase chloride excretion also increase urinary iodide loss[2]; which suggests that these 2 ions are excreted in a similar manner by the kidney. In the work reported here we have re-examined the effects of acute PTU treatment in the rat to determine whether a chloruresis accompanies the increased iodide excretion.

Normal female Wistar rats weighing approximately 250 g maintained on a 41-B diet were used. 14 h preceding an experiment animals were deprived of solid food. On the experimental day each rat was injected s.c. with approximately 3 μc of iodine-131 (Radiochemical Centre, Amersham) in an accurately measured volume of isotonic saline (0.1 ml). 2 h later a 0.1-ml sample of tail blood was obtained and an oral load of distilled water (5 ml) at pH 8.4 containing the PTU was administered by stomach tube; these procedures invariably resulted in the rats urinating. They were then placed in individual metabolism cages and urine collected over a 4-h period at the end of which they were required to breathe ether in order to stimulate emptying of the bladder. A second tail blood sample was then taken (0.1 ml), the animals killed and the thyroids dissected out and homogenized in 10% NaOH. Throughout the 6-h experimental period no food or water was given. In a second series of experiments 20 μg of thyroxine in 0.1 ml distilled water was given i.p. at the time of water loading.

Blood samples, aliquots of urine and thyroid homogenate from each rat, together with an aliquot of the injected iodine were then counted for iodine-131 using a Nuclear Enterprises Gammamatic. The percentage excretion of injected iodine-131 during the collection period was calculated, together with renal iodide clearance values for each rat, determined by the method of ALBERT, TENNEY and LORENZ[3]. Urine was analysed for sodium and potassium by flame photometry, and chloride determined using an 'EEL' chloride meter.

Less than 4 % of the injected iodide accumulated in the thyroids of all animals. All doses of PTU increased significantly the excretion of iodide, sodium, chloride and potassium above control levels ($p < 0.01$, Table I), but did not significantly alter urine flow. The Figure shows the relationship between renal iodide clearance and chloride excretion when the data for individual animals from Table I are plotted. The correlation coefficient is highly significant ($p < 0.001$); the same degree of correlation is also found between iodide clearance and sodium excretion.

The effects of a physiological dose of thyroxine, given at the time of water loading, on electrolyte and urine excretion are shown in Table II. Iodide, sodium, chloride and urine excretion are not significantly different in these thyroxine-treated groups when compared with the corresponding groups in Table I which were not given thyroxine.

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Table I. Effect of acute doses of propylthiouracil on electrolyte and water excretion in water loaded rats

Treatment	No. of rats	Body weight (g)	4-h urinary excretion of Cl⁻ (μEq/100 g body weight)	Na⁺	K⁺	I⁻ (% of injected)	Urine (ml/100 g body weight)	Renal iodide clearance (cm³/min × 100)
Control	8	241 ± 7	23.5 ± 3.6	7.7 ± 1.2	30.7 ± 3.1	7.3 ± 1.5	2.1 ± 0.1	5.6 ± 1.1
10 mg PTU/rat	8	240 ± 7	71.3 ± 13.1	56.7 ± 8.7	75.1 ± 4.2	18.3 ± 2.9	2.2 ± 0.2	12.8 ± 2.0
15 mg PTU/rat	8	258 ± 6	88.8 ± 11.6	70.3 ± 13.0	75.9 ± 4.6	26.7 ± 2.4	2.3 ± 0.1	19.5 ± 2.3
20 mg PTU/rat	8	241 ± 6	122.2 ± 16.3	112.8 ± 14.9	74.9 ± 8.3	31.5 ± 4.1	2.4 ± 0.1	24.4 ± 3.2
30 mg PTU/rat	7	251 ± 6	84.9 ± 20.6	96.3 ± 25.4	72.5 ± 14.8	31.3 ± 3.8	1.5 ± 0.2	26.0 ± 4.9

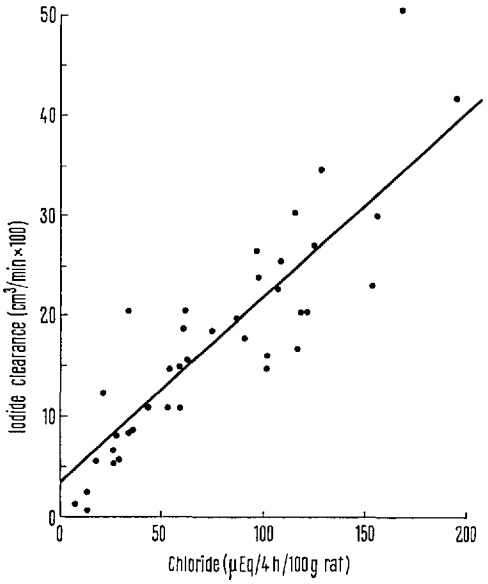
Standard errors of the mean are indicated.

Table II. Effect of thyroxine and propylthiouracil on electrolyte and water excretion in water loaded rats

Treatment	No. of rats	Body weight (g)	4-h urinary excretion of Cl⁻ (μEq/100 g body weight)	Na⁺	K⁺	I⁻ (% of injected)	Urine (ml/100 g body weight)	Renal iodide clearance (cm³/min × 100)
Thyroxine 20 μg/rat	8	239 ± 6	27.2 ± 3.1	8.1 ± 1.3	47.9 ± 2.8[a]	9.7 ± 1.5	2.3 ± 0.1	6.6 ± 1.2
Thyroxine 20 μg/rat + 15 mg PTU/rat	8	258 ± 4	91.1 ± 14.0	62.1 ± 12.9	75.0 ± 6.0	23.2 ± 2.2	1.9 ± 0.2	17.8 ± 2.4

Standard errors of the mean are indicated. [a] Significantly different from control group in Table I. $p < 0.001$.

These experiments confirm the work of BROWN[1] that acute doses of PTU increase iodide excretion by a mechanism which is independant 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 NECHAY[2] 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.



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.

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 animals[4–8]. In the work reported here acute doses of PTU increase urinary electrolyte output in the rat by an extrathyroidal action[9].

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.

A. J. MATTY and R. G. PYE

The Department of Biological Sciences, University of Aston, Birmingham 4 (England), 22 July 1968.

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

The calorigenic effect of noradrenaline has been studied primarily in the new-born of various mammals[1], 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) strain[2] 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 °C[3]. 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 ($cm^3/h \times g$).

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

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