PENTOBARBITONE-BARBITONE ANAESTHESIA AND THYROID FUNCTION IN THE RAT

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There are reports that di-ethyl ether and thiopentone depress thyroid function as measured by $^{131}$I uptake (Wase & Foster, 1956; Oyama, 1957), $^{131}$I incorporation into organic union and release by the gland (Oyama, 1959). However, pentobarbitone (Nembutal) in anaesthetic amounts for short periods is reported to have no significant effect on $^{131}$I release (Perry, 1951; Oyama, 1959). The present investigation describes effects on thyroid hormone metabolism and thyroid function during 8 hr. of surgical anaesthesia in the rat produced by a mixture of pentobarbitone and barbitone.

Sprague–Dawley rats (Holtzman Farms), weighing between 250 and 300 g., were housed individually and fed ad libitum. The animals were injected with 10–20 $\mu$C $^{131}$I (Abbott Laboratories) 48 hr. before the start of the experiment, and 2 mg. methimazole (Tapazole, Lilly) per rat were injected i.p. 24 hr. before and again on the morning of the day of the experiment to prevent re-utilization by the thyroid of $^{131}$I derived from metabolized labelled organic iodine (Premachandra & Turner, 1960). Methimazole has been shown to have no extrathyroidal effects (Grosvenor, 1962). Prolonged anaesthesia was produced by the i.p. injection of a mixture of 22-5 mg. sodium pentobarbitone and 100 mg. sodium barbitone/kg. body weight with supplementary small doses as needed to prevent a righting reflex during an 8-hr. period. Serum protein bound iodine (PBI), thyroidal $^{131}$I and blood precipitable $^{131}$I were measured by conventional techniques (Premachandra, 1965). Thyrotrophic hormone (TSH, NIH) was administered in large doses (500–2000 m-u./rat) and the effect on thyroidal $^{131}$I release and on precipitable $^{131}$I in plasma was studied.

The results are shown in Table 1. Thyroidal $^{131}$I release was significantly ($P < 0.01$) reduced in the anaesthetized rats as compared with the control animals. In control animals there was a decline of 15.2% in radioactivity over the thyroid gland from the initial value during an 8-hr. interval as contrasted with a decrease of 7.7% in anaesthetized animals, this reduction was significant ($P < 0.01$, Table 1). This result was consistent with marked reduction in PBI in anaesthetized animals. PBI at the end of 8 hr. in the treated animals was 2.0 $\mu$g./100 ml. serum compared with 3.0 in control animals ($P < 0.001$). The possibility that enhanced peripheral utilization of thyroid hormone contributed to the decrease in PBI in the anaesthetized—and therefore inactive—rats is very unlikely; furthermore this state would have tended to increase rather than to decrease $^{131}$I secretion by the gland. Impairment of
Table 1. Thyroid function in rats anaesthetized with a mixture of pentobarbitone and barbitone and response to exogenous TSH

<table>
<thead>
<tr>
<th>No. of rats</th>
<th>Control</th>
<th>No. of rats</th>
<th>Anaesthetized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroidal $^{131}$I (controls)</td>
<td>15</td>
<td>(a) (-) 15.2±2.2</td>
<td>14</td>
</tr>
<tr>
<td>Thyroidal $^{131}$I (TSH-treated)</td>
<td>7</td>
<td>(c) (-) 36.3±6.1</td>
<td>7</td>
</tr>
<tr>
<td>Blood precipitable $^{131}$I (TSH-treated)</td>
<td>6</td>
<td>(e) (+) 48.9±6.5</td>
<td>6</td>
</tr>
<tr>
<td>PBI (µg./100 ml.)</td>
<td>15</td>
<td>(g) 3.0±0.2</td>
<td>20</td>
</tr>
</tbody>
</table>

- = decrease in radioactivity in external thyroid counting; + = increase in precipitable $^{131}$I in blood plasma. 't' between (a) and (b) = $P < 0.01$; 't' between (c) and (d) = $P < 0.2$; 't' between (e) and (f) = $P < 0.1$; 't' between (g) and (h) = $P < 0.001$.

respiratory and circulatory processes as well as factors mediated by the kidneys and the adrenal glands contributing to the change in thyroid function in anaesthetized rats cannot be excluded. In any case, our investigations indicate that anaesthesia with a mixture of pentobarbitone and barbitone maintained for 8 hr. has an anti-thyroid effect. The significant reduction in thyroid activity caused by this type of anaesthesia would seem to contrast with the effects of pentobarbitone alone which has been reported to have no influence on thyroidal $^{131}$I release. The absence of -SH groups in pentobarbitone is believed to be the reason for the lack of an anti-thyroidal effect (Oyama, 1959). The -SH grouping is absent in barbitone. Anaesthetics containing -SH groups are metabolized in the body with the production of substances like thiourea (Brodie et al. 1950) that subsequently inhibit thyroid function.

In TSH-treated animals the apparent decline in thyroid radioactivity, at the end of 8 hr. in the anaesthetized group was 24.5% as compared with 36.3% in the controls. There was a similar suggestion of correlation with plasma $^{131}$I values. In control animals treated with TSH, the increase in radioactivity in the precipitable fraction in plasma was 48.9% during an 8-hr. period as compared with an increase of 32.1% in animals under pentobarbitone–barbitone anaesthesia. In both instances the differences were not significant. The maximum response occurred at the dose of 500 m.u./rat. It seems, therefore, that exogenous TSH may be less potent in discharging thyroidal $^{131}$I in anaesthetized animals than in untreated rats. A diminished response of the thyroid in the anaesthetized rat to exogenous TSH may have been an expression of the reduced sensitivity of the thyroid to thyrotrophic stimulation and/or due to an indirect effect of alterations in blood flow through the endocrine glands. (NIH grant A-5107.)

REFERENCES