INTERREGULATORY INFLUENCE OF PARASYMPATHETIC AND
SYMPATHOADRENAL SYSTEM ON THYROID STATUS IN RATS

In vertebrates, thyroid hormones have morphogenic actions (Jones and Chin, 1991) and is
necessary for both normal development and homeostasis (Alderson et al., 1985). Its status
influences variety of metabolic parameters in virtually all mammalian tissues (Oppenheimer,
1979). Thyroid hormone also governs metabolic reactions concerned with glucose uptake,
glycogenolysis and gluconeogenesis (Pilo et al., 1984a). These hormones are known to
regulate metabolic rates of the body in general and oxidative reactions in particular (Guyton,
1981). The primary physiological effect of thyroid hormone on target organ metabolism is
thought to occur through its binding sites in the nucleus with a subsequent alteration in the
rate of synthesis of certain proteins in the cell for example Malic dehydrogenase (Goodridge,
1975; 1978), GH (Martial et al., 1977; Shapiro et al., 1978) and alpha2-globulin (Roy et al.,
1976).

To maintain a normal basal metabolic rate, precisely the right amount of thyroid
hormone must be secreted all the time, and to provide this, a specific feedback mechanism
operates through the hypothalamus and anterior pituitary gland to control the rate of thyroid
secretion (Yanagisawa et al., 1988). The activity of the thyroid gland is regulated by
variations in the plasma levels of TSH (Tong, 1974; Dumont, 1971). In the thyroid gland,,
TSH stimulates cAMP formation (Dumont, 1971), exocytosis of precursor thyroglobulin, and
proteolytic processing of the thyroglobulin to form thyroid hormones (Nielsen et al., 1985).
Thus, the immediate action of this hormone is to release thyroid hormone from the gland.
Subsequently it increases the uptake of iodine from the blood and promotes hyperplasia of
the gland. Moreover, the output of TSH from the anterior pituitary is itself governed by the plasma levels of the thyroid hormones, a fall in the latter increasing the output and a rise diminishing it.

Like in other endocrine glands, both adrenergic innervation (Melander et al., 1972; Melander, 1976a) as well as cholinergic innervation from the vagus (Amenta et al., 1978) of the mammalian thyroid have been studied in some detail. These fibers influence the short term activity of the gland by the former facilitating and the latter inhibiting hormonal release.

Apart form this, thyroid hormone secretion is also regulated by other hormones. There is a body of evidence showing that glucocorticoids have multiple effects on the hypothalamo-pituitary-thyroid axis of some birds and mammals (Decuypere et al., 1983; Cavalieri et al., 1984; Jennings and Ferguson, 1984). Even catecholamine have been reported to exert a variety of stimulatory as well as inhibitory actions on the thyroid (Mills and Sherwin, 1985). Epinephrine and norepinephrine release TSH from monolayer cultures of rat and bovine anterior pituitary cells (Peters et al., 1983; Klibanski et al., 1983). In in vitro epinephrine and TRH act additively to release TSH (Dieguez et al., 1984). Thus epinephrine and hypothalamic neuropeptides might interact to control TSH secretion in vivo (Dieguez et al., 1985).

To determine whether there is an evidence of altered thyroid status in the absence of autonomic system and adrenal gland the present study was undertaken. In this study, the effects of impaired adrenergic and cholinergic systems on TSH release from anterior pituitary level and on the release of thyroid hormones from thyroid were investigated. The loss of cholinergic control was produced by performing subdiaphgramatic vagotony and the adrenergic through chemical sympathectomy. Guanethidine sulphate destroys adrenergic ganglion over four weeks period of time. Along with this, a total sympatho-adrenal influence was removed by subjecting rats to chemical sympathectomy and bilateral adrenalectomy together.

MATERIAL AND METHODS
Albino rats of Charles Foster strain weighing between 120-150 gm severed as experimental model. Rats were maintained in standard laboratory conditions with 12L:12D light regime. They were divided into twelve groups of six animals each and were subjected to various
surgical operations and drug treatments as discussed in materials and methods. Animals subjected to sham operation served as controls.

GROUP I VAGOTOMY (VGX)
GROUP II SHAM VAGOTOMY (VGS)
GROUP III ADRENALECTOMY (ADX)
GROUP IV SHAM ADRENALECTOMY (ADS)
GROUP V VAGOTOMY + ADRENALECTOMY (VGX + ADX)
GROUP VI SHAM VAGOTOMY + SHAM ADRENALECTOMY (VGS + ADS)
GROUP VII CHEMICAL SYMPATHECTOMY (CSX)
GROUP VIII CONTROL CHEMICAL SYMPATHECTOMY (CSS)
GROUP IX CHEMICAL SYMPATHECTOMY + VAGOTOMY (CSX + VGX)
GROUP X CONTROL CHEMICAL SYMPATHECTOMY + SHAM VAGOTOMY (CSS + VGS)
GROUP XI CHEMICAL SYMPATHECTOMY + ADRENALECTOMY (CSX + ADX)
GROUP XII CONTROL CHEMICAL SYMPATHECTOMY + SHAM ADRENALECTOMY (CSS + ADS)

After respective treatments, overnight fasted animals were sacrificed and blood was collected from the jugular vein with utmost care. Serum was extracted by centrifuging the blood in the cold centrifuge at 2000rpm at -10°C. Serum samples were stored in frozen condition prior to analysis.

Serum T3, T4 and TSH level was assayed with tube ELISA kits. The absorbance of the samples were read at 450nm. The average absorbance of experimental and control group serum samples were calculated and the corresponding T4 concentration (µg/dl) was noted from the standard curve

Statistical Analysis
Statistical comparisons were made with Student’s 't' test for respective treatments. Data are presented as the mean ± SEM and P value < 0.05 was considered statistically significant.

RESULTS
Serum T3, T4, T4/T4 ratio and TSH level in response to removal of autonomic nervous system and adrenal gland is depicted in Table 7.1, 7.2 and Figure 7 1-7.8, respectively.
Table 7.1 Serum triiodothyronine (T3), Thyroxine (T4) and Thyroid Stimulating Hormone (TSH) levels in rats subjected to vagal and sympato-adrenal manipulation.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Triiodothyronine (T3) [ng/dl]</th>
<th>Thyroxine (T4) [μg/dl]</th>
<th>T3/T4 (x 100)</th>
<th>TSH [μU/ml]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sham</td>
<td>Experimental</td>
<td>Sham</td>
<td>Experimental</td>
</tr>
<tr>
<td>Vagotomy</td>
<td>51.00 ± 2.51</td>
<td>74.20****</td>
<td>3.04 ± 0.15</td>
<td>1.68 ± 0.045</td>
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<td></td>
<td></td>
<td></td>
<td>2.52** ± 0.10</td>
<td>2.49*** ± 0.15</td>
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<td></td>
<td></td>
<td>1.13 ± 0.054</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>0.78**** ± 0.041</td>
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<tr>
<td>Adrenalectomy</td>
<td>50.60 ± 2.29</td>
<td>60.40**</td>
<td>3.13 ± 0.11</td>
<td>1.62 ± 0.051</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.62** ± 0.14</td>
<td>2.31*** ± 0.13</td>
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<td></td>
<td></td>
<td></td>
<td>1.01 ± 0.052</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.83* ± 0.039</td>
</tr>
<tr>
<td>Vagotomy + Adrenalectomy</td>
<td>48.00 ± 3.21</td>
<td>67.41****</td>
<td>2.93 ± 0.13</td>
<td>1.64 ± 0.053</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3.54** ± 0.16</td>
<td>1.90** ± 0.07</td>
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<td></td>
<td></td>
<td>1.06 ± 0.059</td>
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<td></td>
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<td></td>
<td></td>
<td>0.85** ± 0.042</td>
</tr>
<tr>
<td>Chemical Sympathectomy</td>
<td>53.00 ± 2.43</td>
<td>41.60**</td>
<td>3.12 ± 0.15</td>
<td>1.70 ± 0.062</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>2.54** ± 0.12</td>
<td>1.64 NS ± 0.064</td>
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<td></td>
<td>1.04 ± 0.046</td>
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<td></td>
<td></td>
<td>1.29*** ± 0.060</td>
</tr>
<tr>
<td>Chemical Sympathectomy +</td>
<td>51.80 ± 2.31</td>
<td>34.41****</td>
<td>3.22 ± 0.15</td>
<td>1.61 ± 0.057</td>
</tr>
<tr>
<td>Adrenalectomy</td>
<td></td>
<td></td>
<td>2.56*** ± 0.13</td>
<td>1.35*** ± 0.043</td>
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<td></td>
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<td></td>
<td></td>
<td>1.05 ± 0.059</td>
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<td></td>
<td></td>
<td>1.34*** ± 0.061</td>
</tr>
<tr>
<td>Chemical Sympathectomy +</td>
<td>52.01 ± 2.44</td>
<td>42.00**</td>
<td>2.99 ± 0.11</td>
<td>1.74 ± 0.061</td>
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<tr>
<td>Vagotomy</td>
<td></td>
<td></td>
<td>3.45* ± 0.15</td>
<td>1.22*** ± 0.047</td>
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<td></td>
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<td></td>
<td>1.14 ± 0.065</td>
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<td></td>
<td></td>
<td>0.94* ± 0.051</td>
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</table>

* Values are expressed as mean ± SEM of 6 experiments; * p< 0.05; ** p< 0.02; *** p< 0.01; **** p< 0.001
Table 7.2 Percentage change (compared to controls) in triiodothyronine ($T_3$), thyroxine ($T_4$), $T_3$ to $T_4$ ratio and TSH in rats subjected to autonomic and adrenal manipulation

<table>
<thead>
<tr>
<th>Treatment</th>
<th>$T_3$</th>
<th>$T_4$</th>
<th>$T_3/T_4$</th>
<th>TSH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vagotomy</td>
<td>45&lt;sup&gt;®&lt;/sup&gt; ↓</td>
<td>17&lt;sup&gt;**&lt;/sup&gt; ↓</td>
<td>48&lt;sup&gt;****&lt;/sup&gt; ↑</td>
<td>31&lt;sup&gt;****&lt;/sup&gt; ↓</td>
</tr>
<tr>
<td>Adrenalectomy</td>
<td>19&lt;sup&gt;•&lt;/sup&gt; ↑</td>
<td>17&lt;sup&gt;**&lt;/sup&gt; ↓</td>
<td>43&lt;sup&gt;***&lt;/sup&gt; ↑</td>
<td>18&lt;sup&gt;•&lt;/sup&gt; ↓</td>
</tr>
<tr>
<td>Vagotomy + Adrenalectomy</td>
<td>40&lt;sup&gt;***&lt;/sup&gt; ↑</td>
<td>21&lt;sup&gt;**&lt;/sup&gt; ↑</td>
<td>16&lt;sup&gt;**&lt;/sup&gt; ↑</td>
<td>20&lt;sup&gt;**&lt;/sup&gt; ↓</td>
</tr>
<tr>
<td>Sympathectomy</td>
<td>22&lt;sup&gt;**&lt;/sup&gt; ↓</td>
<td>19&lt;sup&gt;**&lt;/sup&gt; ↓</td>
<td>04&lt;sup&gt;NS&lt;/sup&gt; ↓</td>
<td>24&lt;sup&gt;***&lt;/sup&gt; ↑</td>
</tr>
<tr>
<td>Sympathectomy + Adrenalectomy</td>
<td>34&lt;sup&gt;****&lt;/sup&gt; ↓</td>
<td>20&lt;sup&gt;***&lt;/sup&gt; ↓</td>
<td>16&lt;sup&gt;***&lt;/sup&gt; ↓</td>
<td>28&lt;sup&gt;***&lt;/sup&gt; ↑</td>
</tr>
<tr>
<td>Sympathectomy + Vagotomy</td>
<td>19&lt;sup&gt;**&lt;/sup&gt; ↓</td>
<td>15&lt;sup&gt;•&lt;/sup&gt; ↑</td>
<td>30&lt;sup&gt;***&lt;/sup&gt; ↓</td>
<td>18&lt;sup&gt;•&lt;/sup&gt; ↓</td>
</tr>
</tbody>
</table>

<sup>®</sup> Values corrected to nearest whole number; <sup>•</sup> p<0.05; <sup>**</sup> p<0.02; <sup>***</sup> p<0.01; <sup>****</sup> p<0.001
Figure 7.1 Levels of serum triiodothyronine ($T_3$), thyroxine ($T_4$), thyrotropin (TSH) and $T_3$ to $T_4$ ratio in rats subjected to vagotomy.

** p < 0.02; **** p < 0.001.
Figure 7.2 Levels of serum triiodothyronine (T₃), thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to adrenalectomy.


* p < 0.05; ** p < 0.02; *** p < 0.01.
Figure 3 Levels of serum triiodothyronine ($T_3$), thyroxine ($T_4$), thyrotropin (TSH) and $T_3$ to $T_4$ ratio in rats subjected to vagotomy and adrenalectomy in combination.

** p < 0.02; *** p < 0.01.

$T_3$ Thyroxine (pg/dl) TSH (pU/ml)

$T_4$ Thyroxine (pg/dl)

$T_3/T_4 \times 100$

Control
Experimental

** p < 0.02; *** p < 0.01.
Figure 7.4 Levels of serum triiodothyronine (T₃), thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy.

** p < 0.05; *** p < 0.01; NS Non Significant.
Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.

![Bar graph showing levels of triiodothyronine and thyroxine with statistical significance marks.]

**Note:**
- *** p < 0.01; **** p < 0.001.
- Control: []
- Experimental: [ ]

*Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.*

**Statistical Significance:**

- *** p < 0.01
- **** p < 0.001

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*Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.*

**Note:**
- *** p < 0.01; **** p < 0.001.

*Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.*

**Statistical Significance:**

- *** p < 0.01
- **** p < 0.001

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*Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.*

**Note:**
- *** p < 0.01; **** p < 0.001.

*Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.*

**Statistical Significance:**

- *** p < 0.01
- **** p < 0.001

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*Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.*

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**Statistical Significance:**

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- **** p < 0.001

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*Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.*

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**Statistical Significance:**

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- **** p < 0.001

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*Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.*

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**Statistical Significance:**

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- **** p < 0.001

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*Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.*

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**Statistical Significance:**

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*Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.*

**Note:**
- *** p < 0.01; **** p < 0.001.

*Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.*

**Statistical Significance:**

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- **** p < 0.001

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*Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.*

**Note:**
- *** p < 0.01; **** p < 0.001.

*Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.*

**Statistical Significance:**

- *** p < 0.01
- **** p < 0.001

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*Figure 7.5 Levels of serum triiodothyronine (T₃) thyroxine (T₄), thyrotropin (TSH) and T₃ to T₄ ratio in rats subjected to chemical sympathectomy and adrenalectomy in combination.*

**Note:**
- *** p < 0.01; **** p < 0.001.
Figure 7.6 Levels of serum triiodothyronine ($T_3$), thyroxine ($T_4$), thyrotropin (TSH), and $T_3$ to $T_4$ ratio in rats subjected to chemical sympathectomy and vagotomy in combination.

* $p < 0.05$; ** $p < 0.02$; *** $p < 0.01$. 

Thyroxine (pg/dl) TSH (pU/ml)

- Control
- Experimental
Figure 7.7 Percentage change in serum $T_3$, $T_4$, $T_3/T_4$ ratio and TSH levels in rats subjected to vagotomy (A), adrenalectomy (B), and their combination (C).
Figure 7.8 Percentage change in serum T_{3}, T_{4}, T_{3}/T_{4} ratio and TSH levels in rats subjected to chemical sympathectomy singly (A), and in combination with adrenalectomy (B), and vagotomy (C).
Following subdiaphragmatic vagotomy serum T₃ level increased significantly (P<0.001) compared to sham operated animals. This was accompanied by marked decrease in serum T₄ (P<0.02; Figure 7.1) and TSH level (P<0.001). Thereby, the T₃/T₄ ratio increased by 48%. Identical results were obtained in adrenalectomized rats. Serum T₃ level increased slightly, whereas TSH and T₄ level decreased noticeably by 18% and 16%, respectively (Table 7.2), indicating a marked increase in T₃/T₄ ratio (P<0.001) compared to adrenalectomized rats. But in VGX + ADX individuals both T₃ and T₄ increased concomitantly compared to sham operated animals. Serum T₃ level increased from 48.0 ± 3.21 to 67.41 ± 3.79 (P<0.001) and T₄ level increased from 2.93 ± 0.13 to 3.54 ± 0.16 (P<0.02), respectively (Table 7.1). The overall T₃/T₄ ratio increased significantly (P<0.02). Like VGX and ADX conditions, even in VGX + ADX group of rats, TSH level decreased (P<0.02) after 48hrs.

Guanethidine induced chemical sympathectomy increased serum T₃ and T₄ level decreased remarkably (P<0.02) over four weeks period of time compared to control group of animals injected with 0.9% saline. However, the T₃/T₄ ratio remained unaltered in these rats. But in CSX rats, TSH level increased from 1.04 ± 0.046 to 1.29 ± 0.060 (P<0.01). However, this decrease in thyroid hormones concentration (T₃ and T₄) was more pronounced in CSX + ADX rats (Figure 7.5). In these rats, serum T₃ and T₄ level decreased significantly to P<0.001 and P<0.01, respectively compared to their controls. Even, T₃/T₄ ratio decreased by 16% in these rats (Figure 7.8). Decreased thyroid hormone status in CSX + ADX rats was supported by remarkable increase in serum TSH level (p<0.01). In CSX + VGX rats, serum T₃ level decreased markedly (19%) whereas T₄ level increased slightly (15%). Thereby, T₃/T₄ ratio decreased markedly (P<0.01; Figure 7.6) compare to control group rats. Even TSH level depleted slightly (P<0.05) in these rats.

**DISCUSSION**

Data of the present study revealed an enhanced thyroid hormone status due to suppressed parasympathetic tone following vagotomy. In these rats, level of thyroid stimulating hormone (TSH) and thyroxine (T₄) in the serum depleted, whereas triiodothyronine (T₃) level increased compared to the sham operated rats. This low T₄ level may indicate its greater uptake by the liver and kidney, the two major organs in which much of the deiodination of T₄ and T₃ has been shown to occur in rats (Chiraseveenuprapund *et al.*, 1978; Visser and
Hennemann, 1980; Imai et al., 1981). This in turn, could be the reason of enhanced T₃ level and T₃/T₄ ratio in vagotomized rats. Moreover, enhanced T₃ level might have a negative feedback control on TSH which is mediated through the inhibition on the production of thyrotropin releasing hormone (TRH) by the hypothalamus (Kurihara et al., 1986; Yokokawa et al., 1989). Thus, the interaction of TRH with thyrotroph results in a multi-stepped cascade leading to elevated protein kinase C activity and ultimately to impaired TSH release. This is compatible with the observation of (Melander et al., 1977; Pilo et al., 1984a) in individuals suffering from diabetes mellitus.

Increased thyroid hormone also increases the rates of secretion of most other endocrine glands (viz., pancreas and adrenal), and it also increases the need of the tissues for the hormones. Increased thyroxine secretion increases the rate of glucose metabolism everywhere in the body and therefore causes a corresponding need for increased insulin secretion by the pancreas.

Along with the influence of adrenal hormones on thyroid status, there is a considerable evidence that thyroid hormones also influence the responses of various tissues to catecholamines, both in man and in laboratory animals (Dimitriadis et al., 1991). Thyroid hormones can also potentiate various metabolic effects of catecholamines like lipolysis, glycogenolysis in the heart and during thermogenesis (Landsberg, 1977) it is considered to increase the metabolic activities of almost all tissues of the body.

Also, E and NE have been reported to stimulate colloid droplet formation (Melander et al., 1972) and radioiodide release from thyroid glands of T₄-suppressed mice (Melander, 1976b, iodide organization in mouse (Maayan et al., 1981; 1983) and beef thyroid tissues (Maayan et al., 1973) as well as thyroid cAMP formation in mouse, beef or cat thyroid (Sherwin and Mills, 1980; Maayan et al., 1981). The involvement of adrenal hormones in the regulation of thyroid hormones secretion is highlighted by adrenalectomy. Adrenalectomy nullifies the anabolic impact of adrenal hormones on thyroid functional status. In these rats both sympathetic and parasympathetic components of autonomic nerves were intact. Increased T₃ concentration following adrenal abrogation is supplemented by deiodination of T₄. This might be the reason of decrease in T₄ concentrations. Moreover, inhibitory effect of T₃ inhibits TRH induced TSH release (Melmed et al., 1981) thereby, decreasing serum TSH
concentration in ADX rats. The increased T_{3} level might be exercising translational control, stimulating amino acid transport and generalized protein synthesis (Chapter 3). Also, increased T_{3} level appears to be able to increase the activity of various enzymes involved in lipogenesis (Mariash et al., 1980; Rao et al., 1984). This could be supported by the increased lipid stores in liver of adrenalectomized rats (Chapter 3). Even, T_{3}/T_{4} ratio increased in these rats suggesting deiodination of T_{4} to T_{3}.

When both vagus nerve and adrenal glands are abrogated simultaneously (VGX + ADX), the sympathetic counterpart regulate the metabolic activities. Melander and associates have shown that the sympathetic action does elicit secretion of the thyroid hormones (Melander, 1976a; 1978): The T_{3} and T_{4} releasing response elicited by the sympathetic nerve action has been shown to be considerably faster than that by TSH (Langer et al., 1983a; Nilson and Karlberg, 1983) and this beta adrenergic action is TSH independent (Langer et al., 1983b). This could be the reason of increased T_{3} and T_{4} level in ADX + VGX rats (i.e. enhanced thyroid activity). However, an increase in T_{3} level is more prominent than T_{4}, thereby suggesting the operation of deiodination of T_{4} to T_{3}. This in turn, results in an increased T_{3}/T_{4} ratio in these rats. This increased thyroid status may deplete anterior pituitary TSH secretion through a feedback mechanism controlled by TRH. The enhancement of metabolic rate by thyroid hormone (Barker and Klittgard, 1952) implies an increase in the requirement for cellular glucose uptake and indeed, thyroid hormone has been shown to increase glucose disposal in vivo (Muller et al., 1988b) and to stimulate glucose transport in cultured cells (Segal and Gordon, 1977; Harber et al., 1988). Thus, thyroid hormone appears to play a role in chronic regulation of cellular glucose transport.

The altered function of thyroid glands could at least in part be responsible for the lowered metabolic rate (Melander 1976a; Dumont, 1971). Several neuropharmacological studies in the rat suggest that the central regulation of TSH secretion is under alpha-adrenergic control (Kruklich et al., 1977; 1982; Mannisto et al., 1979; 1981). This view is mainly supported by findings that alpha-adrenergic antagonists lower basal levels of TSH, whereas alpha adrenergic agonist have the opposite effect (Tuomisto et al., 1975; Anunziato et al., 1977; Montoya et al., 1979). Finally it has also been suggested that adrenergic receptor agonist, could exert its stimulatory effect on TSH secretion via hypothalamic serotonin
(Smythe et al., 1982). Thereby, highlighting the influence of adrenergic system on thyroid status.

Also, studies by Melander et al. (1977) have shown that various sympathetic stimuli can influence thyroid activity and increase thyroid hormone secretion. This is more obvious by sympathectomy and by using adrenergic blocking drugs which decrease thyroid hormone secretion. Accordingly, sympathectomy could inactivate thyroid hormone secretion due to increased vagal tone which is in agreement with the present result, as also of Rintamaki (1986), since both $T_3$ and $T_4$ level showed a decrease after guanethidine treatment. Both $T_3$ and $T_4$ level declined significantly ($P<0.02$) after sympathectomy. This decrease may be attributed to a general reduction in the release of hormones from the thyroid gland (Rintamaki, 1986). The reduced thyroxine and triiodothyronine in the serum leads to a tremendous feedback enhancement of TSH secretion by the anterior pituitary gland in sympathectomized animals.

Moreover, the decrease of serum $T_3$ and $T_4$ level following sympathectomy attain higher degree of significance, when adrenalectomy is also performed in these rats. Lack of adrenal hormones and sympathetic tone, reduce the plasma levels of thyroid hormones which in turn influence the gluconeogenic pathway, thereby, reducing glucose mobilization from target tissues (chapter 3). However, the decrease in thyroid hormone levels could also be due to inhibitory influence of existing vagal tone. Decrease in serum $T_3$ level is more pronounced than $T_4$ level, thereby, resulting a concomitant decrease in $T_3/T_4$ ratio. It is possible that lack of thyroid hormone nullifies the feedback inhibition on the anterior pituitary, which in turn may result in an increased serum TSH level in CSX + ADX rats (Weintraub et al., 1981; Faglia et al., 1983). Due to fall in $T_3$ level, a resultant down regulation of glucose transporters in target tissue such as liver, muscle could then serve as a useful adaptation to direct scarce fuel supplies to the glucose dependent central nervous system.

Nevertheless, increased thyroid status in response to the hyperglycaemic state if vagotomized rats can be controlled to some extent by subjecting the same to chemical sympathectomy. In these rats, the metabolic control is mainly through the adrenal cortical and medullary hormones. The depressive effect of corticosteroids on the activity of the hypothalamo-pituitary-thyroid axis (Leatherland and Lam, 1971; Van Overbeeke and
McBride, 1971) is giving rise to a lowering of serum thyroid hormone level. This was indicated by significant decrease in serum T₃ level. Whereas, serum T₄ level increased slightly. In these rats, the peripheral deiodination of T₄ to T₃ to replenish the depleting T₃ level might not be required. As a result of this, T₃/T₄ ratio decreased in these animals. Moreover, catecholaminergic control of TSH secretion appears to act to reduce TSH secretion in hypothyroidism, a function that appears at odds with homeostasis. In addition, TSH stimulates not only enzyme that converts T₄ to T₃ but also the degradation of T₃ to T₂ (Wu, 1983). Thus, the activation of T₃ synthesis and degradation is TSH stimulated. Therefore, reduced TSH level in rats subjected to chemical sympathectomy and vagotomy together, hinders the conversion of T₄ to T₃ thereby, resulting in reduced serum T₃ level and higher T₄ level.

These data taken together, suggest the antagonistic effects of sympathetic and parasympathetic nervous system on thyroid status. Along with this, it can be concluded that hypo- and hyper-thyroidism have a multifarious effect on the liver metabolism and in turn in maintaining glucose homeostasis. As, diabetes and hyperthyroidism exist together, a decreased thyroid hormone secretion could be of help to arrest diabetes. Guanethidine induced chemical sympathectomy arrests thyroid secretion directly as well as by affecting hypothalamo-pituitary-thyroid axis. This decrease in thyroid status was more pronounced when adrenalectomy was performed along with chemical sympathectomy. This means that reduction in both plasma catecholamine and corticoid levels as well as sympathetic tone shall produce a hypothyroidic condition and in the reverse, an increased sympathetic activity together with increased adrenal hormone secretion shall cause hyperthyroidism. Thus, hyperthyroidic condition can lead to diabetic state or atleast aggravate it.