A. Methods of Measurement and Normal Values

Conventionally daily production rates (PR) of T₃S are measured by means of disposal rates (DR), which equal PR under steady state conditions. The disposal rate (DR or PR) is calculated by multiplying the serum concentration of iodothyronine (T₃ or rT₃) by its metabolic clearance rate (MCR); MCR refers to the volume of plasma from which iodothyronine is cleared irreversibly per unit time.

Table 5.1 lists several estimates of MCR and the values of T₃S (T₃ and rT₃). The mean normal MCR of T₃ has been estimated to vary between 16 and 27 liters/day, while that of rT₃ has varied between 82 and 131 liters/day. The estimates of mean normal PR of T₃ have varied in recent studies between 23 and 60 µg/day, while those of rT₃ have varied between 21 and 52 µg/day. In comparison, the normal MCR of T₄ has been estimated at about 0.9–1.2 liters/day, while the normal PR of T₄ approximates 90–110 µg/day. The relatively more marked variations in PRs of T₃ and rT₃ reflect the uncertainties in measurement of serum concentration as well as of MCR. The information on the methods of measurement of serum concentration of T₃S has been reviewed in Chap. 4 and that on the measurements of MCRs is discussed below.

In most studies of iodothyronine turnover, a single (pulse) injection of labeled (radioactive) iodothyronine is administered intravenously. The thyroidal uptake of radioactivity is blocked by the oral administration of a saturated solution of potassium iodide, and serial blood samples are obtained at intervals for a few days. The concentration of radioactive iodothyronine at various sampling times is determined and the data are treated mathematically, using one of the several model systems to calculate the rate of disappearance (clearance) of the iodothyronine.

Most of the initial studies employed the single compartment (SC) model for calculating MCR. In this model, it is assumed that iodothyronine is distributed in a single homogeneous and rapidly equilibrating compartment from which it is removed at a constant fractional rate. Using this model, only the terminal slope of the plasma disappearance curve of the labeled iodothyronine is utilized to derive the iodothyronine kinetic parameters. The formulas employed include volume of distribution (VD) = dose divided by zero time intercept of final exponential curve; fractional catabolic rate (FCR) = 0.693/t_{1/2}; MCR = VD × FCR. Unsatisfied by the assumptions of a single compartment model, some investigators employed two or three models, assuming two or three distinct but interconnected compartments, to define the kinetics of iodothyronine distribution (Cavalieri et al. 1970; Koutras et al. 1970). Others employed noncompartmental (NC) techniques for estimation of MCR. One NC technique, which is similar to the method of Tait (1963) used in...
Table 5.1. Published data on kinetics of extrathyroidal metabolism of $T_3$ and reverse $T_3$

<table>
<thead>
<tr>
<th>Reference</th>
<th>Serum concentration (ng/100ml)</th>
<th>TDV&lt;sup&gt;a&lt;/sup&gt; (liters/day)</th>
<th>FCR&lt;sup&gt;a&lt;/sup&gt; (liters/day)</th>
<th>MCR&lt;sup&gt;a&lt;/sup&gt; (liters/day)</th>
<th>PR&lt;sup&gt;a&lt;/sup&gt; (μg/day)</th>
<th>Mean-residence time (h)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Extra-thyroid-pool (μg/day)</th>
<th>Method of calculation of MCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sterling et al. 1954</td>
<td>–</td>
<td>–</td>
<td>0.27</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>SC</td>
<td>SC</td>
</tr>
<tr>
<td>Wiswell and Coronho 1962</td>
<td>–</td>
<td>–</td>
<td>0.53</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>SC</td>
<td>SC</td>
</tr>
<tr>
<td>Fisher and Oddie 1964</td>
<td>–</td>
<td>31.0</td>
<td>0.53</td>
<td>16.4</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Whole body counting following single injection</td>
</tr>
<tr>
<td>Gregerman and Solomon 1967</td>
<td>–</td>
<td>18.1</td>
<td>0.51</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>SC</td>
</tr>
<tr>
<td>Surks and Oppenheimer 1969</td>
<td>–</td>
<td>38.1</td>
<td>0.47</td>
<td>18.0</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>SC</td>
</tr>
<tr>
<td>Woeber et al. 1970</td>
<td>273</td>
<td>43.4</td>
<td>0.52</td>
<td>22.3</td>
<td>60.0</td>
<td>–</td>
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<tr>
<td>Cavalieri et al. 1971</td>
<td>35.1</td>
<td>0.75</td>
<td>27.2</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>SC</td>
</tr>
<tr>
<td></td>
<td>27.8</td>
<td>0.86</td>
<td>26.1</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>NC following constant infusion</td>
</tr>
<tr>
<td>Oddie et al. 1971</td>
<td>97</td>
<td>34.8</td>
<td>0.75</td>
<td>26.1</td>
<td>22.6</td>
<td>–</td>
<td>–</td>
<td>Whole body counting after single injection</td>
</tr>
<tr>
<td>Nicoloff et al. 1972</td>
<td>106</td>
<td>36.6</td>
<td>0.68</td>
<td>24.9</td>
<td>26.3</td>
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<td>–</td>
<td>SC</td>
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<td>Inada et al. 1975</td>
<td>142</td>
<td>31.0</td>
<td>0.71</td>
<td>19.8</td>
<td>28.0</td>
<td>–</td>
<td>–</td>
<td>Three compartmental (single injection)</td>
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<td>Oppenheimer et al. 1975 b, c</td>
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<td>21.0</td>
<td>0.72</td>
<td>22.4</td>
<td>–</td>
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<td>NC (single injection)</td>
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<td>Gavin et al. 1977</td>
<td>104</td>
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<td>24.0</td>
<td>21.2</td>
<td>–</td>
<td>29.3</td>
<td>NC (single injection)</td>
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<tr>
<td>Suda et al. 1978b</td>
<td>173&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>24.0</td>
<td>40.7&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>–</td>
<td>NC (single injection)</td>
</tr>
<tr>
<td>Bianchi et al. 1978</td>
<td>150</td>
<td>27.0</td>
<td>0.98</td>
<td>26.5</td>
<td>41.0</td>
<td>24.7</td>
<td>41.9</td>
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