Physiological effects of nonthyroidal illness syndrome in patients after cardiac surgery


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Spratt DI, Frohnauer M, Cyr-Alves H, Kramer RS, Lucas FL, Morton JR, Cox DF, Becker K, Devlin JT. Physiological effects of nonthyroidal illness syndrome in patients after cardiac surgery. Am J Physiol Endocrinol Metab 293:E310–E315, 2007. First published April 10, 2007; doi:10.1152/ajpendo.00687.2006.—In a prospective randomized placebo-controlled study, we assessed potential physiological effects of nonthyroidal illness syndrome (NTIS) in acute illness. Coronary artery bypass graft surgery was employed as a prospective model of acute illness and NTIS. Triiodothyronine (T3) or placebo was infused for 24 h after surgery, with a T3 dose selected to maintain postoperative serum T3 concentrations at preoperative levels. Patients were evaluated before coronary artery bypass graft and during the postoperative period. Cardiovascular function was monitored with Swan-Ganz catheter measurements and ECG. Urinary nitrogen excretion and L-[1-13C]leucine flux were used to evaluate protein metabolism. Serum measurements of relevant hormones, iron, and total iron-binding capacity were used to assess effects on sex steroid, growth hormone axis, and iron responses to illness. Cardiovascular function was not affected by T3 infusion, except for a transient higher cardiac index in the T3 group 6 h after surgery (3.04 ± 0.12 for T3 and 2.53 ± 0.08 for placebo, P = 0.0016). Protein metabolism was not affected; changes in urinary nitrogen excretion and L-[1-13C]leucine flux were equivalent in the two groups (P = 0.35 and P = 0.95, respectively). No differences were observed in changes in testosterone, estrogens, growth hormone, insulin-like growth hormone I, iron, or total iron-binding capacity between T3 and placebo groups. We conclude that, in the early stages of major illness, the decrease in circulating T3 concentrations in NTIS has only a minimal transient physiological impact on cardiac function and plays no significant role in protecting against protein catabolism or modulating other endocrine responses or iron responses to illness.

euthyroid sick syndrome was first described nearly three decades ago. Its most prominent feature is a marked decrease in circulating triiodothyronine (T3) levels with the onset of illness or fasting (19). Recently, a change in terminology from euthyroid sick syndrome to “nonthyroidal illness syndrome” (NTIS) has been adopted by many (8). This change in nomenclature reflects an underlying controversy as to whether NTIS is truly a euthyroid state or deserves therapy with thyroid hormone (8, 10, 11, 35, 37). Previous data addressing this question are scant. In some studies, T3 was administered to patients after coronary artery bypass graft (CABG) surgery or to heart transplant donors and recipients, both of which have NTIS (4, 5, 13, 17, 27, 28, 30, 36). Mild improvement in cardiac function was reported. However, in most of these studies, supraphysiological doses of T3 were used for short durations. Another study suggested that NTIS may protect against catabolism in healthy fasting subjects (12).

To further evaluate the physiological effects of NTIS in the early stages of major illness, we employed a prospective model of patients undergoing CABG, a major surgical procedure that predictably induces NTIS (7, 14, 29). We monitored selected physiological processes that are known to be altered simultaneously with the onset of NTIS (9, 26, 31) and for which there is established or circumstantial evidence for modulation by T3 in other settings (16, 18, 23). These processes included cardiovascular function and protein metabolism, as well as sex steroid, growth hormone (GH) axis, and iron responses to illness. T3 was infused for 24 h at a dose previously demonstrated to maintain T3 levels in the midnormal range in an unpublished trial (unpublished observation, SmithKline).

These observations can help further determine whether NTIS is indeed a euthyroid state in acute illness. They can provide additional information regarding questions of benefit (enhanced cardiovascular function) or harm (worsened catabolism) of administering T3 to patients with NTIS. These questions remain relevant as trials of T3 in cardiac surgery continue (2, 3).

METHODS

Patient Population

Fifty-nine patients (7 women and 52 men) undergoing elective CABG were included in the study. Because the primary aim of this study was to evaluate physiological effects of NTIS, volunteers were selected to provide a relatively healthy baseline (with no evidence of NTIS before surgery). We did not intend to answer clinical questions regarding the use of T3 in patients with markedly compromised preoperative cardiac function. Inclusion criteria were as follows: ≤80 yr of age, ambulatory before surgery with New York Heart Association classification I or II, preoperative ejection fraction ≥40%, no active endocrine illness as assessed by history and by serum levels of thyroxine (T4), T3, thyroid-stimulating hormone (TSH), testosterone (T), GH, and IGF-I within the normal range before surgery, no major illness other than cardiac disease, and no therapy with thyroid hormone, amiodarone, glucocorticoids, or sex steroids within the past year. Body mass index of patients ranged from 22 to 42. Baseline characteristics of patients are displayed in Table 1. A single group of five cardiovascular surgeons was involved with similar strategies for postoperative management of patients. The study was approved by the

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**Table 1. Baseline patient characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Age, yr</th>
<th>BMI, kg/m²</th>
<th>Women/Men</th>
<th>EF, %</th>
<th>CI, l·min⁻¹·m⁻²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>59.4±2.4</td>
<td>29.3±0.9</td>
<td>3/30</td>
<td>55.7±2.7</td>
<td>2.4±0.1</td>
</tr>
<tr>
<td>T₃</td>
<td>63.7±1.7</td>
<td>27.8±0.6</td>
<td>4/28</td>
<td>55.0±2.7</td>
<td>2.6±0.1</td>
</tr>
</tbody>
</table>

Values are means ± SE. BMI, body mass index; EF, ejection fraction; CI, cardiac index; T₃, triiodothyronine.

Maine Medical Center Institutional Review Board, and all patients provided written informed consent.

**Administration of T₃ or Placebo**

Patients were randomized in double-blind fashion to treatment or placebo groups. Patients in the T₃ group received a bolus dose of 0.2 μg/kg at the time of cross-clamp (CC) removal followed by an infusion of 0.8 μg/kg over the subsequent 24 h. Placebo was administered in identical infusions. Dosing was selected to maintain serum T₃ levels within the normal range on the basis of an unpublished previous multicenter trial (SmithKline) in which serum levels of T₃ were assessed using bolus doses of 0.1, 0.4, and 0.8 μg/kg matched with infusion doses of 0.1, 0.4, and 0.8 μg/kg over 6 h after CABG.

**Monitoring of Hemodynamics, ECGs, Cardiac Rhythms, and Cardiac Drugs**

Cardiac output (CO), mean arterial pressure (MAP), central venous pressure (CVP), and mixed venous O₂ saturation were measured via an indwelling Swan-Ganz catheter upon insertion of the catheter and 1, 6, 12, and 18 h after CC removal. Derivative measurements were cardiac index (CI), calculated as CO/body surface area) and systemic vascular resistance [calculated as (MAP - CVP)/CO].

ECGs were performed just before admission and 36 h after CC removal to monitor heart rate (HR) and evidence of ischemia or myocardial damage. Arrhythmias as recorded by telemetry were monitored for 24 h after CC removal. In addition, in the first 20 patients, cardiac activity was recorded by Holter monitor for the 6 h before CABG and for 24 h after CABG.

Administration of the following classes of drugs was monitored for the 24 h after CC removal: 1) vasodilators (primarily nitrates), 2) inotropes (primarily dopamine), 3) cardiac glycosides, 4) antihypertensives (primarily nitroprusside), 5) β-blockers, 6) calcium channel blockers, 7) angiotensin-converting enzyme inhibitors, 8) antiarrhythmics, and 9) diuretics.

**Evaluation of Protein Catabolism**

Protein metabolism was evaluated in a subset of 20 patients (10 each in placebo and T₃-treated groups). These 20 patients were entered consecutively into the protein protocol during routine recruitment for the larger study. Inclusion criteria were as stated above. Evaluation was accomplished by measurement of urinary nitrogen excretion (Uₙ) and L-[¹³C]leucine flux.

\[ \text{Ur} \] At 9 h before the start of each leucine infusion, 12-h urine collections were initiated for determination of \( \text{Ur} \). \( \text{Ur} \) was determined by a macro-Kjeldahl method, but copper sulfate was used as the catalyst (1).

\[ \text{L-[¹³C]leucine flux} \] Leucine tracer kinetics were determined in each patient within 14 days before surgery after a 10-h overnight fast and again 20–24 h after surgery. At the time of postoperative testing, patients had been without oral intake for 36 h. Any solutions containing dextrose (with the exception of nitroglycerin) were discontinued 3 h before the leucine infusion. L-[¹³C]leucine (99% \(^{13}C\)) was prepared as previously described (24, 25) and infused in a bolus of 2 μmol/kg followed by infusion of 2.4 μmol·kg⁻¹·h⁻¹ for 3 h. Blood samples drawn at 0, 135, 150, 165, and 180 min after administration of the L-[¹³C]leucine bolus were placed in iced tubes, and an equal volume of 10% sulfosalicylic acid was added. Plasma was analyzed for α-ketoisocaproate (KIC) by gas chromatography-mass spectrometry (24, 25). Rate of appearance (Rₐ) or “flux” of leucine into plasma was defined as

\[ \text{R}_a = \frac{\text{I}_{iv}E_{iv}}{E_p - 1} \]

where \( \text{I}_{iv} \) is the infusion rate of L-[¹³C] leucine, \( E_{iv} \) is the enrichment of the leucine infused, and \( E_p \) is the enrichment of plasma leucine.

**Monitoring of Serum Hormone Levels and Iron-Handling Parameters**

Concentrations of T₃, TSH, total T, GH, IGF-I, and iron, as well as total iron-binding capacity (TIBC), were measured on serum samples obtained from patients within the week before surgery and then following CC removal after surgery (Table 2). We did not monitor serum levels of T₄, because we and other groups previously reported that serum levels of T₄ declined in parallel with T₃ (but to a lesser degree) after CABG (7, 14, 33). We also did not measure serum concentrations of free T or sex hormone-binding globulin, because we and others previously reported that serum levels of free T decreased in parallel with total T after CABG (22, 33).

**Table 2. Scheme for measurement of hemodynamic and serum parameters**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>PreOp</th>
<th>1 h</th>
<th>6 h</th>
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<th>18 h</th>
<th>24 h</th>
<th>36 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>59</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>T₃</td>
<td>59</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>TSH</td>
<td>59</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>GH, IGF-I</td>
<td>30</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Iron, TIBC</td>
<td>20</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

CC, cross-clamp; HD, hemodynamic measurement; PreOp, preoperatively; TSH, thyroid-stimulating hormone; T, testosterone; E₁, estrone; E₂, estradiol; IGF-I, insulin-like growth factor I; GH, growth hormone; TIBC, total iron-binding capacity. Urinary nitrogen excretion and L-[¹³C]leucine flux were measured before and 12–24 h after coronary artery bypass graft.
treatment groups at 6 h after CC removal, these values were compared using a two-tailed paired $t$-test.

**RESULTS**

**Serum T3 and TSH Concentrations**

Figure 1 displays serum T3 concentrations throughout the study in the placebo and T3 groups. As anticipated, serum T3 levels decreased markedly in the placebo group but remained at baseline levels in the T3 group until discontinuation of the infusion at 24 h. TSH remained within the normal range in all patients in the placebo group at 24 h after surgery (1.81 ± 0.22 (0.43–3.84) μU/ml). TSH in the T3 group was 0.57 ± 0.07 (0.19–1.18) μU/ml, with values slightly below the lower limit of normal (0.4 μU/ml) in seven patients. TSH was significantly lower in the T3 than in the placebo group ($P < 0.0001$).

**Hemodynamic Parameters**

CI was increased over baseline values by 1 h after CC removal in the placebo and T3 groups (Fig. 2; $P < 0.001$). No significant difference in mean CI values was observed between the two groups, except at 6 h after CC removal, when CI in the placebo group fell below CI in the T3 group (2.53 ± 0.08 vs. 3.04 ± 0.12 l/min$^{-1}$·m$^{-2}$, $P = 0.0016$). Values for systemic vascular resistance and mixed venous $O_2$ saturation were also equivalent in the placebo and T3 groups (Table 3). ECG data demonstrated similar increases in HR after CABG in the placebo (19.2 ± 2.9 beats/min) and T3 (22.4 ± 2.1 beats/min) groups. Holter monitor data confirmed this finding, with increases in HR of 24.8 ± 2.3 and 27.6 ± 2.5 beats/min in the placebo and T3 groups ($P = 0.43$). ECG data also demonstrated no ischemic damage in either group.

**Arrhythmias and Drug Administration**

No differences in the incidence of arrhythmias were noted postoperatively between the placebo and T3 groups. Particularly, no decrease in the incidence of atrial fibrillation was observed in the T3 group.

Very few patients in these populations received dopamine. T3 and placebo patients were equally likely to receive dopamine, and only small “renal” doses (≤5 μg·kg$^{-1}$·h$^{-1}$) were administered. Placebo and T3 patients were also equally likely to receive 1) vasodilators, 2) inotropes, 3) cardiac glycosides, 4) antihypertensives (primarily nitroprusside), 5) β-blockers, 6) calcium channel blockers, 7) angiotensin-converting enzyme inhibitors, 8) antiarrhythmics, and 9) diuretics.

**Protein Catabolism**

$U_N$ values were not significantly increased postoperatively in the placebo or the T3 group. Pre- and postoperative $U_N$ values were 6.27 ± 0.79 and 7.25 ± 1.13 g/24 h ($P = 0.19$) in the placebo group and 5.36 ± 0.58 and 5.46 ± 0.50 g/24 h ($P = 0.86$) in the T3 group. No significant difference was observed in the pre- to postoperative change in $U_N$ excre-

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**Table 3. SVR and $\bar{SVO}_2$, in placebo and T3 groups**

<table>
<thead>
<tr>
<th></th>
<th>PreOp</th>
<th>1 h</th>
<th>6 h</th>
<th>12 h</th>
<th>18 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR, dyn·s·cm$^{-5}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>1.116±0.66</td>
<td>981±176</td>
<td>995±51</td>
<td>931±51</td>
<td>962±52</td>
</tr>
<tr>
<td>T3</td>
<td>1.115±0.77</td>
<td>810±57</td>
<td>949±53</td>
<td>966±49</td>
<td>942±42.6</td>
</tr>
<tr>
<td>$\bar{SVO}_2$, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>0.81±0.5</td>
<td>0.75±0.1</td>
<td>0.64±0.1</td>
<td>0.65±0.1</td>
<td>0.63±0.2</td>
</tr>
<tr>
<td>T3</td>
<td>0.82±0.6</td>
<td>0.77±0.1</td>
<td>0.66±0.2</td>
<td>0.68±0.1</td>
<td>0.64±0.2</td>
</tr>
</tbody>
</table>

Values are means ± SE. SVR, systemic vascular resistance; $\bar{SVO}_2$, mixed venous $O_2$ saturation.
Fig. 4. Change from baseline in serum concentrations of testosterone (A) and estrone (E1; B) in placebo and T3-treated patients before and 1 h, 2 h, 3 h, 6 h, 12 h, 24 h, and 36 h after CABG. Values are means ± SE. Decreases in testosterone were not significantly different between the placebo and the T3 group (P = 0.11). Increases in E1 were not significantly different between the placebo and the T3 group (P = 0.31).

Table 4. Serum E3 levels

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>T3</th>
</tr>
</thead>
<tbody>
<tr>
<td>PreOp</td>
<td>22.0±2.8</td>
<td>23.7±2.4</td>
</tr>
<tr>
<td>1 h</td>
<td>16.5±2.5</td>
<td>21.1±2.6</td>
</tr>
<tr>
<td>2 h</td>
<td>26.2±3.1</td>
<td>27.0±2.7</td>
</tr>
<tr>
<td>3 h</td>
<td>27.8±5.4</td>
<td>26.3±3.1</td>
</tr>
</tbody>
</table>

Values are means ± SE in pg/ml.

Table 5. GH and IGF-I in placebo and T3 groups

<table>
<thead>
<tr>
<th></th>
<th>PreOp</th>
<th>1 h</th>
<th>24 h</th>
<th>36 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>GH, μg/l</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>1.6±0.4</td>
<td>4.1±0.9</td>
<td>1.4±0.3</td>
<td>1.6±0.5</td>
</tr>
<tr>
<td>T3</td>
<td>2.0±0.4</td>
<td>4.6±1.0</td>
<td>2.3±0.6</td>
<td>1.1±0.2</td>
</tr>
<tr>
<td>IGF-I, μg/l</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>121.7±16.2</td>
<td>60.6±13.1</td>
<td>67.7±6.4</td>
<td>62.7±2.7</td>
</tr>
<tr>
<td>T3</td>
<td>127.8±17.0</td>
<td>66.7±11.3</td>
<td>80.1±7.8</td>
<td>75.2±3.1</td>
</tr>
<tr>
<td>IGF-I/GH ratio</td>
<td>102.6±16.7</td>
<td>28.5±7.5</td>
<td>83.7±26.2</td>
<td>62.2±21.8</td>
</tr>
</tbody>
</table>

Values are means ± SE.

measures ANOVA showed no difference between time points within each group.

L-[1-13C]leucine flux (μmol·kg⁻¹·min⁻¹) increased slightly postoperatively in the placebo group: from 121 ± 4 to 139 ± 8 (P = 0.05; Fig. 3). In the T3 group, the difference between pre- and postoperative values (126 ± 9 and 145 ± 8, respectively) was not significant (P = 0.13). Postoperative changes in L-[1-13C]leucine flux in the placebo group were not significantly different from those in the T3 group (18.2 ± 17.7 and 19.0 ± 31.1, respectively, P = 0.95).

Sex Steroids

T decreased profoundly in the placebo and T3 groups to similar nadir levels within the range of prepubertal values (Fig. 4A). In the placebo group, serum T decreased from a preoperative value of 3.5 ± 0.9 ng/ml to a nadir postoperative value of 0.9 ± 0.4 ng/ml (P < 0.0001) and in the T3 group from 4.0 ± 1.4 to 0.8 ± 0.3 ng/ml (P < 0.0001). These decreases were statistically the same for both groups (P = 0.11).

In contrast to T, serum E1 levels rose in the placebo and T3 groups (Fig. 4B). The increase in the T3 group (from 34.7 ± 2.6 to 90.2 ± 9.0 pg/ml) was not significantly greater than the increase in the placebo group (from 35.3 ± 3.0 to 70.2 ± 9.1 pg/ml, P = 0.31). Serum levels of E2 did not rise significantly in either group, with similar values observed in both groups (Table 4).

GH Axis and Serum Iron and TIBC

Serum GH levels increased and IGF-I levels decreased in placebo and T3 patients (Table 5). No significant differences between these changes were observed between the two groups.

Table 6. Serum iron concentrations and TIBC in placebo and T3 groups

<table>
<thead>
<tr>
<th></th>
<th>PreOp</th>
<th>1 h</th>
<th>24 h</th>
<th>36 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron, μg/dl</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>73.6±11.3</td>
<td>57.8±10.4</td>
<td>17.4±5.7</td>
<td>12.5±2.1</td>
</tr>
<tr>
<td>T3</td>
<td>100.9±12.4</td>
<td>62.0±12.0</td>
<td>17.9±3.3</td>
<td>15.2±2.9</td>
</tr>
<tr>
<td>TIBC, μg/dl</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>296±22</td>
<td>105±26</td>
<td>135±21</td>
<td>172±15</td>
</tr>
<tr>
<td>T3</td>
<td>312±23</td>
<td>82±18</td>
<td>156±15</td>
<td>173±7</td>
</tr>
</tbody>
</table>

Values are means ± SE.
The decrease in the GH/IGF-I ratio was also equivalent in both populations (P = 0.30).

Decreases in serum iron concentrations and TIBC were observed after CABG (Table 6). No statistical difference was observed in changes in iron (P = 0.49) or TIBC (P = 0.40) between the placebo and the T3 group.

DISCUSSION

These data demonstrate that preventing the decrease in T3 during the early stages of NTIS in acute illness has minimal effects on the physiological processes evaluated in our study; there was only a slight transient enhancement in cardiac function. No effect on protein metabolism was evident. Similarly, we observed no evidence of NTIS modulation of the sex steroid, GH-IGF-I axis, or iron responses to acute illness. Thus, although NTIS does not appear to be an entirely euthyroid state, in at least this circumstance (early stages of major illness of moderate severity), physiological effects appear to be minimal. Whether this is true for less healthy patients or for more extended illnesses has yet to be determined.

With respect to cardiac function, one previous study in which a T3 dose similar to that in this study was used also reported a mild inotropic effect reflected by increased CI and decreased use of dopaminergic agents (28). Other studies in which much higher doses were used for a 6 h still reported only minimal increases in CI (4, 17). Thus it is reasonable to assume that any hypothyroid effect of NTIS on cardiovascular function is minimal. The therapeutic effects of T3 supplementation appear to be clinically inconsequential, particularly compared with standard inotropic agents such as dopaminergic drugs.

With respect to protein metabolism, we did not confirm the previous study suggesting that NTIS is protective against catabolism (12). That study employed a model of fasting in seven healthy subjects, rather than acute illness. The dose of T3 resulting in T3 levels slightly above baseline and suppressed TSH values, indicating that a mildly hyperthyroid state may have been induced. Only urinary urea nitrogen excretion was monitored, rather than the more sophisticated parameters of UN and l-[1-13C]leucine flux that are now available. In our study, we were able to maintain serum T3 concentrations at preoperative levels. TSH remained within the normal range or minimally suppressed, with a lower mean TSH value in the T3 than in the placebo group. No trend in increased protein catabolism (measured by UN or 1-[1-13C]leucine flux) was evident in our T3 patients compared with placebo patients. Therefore, it is unlikely that a larger study of similar patients would reveal a protective effect of NTIS on protein catabolism in the early stages of illness. Whether results with illness of greater severity or longer duration would differ was not addressed by the present study.

The lack of any discernable effect of T3 administration on other endocrine responses to acute illness rules against a role of NTIS in modulating those responses. The decrease in serum T and rise in E1 were not different between the T3 and placebo groups. Thus the hypogonadotropism and decreased testicular responsiveness to luteinizing hormone (6, 22, 32, 33) seem to occur independently from NTIS. Nor does the increased aromatase activity that results in rising estrogen production with acute illness (34) appear to be blunted by NTIS. Similarly, we found no evidence that increased pituitary GH secretion, decreased hepatic responsiveness to GH, or iron handling is affected by NTIS.

Our data indicate that T3 supplementation is safe with respect to protein catabolism, cardiac arrhythmias, and myocardial ischemia after successful CABG. However, they also argue against continued trials of T3 therapy in CABG patients because of the lack of discernable benefits. A similar lack of benefit has been observed in children undergoing cardiac surgery (5). It is possible that a trial including only CABG patients with clearly compromised cardiac function postoperatively may demonstrate a clinical benefit. Until such results are available, T3 therapy should not be used in CABG patients. Results in transplant donors remain unresolved (15, 27, 30).

In summary, our data indicate that NTIS with marked decreases of serum T3 in the early stages of illness is accompanied only by minimal effects of hypothyroidism limited to a transient mild suppression of CI. No effects on protein catabolism, other endocrine responses to acute illness, or iron parameters were observed. The consistent onset of NTIS with illness is suggestive of an adaptive advantage at some point in evolution. Possibly NTIS was of greater importance in settings of marginal nutrition where humans lived (or live) on the edge of a catabolic state. Thus future studies of patients who are more nutritionally compromised before and during their illnesses may be of interest. The present data do not clearly indicate that NTIS is accompanied by significant physiological hypothyroid effects.

ACKNOWLEDGMENTS

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REFERENCES