

# Clinical Investigation

## Thyroid Hormone Levels in the Acquired Immunodeficiency Syndrome (AIDS) or AIDS-Related Complex

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*Hypothalamic-pituitary dysfunction and thyroid gland cytomegalovirus inclusions have been described in patients with the acquired immunodeficiency syndrome (AIDS) and AIDS-related complex (ARC). We evaluated 80 patients with AIDS or ARC for the frequency of hypothalamic-pituitary or thyroid gland failure and altered serum thyroid hormone levels due to nonthyroidal disorders. One patient had subclinical hypothyroidism. Of these patients, 60% had low free triiodothyronine ( $T_3$ ) index values and 4% had low free thyroxine ( $T_4$ ) indexes; none of the latter had hypothalamic-pituitary or thyroid gland failure, since all serum cortisol values were  $\geq 552$  nmol per liter ( $\geq 20$   $\mu$ g per dl) and all thyrotropin levels were  $\leq 3$  mU per liter ( $\leq 3$   $\mu$ U per ml), respectively. Those who died had lower total  $T_4$  and  $T_3$ , free  $T_3$  index, and albumin levels than those discharged from hospital. Serum total  $T_4$  and  $T_3$  levels correlated with albumin levels and total  $T_3$  with serum sodium levels. Serum total  $T_3$  levels best predicted the outcome of the hospital stay (accuracy = 82%). Thus, abnormal serum thyroid hormone levels in AIDS or ARC patients are most frequently due to nonthyroidal disorders, but hypothalamic-pituitary or thyroid gland failure may occur.*

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Multiple endocrine abnormalities occur in patients with the acquired immunodeficiency syndrome (AIDS) or AIDS-related complex (ARC),<sup>1-7</sup> including hypothalamic dysfunction,<sup>6,7</sup> anterior pituitary insufficiency,<sup>1-5</sup> and adrenal or testicular failure.<sup>2-6</sup> At autopsy, pituitary lesions found include basophilic infiltration (22%), adenomas (15%), infarction (7%), and infection (1%).<sup>8</sup> In addition, cytomegalovirus (CMV) inclusions are present in the thyroid gland (14% to 71%), as well as in the adrenal (40% to 80%) and parathyroid glands (3%)<sup>9-11</sup> and in the testes.<sup>11,12</sup> These lesions of the hypothalamus, pituitary, and thyroid glands theoretically could result in an increased frequency of hypothyroidism in patients with AIDS or ARC. Because hypothyroidism may be overlooked clinically in severely ill patients, the diagnosis would depend on laboratory detection and confirmation.<sup>13,14</sup>

In the absence of hypothalamic-pituitary or thyroid gland failure, alterations of serum thyroid hormone levels due to nonthyroidal disorders would be expected to occur in patients with AIDS or ARC. These patients frequently have systemic infections, malignant neoplasms, and malnutrition—disorders known to be associated with reduced serum total triiodothyronine ( $T_3$ ), free  $T_3$  index, total thyroxine ( $T_4$ ), and free  $T_4$  index values in the absence of hypothyroidism.<sup>15,16</sup> The magnitude of changes in serum thyroid hormone values would be

predicted to be related to the severity of illness in patients with AIDS or ARC, as reflected by the degree of malnutrition, the presence of hyponatremia,<sup>5,17-19</sup> and the outcome of the hospital stay.<sup>15,20</sup>

We studied 80 patients in hospital with AIDS or ARC to determine the frequency of altered serum thyroid hormone levels due to hypothyroidism or to nonthyroidal disorders and to evaluate the relationships of these alterations to the severity of nonthyroidal illness.

### Materials and Methods

Serum thyroid hormone values were determined in 80 patients with AIDS or ARC admitted to the Internal Medicine service of the University of Southern California/Los Angeles County Medical Center between October 1 and December 31, 1986; of the 80, 6 men were admitted twice and had two sets of serum thyroid hormone levels done. All patients had serum total thyroxine, triiodothyronine uptake ratio, and serum thyrotropin (TSH) levels determined, and 50 patients had serum total triiodothyronine levels measured. All patients gave informed consent for inclusion into the study.

The study population consisted of 78 men and 2 women whose mean age was  $36 \pm 1$  (standard error) years (range 19 to 60). The patients were white (46%), Hispanic (34%),

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## ABBREVIATIONS USED IN TEXT

AIDS = acquired immunodeficiency syndrome  
 ARC = AIDS-related complex  
 CMV = cytomegalovirus  
 $T_3$  = triiodothyronine  
 $T_4$  = thyroxine  
 TRH = thyrotropin-releasing hormone  
 TSH = thyrotropin

black (19%), and Oriental (1%). The diagnosis of AIDS or ARC was based on the Centers for Disease Control criteria.<sup>21,22</sup> Patients had been diagnosed with AIDS or ARC for  $4 \pm 1$  months before the current hospital stay. The risk factors for AIDS or ARC in the 78 men included 62 with homosexuality or bisexuality (80%), 5 with intravenous drug abuse (6%), 5 with both homosexuality and intravenous drug abuse, and 1 with blood transfusion; the other patients denied having any of the known risk factors. The two women had relationships with bisexual men. The diagnosis at the time of discharge or death after  $18 \pm 1$  days in hospital included 79 with systemic infections (99%), 15 with malignant neoplasms (19%), and 8 with neurologic disease (10%).

Of these 80 patients, 68 (85%) has serum thyroid hormone levels measured to exclude hypothyroidism as a cause of hyponatremia, and the others had levels measured for other reasons. Hyponatremia was defined as a serum sodium concentration of less than 135 mmol per liter ( $< 135$  mEq per liter) on two consecutive measurements (mean  $\pm$  SE  $127 \pm 1$  mmol per liter); the patients with normal serum sodium levels had a mean value of 137 mmol per liter ( $137 \pm 1$  mEq per liter). All patients were clinically euthyroid without symptoms or signs of hypothalamic-pituitary or adrenal insufficiency. Thyroid gland failure was defined as a serum thyrotropin level above 20 mU per liter or between 10 and 20 mU per liter in association with an exaggerated TSH response to thyrotropin-releasing hormone (TRH), with a normal or reduced free  $T_4$  index.<sup>13-16,23</sup>

Serum biochemical values were measured using an autoanalyzer SMAC II (Technicon Instrument Corporation, Tarrytown, NY). Serum total  $T_4$ , total  $T_3$ , TSH, and  $T_3$  uptake values were measured by commercial antibody-coated tube methods (ICN Micromedic Systems, Horsham, Pa). The  $T_3$  uptake values were calculated as the antibody uptake of  $T_3$  labeled with iodine 125 divided by the total  $^{125}\text{I}-T_3$  added to the specimen (bound/total); this method is most commonly used in clinical practice. The  $T_3$  uptake values were also calculated by dividing the antibody uptake of the  $^{125}\text{I}-T_3$  by the residual serum protein-bound counts (bound/serum); this ratio corresponds much more closely to the predictions of the mass action law on which these procedures are based.<sup>24</sup> These  $T_3$  uptake values were normalized to a ratio by using a pooled reference standard. The free  $T_4$  index and free  $T_3$  index values were calculated as the product of the total hormone concentration and the  $T_3$  uptake ratio (bound/total or bound/serum).

Serum sodium and age were expressed as the mean  $\pm$  standard error. Because the thyroid hormone values and albumin concentrations were better described by log distributions, logarithmic transformations were used for the purpose of analysis. Statistical differences between groups were evaluated using unpaired Student's *t* tests adjusted for variances or unpaired ranked-sum tests for data that were not normally distributed. Categorical variables were compared by the  $\chi^2$  or

Fisher's exact test. The relationships between continuous variables were assessed by linear regression analysis. A *P* value less than .05 was considered to be significant. These computational analyses were carried out using the CLINFO computer package of the Clinical Research Center at the University of Southern California. Logistic regression analysis was used to model the probability of outcome as a function of risk factors, clinical characteristics, and therapeutic interventions<sup>25</sup> using the Statistical Analysis System on the IBM mainframe computer of the University of Southern California.

## Results

The mean serum thyroid hormone values for the study population are presented in Tables 1 and 2. Because the mean bound/total and bound/serum values for the  $T_3$  uptake ratio, free  $T_4$  index, and free  $T_3$  index were similar, only the bound/total values are provided in the text. The mean serum total  $T_4$  value (94 nmol per liter [ $7.3 \mu\text{g}$  per dl]),  $T_3$  uptake ratio (1.13), free  $T_4$  index (8.3), and TSH value (1.7 mU per liter [ $\mu\text{U}$  per ml]) were within the laboratory reference range for the total population, while the mean serum total  $T_3$  value (0.7 nmol per liter [ $47 \text{ ng}$  per dl]) and free  $T_3$  index (52) were below the laboratory reference range. Calculating the  $T_3$  uptake ratio values as bound/serum instead of bound/total resulted in a significantly larger number of elevated values (57% versus 38%,  $P < .02$ ). The number of patients with abnormal free  $T_4$  or free  $T_3$  indexes was not substantially changed, however, when calculated by the bound/serum compared with the bound/total method (free  $T_4$  index: 2.3% versus 4.7%, and free  $T_3$  index: 72.5% versus 75.0%, respectively).

There were three patients with free  $T_4$  indexes below the lower normal reference range of 4.5, with values of 2.0, 3.7, and 4.1, respectively; their serum TSH values were 1.0, 1.0, and 2.3 mU per liter ( $\mu\text{U}$  per ml), and morning serum cortisol values were 541, 563, and 709 nmol per liter (19.6, 20.4, and  $25.7 \mu\text{g}$  per dl), respectively; all three patients had normal or elevated blood glucose levels. One patient had a high free  $T_4$  index of 13.8 and a serum free  $T_3$  index of 67, without clinical evidence of hyperthyroidism. This patient had AIDS and died three days after admission—before a TRH stimulation test could be done. Of the 50 patients studied, 30 (60%) had free  $T_3$  indexes below the normal reference range of 70, and 40 (80%) had values below 100. There were five patients with TSH values above the upper normal range of 5 mU per liter. In the four patients with TSH values ranging from 5.1 to 9.3 mU per liter (mean: 6.5 mU per liter), total  $T_4$  and free  $T_4$  index values were within the normal range (mean: 77.2 nmol per liter [ $6.0 \mu\text{g}$  per dl] and 7.0, real ranges: 57.9 to 114.5 nmol per liter [ $4.5$  to  $8.9 \mu\text{g}$  per dl] and 5.7 to 8.6, respectively), and were considered to be euthyroid.<sup>23</sup> The patient with the serum TSH value of 14.3 mU per liter had a total  $T_4$  of 60.5 nmol per liter ( $4.7 \mu\text{g}$  per dl), a free  $T_4$  index of 5.7, and an increase of the TSH from 11.7 to 39.1 mU per liter 30 minutes after receiving 250  $\mu\text{g}$  of TRH intravenously; this patient was severely ill with *Pneumocystis carinii* pneumonia. These findings are compatible with subclinical hypothyroidism due to thyroid gland failure.<sup>13,23</sup>

Patients with AIDS did not differ significantly from those with ARC with respect to serum thyroid hormone levels (Tables 1 and 2). The mean serum albumin concentration,

TABLE 1.—Serum Thyroid Hormone and Albumin Values\* in Patients With the Acquired Immunodeficiency Syndrome (AIDS) or AIDS-Related Complex (ARC)

Thyroid and Albumin Values	Total Population (N=80)	AIDS Patients (N=66)	ARC Patients (N=14)	Hyponatremia	Normonatremia	Outcome		Laboratory Range
						Died (N=23)	Discharged (N=57)	
(Number of specimens) . . . . .	(86)	(71)	(15)	(74)	(12)	(23)	(63)	
Total T <sub>4</sub> , µg/dl . . . . .	7.3†	7.4	7.1	7.1‡	9.0	6.3‡	7.8	4.5 -13.2
	5.0-10.7§	5.0 -11.0	5.4 - 9.4	4.8 -10.5	7.2 -11.2	3.8 -10.3	5.7 -10.6	
T <sub>3</sub> Uptake B/T . . . . .	1.13†	1.14	1.11	1.16‡	1.00	1.23‡	1.10	0.88- 1.19
Ratio	0.99- 1.30§	0.99- 1.31	0.99- 1.25	1.02- 1.31	0.86- 1.16	1.08- 1.41	0.97- 1.24	
B/S . . . . .	1.24†	1.25	1.20	1.28‡	1.02	1.44‡	1.18	
	0.99- 1.57§	0.99- 1.59	1.00- 1.45	1.04- 1.59	0.81- 1.28	1.13- 1.83	0.96- 1.44	
Free T <sub>4</sub> B/T . . . . .	8.3†	8.4	7.9	8.2	9.0	7.8	8.5	4.5 -13.2
Index	6.1 -11.3§	6.1 -11.6	6.4 - 9.8	5.9 -11.4	7.5 -10.9	5.2 -11.6	6.5 -11.0	
B/S . . . . .	9.1†	9.3	8.6	9.1	9.1	9.1	9.2	
	6.9 -12.1§	6.9 -12.4	7.0 -10.5	6.8 -12.2	7.4 -11.3	6.5 -12.7	7.1 -11.9	
TSH, µU/ml . . . . .	1.7†	1.7	2.4	1.8	1.5	1.5	1.9	≤5.0
	1.0 - 3.1§	1.0 - 2.8	1.1 - 5.3	1.0 - 3.2	1.0 - 2.5	1.0 - 2.2	1.0 - 3.5	
Albumin, grams/dl . . . . .	2.7†	2.6†	3.0	2.6‡	3.4	2.2‡	2.9	3.9 - 5.0
	2.0 - 3.5§	1.9 - 3.5	2.6 - 3.5	2.0 - 3.3	2.8 - 4.0	1.7 - 2.9	2.3 - 3.6	

B/S=bound/serum, B/T=bound/total, T<sub>3</sub>=triiodothyronine, T<sub>4</sub>=thyroxine, TSH=thyrotropin

\*To convert to SI units: for total T<sub>4</sub> value and free T<sub>4</sub> index (µg/dl), multiply by 12.87 to get nmol/liter; for TSH value (µU/ml), multiply by 1.00 to get mU/liter; for albumin value (grams/dl), multiply by 10 to get grams/liter.

†The numbers represent the geometric mean.

‡P < .05 comparing either the groups with AIDS with those with ARC, hyponatremia with normonatremia, or survivors with nonsurvivors.

§The numbers represent the antilogarithmic values of 1 standard deviation about the logarithmic mean.

¶P < .001 comparing either the groups with AIDS with those with ARC, hyponatremia with normonatremia, or survivors with nonsurvivors.

¶P < .01 comparing either the groups with AIDS with those with ARC, hyponatremia with normonatremia, or survivors with nonsurvivors.

TABLE 2.—Serum Triiodothyronine (T<sub>3</sub>) Values\* in Patients With the Acquired Immunodeficiency Syndrome (AIDS) or AIDS-Related Complex (ARC)

T <sub>3</sub> Values, ng/dl	Total Population (N=80)	AIDS Patients (N=66)	ARC Patients (N=14)	Hyponatremia	Normonatremia	Outcome		Laboratory Range, ng/dl
						Died (N=23)	Discharged (N=57)	
(Number of specimens) . . . . .	(50)	(43)	(7)	(43)	(7)	(10)	(40)	
Total T <sub>3</sub> . . . . .	47†	45	63	41‡	108	22‡	53	70-200
	21-105§	20-100	30-133	19-88	74-157	12-42	23-121	
Free T <sub>3</sub> B/T . . . . .	52†	50	72	47‡	108	27‡	59	70-200
Index . . . . .	26-106§	25-101	35-148	24-94	79-146	15-48	28-124	
B/S . . . . .	57†	54	79	52‡	109	31‡	63	
	30-109§	29-103	39-159	27-98	80-149	18-54	31-128	

B/S=bound/serum, B/T=bound/total

\*To convert total T<sub>3</sub> value and free T<sub>3</sub> index (ng/dl) to SI units, multiply by 0.01536 to get nmol/liter.

†The numbers represent the geometric mean.

‡P < .01 comparing either the groups with AIDS with those with ARC, hyponatremia with normonatremia, or survivors with nonsurvivors.

§The numbers represent the antilogarithmic values of 1 standard deviation about the logarithmic mean.

however, was lower in patients with AIDS (26 grams per liter [2.6 grams per dl]) than in those with ARC (34 grams per liter [3.4 grams per dl], P < .005).

Because hyponatremia may reflect the severity of illness in patients with AIDS or ARC<sup>5,17-19</sup> and alterations of serum thyroid hormone levels in euthyroid patients with nonthyroidal illnesses are related to the severity of illness,<sup>15</sup> serum thyroid hormone values from hyponatremic and normonatremic patients were compared (Tables 1 and 2). The mean serum total T<sub>4</sub>, total T<sub>3</sub>, and free T<sub>3</sub> index values of the hyponatremic group were lower than those of the normonatremic group, while free T<sub>4</sub> indexes did not differ significantly. The T<sub>3</sub> uptake ratios were higher in the hyponatremic group. Of the 74 hyponatremic patients, 21 (28%) died during their hospital stay, as did 2 of the 12 normonatremic patients (17%); this difference was not statistically significant.

In all, 23 patients died during their hospital stay, and the other 57 were discharged. There were no differences in age,

duration of diagnosis of AIDS or ARC, or serum sodium concentrations between those who were discharged and those who died. Serum total T<sub>4</sub>, total T<sub>3</sub>, free T<sub>3</sub> index values, and albumin levels were significantly lower and T<sub>3</sub> uptake ratios higher, however, in those who died, while free T<sub>4</sub> indexes were not different. In addition, all 23 patients who died but only half of those who were discharged (28) had serum total T<sub>3</sub> levels below 1.08 nmol per liter (70 ng per dl, P = .006), and T<sub>3</sub> uptake ratios were elevated in 17 patients who died (74%) and 14 of those who were discharged (25%, P < .001).

There were positive correlations of concentrations of serum albumin with those of serum total T<sub>4</sub>, total T<sub>3</sub>, and sodium levels, and inverse correlations of concentrations of albumin with T<sub>3</sub> uptake ratio (Table 3). In addition, a significant direct relationship was present between total T<sub>3</sub> and serum sodium concentrations (Table 3). Finally, serum total T<sub>4</sub> levels correlated with serum total T<sub>3</sub> values (r = .58, P < .001).

TABLE 3.—Correlations of Serum Thyroid Hormone Levels With Serum Albumin and Sodium Levels

	Serum Albumin		Serum Sodium	
	r*	Equation†	r*	Equation†
Total thyroxine (T <sub>4</sub> ) . . . . .	.60	ln T <sub>4</sub> =1.19+0.83 ln Albumin	.35	
Total T <sub>3</sub> . . . . .	.80	ln T <sub>3</sub> =1.25+2.53 ln Albumin	.58	ln T <sub>3</sub> = -8.39+0.095 Sodium
T <sub>3</sub> uptake ratio (B/T) . . . . .	-.67	ln T <sub>3</sub> UR=0.45-0.33 ln Albumin	-.34	
T <sub>3</sub> uptake ratio (B/S) . . . . .	-.68	ln T <sub>3</sub> UR=0.78-0.57 ln Albumin	-.38	
Sodium . . . . .	.44			

B/S=bound/serum, B/T=bound/total, ln=natural logarithm, T<sub>3</sub>UR=triiodothyronine uptake ratio

\*All r values are significant at the P<.01 level.  
†Equations are given only for relationships with r values ≥ .50 and are given for metric units.

Using logistic regression analysis, the total T<sub>3</sub> measurement was the best prognostic indicator with an overall classification accuracy of 82%, with a 17.0% falsely abnormal (false-positive) rate (patients who were discharged but were predicted to die) and a 33.3% falsely normal (false-negative) rate (patients who died but were predicted to be discharged). Sensitivity was high, therefore, at 97.5%, and specificity was low at 20%. Serum albumin concentration, which was highly correlated with total T<sub>3</sub>, was the next best predictor of outcome, with an overall classification accuracy of 76% and a 22% false-positive rate and a 42% false-negative rate. Sensitivity was also high at 92%, and specificity was low at 30%. Using the population means for serum total T<sub>3</sub> and albumin as arbitrary cutoff points, 39.1% of patients with a total T<sub>3</sub> value of 0.7 nmol per liter (47 ng per dl) or less and 3.7% with a value above 0.7 nmol per liter died ( $P < .01$ , sensitivity = 67.5%, specificity = 90%), and 46.2% with a serum albumin of 27 grams per liter (2.7 grams per dl) or less and 10.6% with a value above 27 grams per liter died ( $P < .001$ , sensitivity = 66%, specificity = 78%).

## Discussion

Our findings indicate that serum thyroid hormone values are frequently altered in patients with AIDS or ARC and that these changes are most commonly due to the nonthyroidal illnesses and much less frequently to impaired hypothalamic-pituitary or thyroid gland function, as in other nonthyroidal illnesses.<sup>15,16,26</sup>

Although CMV inclusion bodies have been described in the thyroid gland,<sup>9,11</sup> overt thyroid gland failure was not found in patients previously studied or in our 80 patients with AIDS or ARC. One of our patients with AIDS, however, had subclinical hypothyroidism.<sup>13,23</sup> The cause of this patient's thyroid gland failure was not determined and may represent either a coincidental occurrence of hypothyroidism or may be due to an AIDS-related thyroid gland destruction. Thyroid gland failure occurs in 0.6% to 1.1% of the general population,<sup>13,27,28</sup> is twice as frequent in women as in men,<sup>13</sup> and is much more common in the elderly (4.4% to 5.9%).<sup>28</sup> Thus, the frequency of hypothyroidism in young men would be expected to be less than 0.5%. Our study population was too small to determine whether an increased prevalence of primary hypothyroidism was present in patients with AIDS or ARC. Further, although hypothalamic dysfunction<sup>6,7</sup> and pituitary failure are reported to occur in persons with AIDS or ARC,<sup>1-6</sup> none of our patients had hypothyroidism due to overt hypothalamic-pituitary failure, and only one case of central hypothyroidism due to toxoplasmosis is reported in the literature.<sup>1</sup> Thus, although hypothyroidism may occur secondary to hypothalamic-pituitary or thyroid gland lesions

in patients with AIDS or ARC, requiring levothyroxine replacement therapy,<sup>13</sup> the frequency appears to be relatively low.

Reduced serum total T<sub>3</sub> levels and free T<sub>3</sub> indexes were the most frequent alterations observed in our euthyroid patients in hospital with AIDS or ARC. This is consistent with previously described patients with other nonthyroidal disorders including infections, malignant neoplasms, and malnutrition, where the earliest and most common alterations of serum thyroid hormone levels are decreased total and free T<sub>3</sub> concentrations resulting from a reduced peripheral conversion of T<sub>4</sub> to T<sub>3</sub>.<sup>15,16</sup> These changes in T<sub>3</sub> metabolism are considered to be adaptive by minimizing protein breakdown, and patients with the low T<sub>3</sub> state of nonthyroidal illness have not been shown to benefit from thyroid hormone replacement therapy.<sup>15,16</sup> These findings also may be important to consider when treating patients infected with the human immunodeficiency virus.

Abnormalities of serum total T<sub>4</sub> levels were detected in six of our euthyroid patients and included increased as well as reduced total T<sub>4</sub> and free T<sub>4</sub> index values without clinical or biochemical evidence of hyperthyroidism or hypothyroidism. Elevated serum total T<sub>4</sub> and free T<sub>4</sub> index values have been noted to occur transiently in euthyroid patients with mild to moderate nonthyroidal illnesses and may be related to a reduced clearance of T<sub>4</sub> from the body rather than to an increased thyroid gland production of T<sub>4</sub>.<sup>15</sup> Thus, these patients should be differentiated from those with hyperthyroidism to avoid unnecessary and potentially harmful therapy.<sup>15,23</sup>

The patients with reduced total T<sub>4</sub> and free T<sub>4</sub> index values had serum TSH levels below 10 mU per liter ( $\mu$ U per dl) and did not have clinical or biochemical evidence of overt hypopituitarism. These laboratory findings are compatible with the low total T<sub>4</sub> state of severe nonthyroidal illness, which is primarily due to a reduced binding of T<sub>4</sub> to serum carrier proteins rather than to decreased thyroid gland production of T<sub>4</sub>.<sup>15,16,23</sup> and does not require or benefit from levothyroxine therapy.<sup>15,16</sup> The minor elevations of serum TSH levels may be due to TSH, which is immunoactive but not bioactive.<sup>15</sup>

The recalculation of the T<sub>3</sub> uptake ratio, free T<sub>4</sub> index, and free T<sub>3</sub> index values by the bound/serum method significantly increased the number of high T<sub>3</sub> uptake ratios but did not significantly reduce the number of low free T<sub>4</sub> and free T<sub>3</sub> indexes. Thus, although theoretically the bound/serum method is a more accurate calculation of the T<sub>3</sub> uptake ratio,<sup>24</sup> it is not used frequently in clinical practice and may be of minimal benefit in screening persons with AIDS or ARC for the presence of thyroid dysfunction.

Serum total  $T_4$ , total  $T_3$ , and  $T_3$  uptake ratio values in our patients admitted to hospital with AIDS or ARC were related to serum albumin and sodium concentrations, as well as to death during the hospital stay. Similar relationships of serum total  $T_4$  and total  $T_3$  levels with albumin concentrations have been reported in patients with other nonthyroidal disorders.<sup>26</sup> Serum albumin levels reflect the nutritional state,<sup>29</sup> and malnutrition and catabolism are known to decrease serum total  $T_3$  and total  $T_4$  levels.<sup>15,16</sup> Thus, these alterations may be causally related. The  $T_3$  uptake ratios are inversely related to serum thyroxine-binding globulin concentrations,<sup>13</sup> and thyroxine-binding globulin, as well as albumin, is synthesized by the liver; thus, both measurements may reflect alterations in the visceral protein state in patients with AIDS or ARC. These alterations in nutritional variables may, in turn, be related to the severity of the illness.

Hyponatremia has been previously reported to relate to the severity of myocardial infarction,<sup>17</sup> and in patients with a variety of nonendocrine disorders may be an indicator rather than a cause of a poor prognosis and death.<sup>18,19</sup> Similarly, in patients with AIDS or ARC studied at our institution, death during a hospital stay was higher in those with hyponatremia (30%) than with normonatremia (16%).<sup>5</sup> Although the same trend was observed—28% versus 17%, respectively—in our group, the difference in mortality was not significant owing to the smaller population studied. The relationship between serum total  $T_3$  and sodium levels in our study most likely indicates that hyponatremia and reduced serum total  $T_3$  levels reflect the severity of the nonthyroidal illness; these alterations are unlikely to be causally related.

Serum total  $T_4$  and total  $T_3$  levels were lower and  $T_3$  uptake ratios higher in patients with AIDS or ARC who died during their hospital stay, a finding similar to that in those who die of acute critical nonthyroidal illnesses.<sup>20</sup> In the latter group, serum total  $T_4$  levels were better than the total  $T_3$  values as predictors of survival during the hospital stay,<sup>20</sup> while in this study, serum total  $T_3$  levels were better indicators. In the seriously ill patients described in 1982, 43% had reduced total  $T_4$  and 68% had decreased total  $T_3$  levels below the normal reference range, compared with 7% and 62%, respectively, in this study. The low frequency of reduced total  $T_4$  levels in these patients with AIDS or ARC may account for its poor predictive ability. Because the serum total  $T_3$  level appears to reflect the severity of malnutrition and nonthyroidal illness in in-hospital patients with AIDS or ARC, its measurement might prove useful in evaluating the efficacy of nonendocrine therapy.

Differentiating decreased total  $T_4$  and free  $T_4$  index values due to hypothalamic-pituitary or thyroid gland failure from reduced serum levels in euthyroid patients with nonthyroidal disorders is of clinical importance because hypothyroidism may contribute to morbidity and mortality if untreated and can be reversed by levothyroxine therapy.<sup>13,14</sup> On the other hand, patients with low total  $T_4$  and free  $T_4$  index values due to nonthyroidal disorders are clinically and biochemically euthyroid<sup>15,16</sup> and do not require thyroid hormone therapy. Indeed, administering thyroid hormones to euthyroid patients with nonthyroidal disorders has not been proved to be beneficial and may increase catabolism, as well as contributing to morbidity and mortality.<sup>15,16</sup> Consequently,

the differentiation of hypothyroidism from alterations due to nonthyroidal disorders should be an integral part of the evaluation of patients with AIDS or ARC who have reduced free  $T_4$  index values. Because hypothyroidism can be overlooked, particularly in patients with severe concurrent nonthyroidal illnesses,<sup>13,14</sup> the diagnosis depends on laboratory screening and confirmation.<sup>23,30</sup>

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