

Clinical Endocrinology

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4 med. 62-155

Editorial Assistant
W. F. Kelly

*39
1993*

Volume 39
1993

BLACKWELL SCIENTIFIC PUBLICATIONS
OXFORD LONDON EDINBURGH BOSTON
MELBOURNE PARIS BERLIN VIENNA

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Blackwell Scientific Publications
Oxford London Edinburgh Boston
Melbourne Paris Berlin Vienna

ISSN 0300-0664



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Thyroid dysfunction in African trypanosomiasis: a possible role for inflammatory cytokines

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(Received 11 December 1992; returned for revision 1 March 1993; finally revised 26 April 1993; accepted 13 May 1993)

Summary

OBJECTIVE Sleeping sickness (African trypanosomiasis) is an anthroponozoonosis transmitted by the tsetse fly. The treatments of choice are the antiparasitic agents suramin and/or melarsoprol. Experimental infection of animals with *Trypanosoma brucei* results in inflammatory lesions in the pituitary and/or the thyroid gland. In biochemical terms, these animals have hypothyroidism. We evaluated the functional integrity of the hypothalamic–pituitary–thyroid axis in patients with African trypanosomiasis before, during and after specific therapy.

DESIGN Prospective, controlled, cross-sectional study.

PATIENTS AND MEASUREMENTS Sixty-five patients with sleeping sickness (31 female, 34 male; aged 18–66; 32 with haemolympathic sleeping sickness receiving suramin i.v., 33 with cerebral sleeping sickness receiving melarsoprol) and 13 control subjects (6 female, 7 male; aged 21–60) were enrolled in a cross-sectional study after giving informed consent. Fourteen patients were studied shortly after admission for sleeping sickness, 19 in the middle of the course of treatment, 18 at the end of the 5-week treatment period, and 14 patients after cure. All subjects underwent a TRH stimulation test at 1200 with bolus injection of 400 µg TRH i.v. Blood was drawn for determination of fT3, fT4, TSH, rT3, TNF-α, IL-1 and IL-6 at 0 minutes and TSH at 60 minutes. All hormones and cytokines were determined by RIA or ELISA.

RESULTS Baseline TSH concentrations (mean ± SEM) were elevated in unmedicated patients with sleeping

sickness compared to normal subjects (2.6 ± 0.4 vs 1.4 ± 0.2 mU/l; $P = 0.01$), whereas fT3 (2.7 ± 0.5 vs 5.8 ± 0.3 pmol/l; $P = 0.0002$) and fT4 concentrations (10.3 ± 1.2 vs 15.4 ± 0.8 pmol/l; $P = 0.007$) were low. Stimulated TSH concentrations did not significantly differ from normal controls. Reverse T3 concentration in patients with sleeping sickness were normal (2.2 ± 0.3 vs 2.4 ± 0.2 nmol/l; $P = \text{NS}$). During the course of treatment, baseline TSH, fT3 and fT4 concentrations slowly returned to normal and were indistinguishable from controls after cure. Plasma concentrations of TNF-α (16.0 ± 4.1 vs 2.9 ± 1.4 ng/l in controls; $P = 0.003$) and interleukin-6 (19.2 ± 7.3 vs 1.3 ± 0.2 ng/l; $P = 0.0001$), but not interleukin-1β (2.0 ± 0.2 vs 0.9 ± 0.2 , ng/l $P = \text{NS}$), were elevated, when thyroid function impairment and disease activity were at their maximum, but gradually decreased into the normal range with therapy. We found a negative correlation between baseline cytokine concentrations and fT3 concentrations (TNF-α: $r = -0.34$, $P = 0.003$; IL-6: $r = -0.43$, $P = 0.0001$).

CONCLUSIONS We conclude that unmedicated sleeping sickness is associated with significant impairment of thyroid function, which is reversed with specific therapy. Elevated TSH concentrations and low fT3 and fT4 concentrations suggest primary hypothyroidism in patients with sleeping sickness. However, an additional pituitary and/or hypothalamic component cannot be excluded. This impairment may be due to the elevated plasma cytokine concentrations found in these patients or may be the result of parasitic thyroiditis.

African sleeping sickness (SS) is caused by *Trypanosoma brucei*, an extracellular protozoan parasite transmitted by the bite of the tsetse fly (Manson-Bahr & Apted, 1982; Hunter *et al.*, 1984). Approximately 20 000 new cases are reported each year to the WHO, although there is considerable fluctuation due to epidemic outbreaks (WHO, 1987; 1990). Clinically, the early acute disease is characterized by haemolympathic involvement with predominant invasion of lymphatic tissue, whereas pancarditis, glomerulonephritis and hepatitis are observed less frequently. After invasion of the central nervous system by the parasite, a meningoencephalitis, with a broad spectrum of neurologic and psychiatric symptoms, evolves. Untreated, the disease is fatal and death is due to secondary bacterial infection, coma, or cachexia.

Recent work has pointed to the importance of interaction

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Table 1 Clinical profile of patients and controls

	<i>n</i>	Sex (female/male) (<i>n</i>)	Haemolympathic stage (<i>n</i>)	Cerebral stage (<i>n</i>)	Age (mean, range) (years)	Time of test after onset of therapy (mean, range)	Day time of test (mean \pm SD) (hour/min)
Normal controls	13	6/7	—	—	34 (21–60)	—	11:34 \pm 1:05
Patients shortly after admission	14	5/9	6	8	31 (18–60)	4.0 (2–7) d	12:05 \pm 1:10
Patients after 2 weeks of therapy	19	10/9	10	9	36 (21–56)	15.0 (9–22) d	11:45 \pm 0:53
Patients after 4 weeks of therapy	18	9/9	10	8	37 (18/65)	28.0 (23–38) d	12:00 \pm 0:55
Patients after cure	14	7/7	6	8	39 (20–65)	22 (6–37) mo	11:31 \pm 0:53

d, Days; mo, months.

between the immune and neuroendocrine system (Imura *et al.*, 1991; Chrousos & Gold, 1992). It is well known that serum thyroid hormone levels change in severe illness (Wartofsky & Burman, 1982). Such abnormalities of thyroid hormone tests, including low normal TSH, low normal fT4, low T3 and high reverse T3, designated 'euthyroid sick syndrome', are considered to be partly mediated by the effects of the inflammatory cytokines on the hypothalamic-pituitary-thyroid (HPT) axis. *In vivo* and *in vitro*, interleukin-1 β (IL-1 β) and tumour necrosis factor- α (TNF- α) inhibit TSH secretion as well as thyroid hormone release (Dubuis *et al.*, 1988; Van Der Poll *et al.*, 1990; Ozawa *et al.*, 1988), whereas the effects of interleukin-6 (IL-6) on the HPT axis have not been studied in detail.

Endocrine abnormalities in African SS have been observed since the early 1950s and include hypothyroidism, hypogonadism and mild adrenocortical insufficiency (Apted, 1953; Ridet, 1953; Emeh & Nduka, 1983; Hublart *et al.*, 1988; Reincke *et al.*, 1992). Patients with SS frequently suffer from lethargy, skin pallor, cold intolerance and hypothermia, suggestive of hypothyroidism (Noireau *et al.*, 1988). Experimental trypanosomiasis in animals has been associated with inflammatory changes in the pituitary and/or the thyroid gland (Murray, 1974; Morrison *et al.*, 1981), and goats infected with *Trypanosoma congolense* had very low thyroxine concentrations (Mutayoba *et al.*, 1988). The pathogenesis of these abnormalities in humans has not been elucidated; however, experimental data in animals suggest a direct effect of the parasite on the pituitary and/or the thyroid gland (Ikede & Losos, 1975). In addition, inflammatory cytokines are elevated in African trypanosomiasis and may play a role in the thyroid hormone abnormalities of these patients. We investigated the interaction between the HPT axis and the inflammatory cytokines TNF- α , IL-1 β and IL-6 in 65 patients with African trypanosomiasis and compared the results with those of 13 normal Ugandan controls.

Patients and methods

Patients and controls

Patients and controls were recruited through the National Sleeping Sickness Control Program in south-east Uganda. The diagnosis of SS was established by microscopical demonstration of parasites in the peripheral blood (haemolympathic stage), and/or in cerebrospinal fluid obtained by lumbar puncture (cerebral stage). All patients with SS received initially a small dosage of suramin (day 1, 0.25 g; day 3, 0.5 g i.v.). Thereafter, patients without cerebral involvement (haemolympathic stage) received weekly 1-g injections of suramin up to a total dose of 5.75 g, whereas patients with cerebral SS were treated with a 5-week course of melarsoprol (total dose: 20 mg/kg body weight).

A total of 65 patients with *Trypanosoma brucei rhodesiense* infection and 13 healthy Ugandan control subjects were studied after giving informed consent (clinical data, see Table 1). None of the healthy subjects had a previous history of SS, thyroid disease or had received suramin, melarsoprol or thyroxine treatment. Using a cross-sectional study design, every patient was studied once during the course of treatment, on each of the following occasions:

- (1) while acutely ill, within the first 7 days from admission to the health care centre
- (2) in the middle of the course of treatment (days 9–22)
- (3) at the end of the treatment period (days 23–38)
- (4) after permanent cure (at least 6 months after end of treatment)

The patients had no clinically apparent signs of thyroid involvement. None of the patients had a goitre or complained of local tenderness over the thyroid region.

The study was approved by the ethics committee of the University of Köln and by the Ministry of Health, Uganda, and *post hoc* by the ICRS of the NICHD.

All patients and controls underwent a TRH stimulation

test between 1000 and 1400 h. In addition, the patients received hCRH (100 µg i.v.; results reported elsewhere (Reincke *et al.*, 1992)). After placing an indwelling catheter in the forearm blood was drawn for determination of TSH, T3, T4, rT3 at baseline and 30 minutes after a bolus injection of 400 µg TRH i.v. (protirelin, TRH Relefact, Hoechst, Frankfurt, FRG). The concentrations of TNF-α, IL-1β and IL-6 were determined in the baseline samples.

The samples were stored on ice for up to 6 hours, then centrifuged and stored at -20°C. After transportation to FRG or USA on dry ice, all samples from a single patient were run in the same assay.

Assays

Serum TSH was determined in duplicate by a commercial two-site immunoradiometric assay (Nichols, Bad Nauheim, FRG). The interassay and intra-assay variabilities were 6.8 and 4.5%, respectively. Free T3 and fT4 concentrations were determined directly by 'solid-phase technique' RIAs (Henning, Berlin, FRG). The interassay and intra-assay variabilities were 9.1 and 5.2%, and 7.4 and 4.5%, respectively. Reverse T3 was measured by RIA as described elsewhere (Bagni *et al.*, 1977). The inter and intra-assay variabilities were 14.2 and 11.9%. Cross-reactivities of the antiserum with L-thyroxine, L-3,5,3'-triiodothyronine, L-3,5-diiodothyronine and L-3,3'-diiodothyronine were 0.08, 0.002, 0.0006 and 0.03%, respectively. TNF-α, IL-1β and IL-6 were determined by specific ELISA using commercial assays (R&D Systems, Minneapolis, USA). The lower limits of detection of these assays were, respectively, 2.8, 1.0 and 1.0 ng/l, and the inter and intra-assay variability 6.4 and 7.8, 3.0 and 5.0, and 7.8 and 7.5%.

Statistics

The data of patients with haemolymphatic and cerebral SS were analysed separately to exclude effects of disease stage and treatment on the HPT axis. Since no significant differences were found, the combined data of both groups are shown. All data are expressed as mean ± SEM, if not otherwise stated. The normal range of hormones and peptides was defined as the mean of the controls ± 2 standard deviations. Differences between group means were assessed using a non-parametric one-way ANOVA (Kruskal-Wallis test) and the Mann-Whitney *U*-test for unpaired data, as appropriate. Correlations were examined with linear regression analysis, after logarithmic transformation of cytokine concentrations when the arithmetic values did not have a Gaussian distribution, and expressed as Pearson's correlation coefficient. $P \leq 0.05$ was considered as statistically significant.

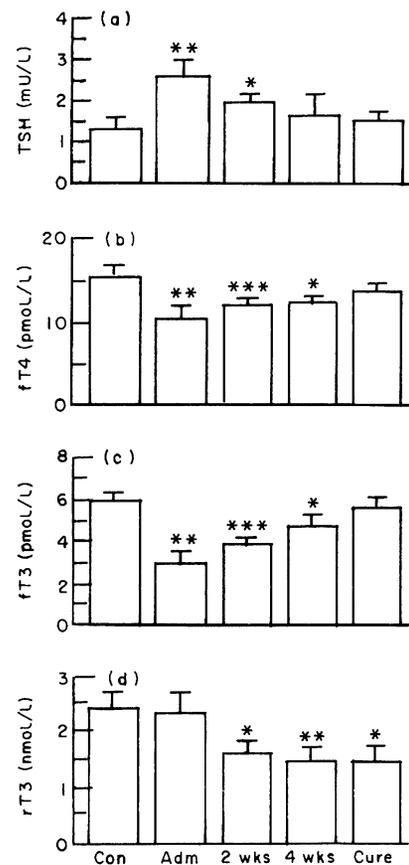


Fig. 1 Mean (\pm SE) a, baseline TSH; b, fT4; c, fT3; and d, rT3 concentrations in 65 African patients with SS and 13 age and sex-matched controls. CON, controls; ADM, newly admitted patients with SS; 2 WKS, 4 WKS, after 2 and 4 weeks of treatment. The symbols denote significant changes between patients and controls. * $P \leq 0.05$; ** $P \leq 0.01$; *** $P \leq 0.005$.

Results

Baseline thyroid function

In 65 patients with SS and 13 age and sex-matched normal Ugandan controls baseline TSH, fT3, fT4 and rT3 were determined (Fig. 1). For TSH concentrations (Kruskal-Wallis test, $P = 0.04$), fT3 ($P \leq 0.0001$), fT4 ($P = 0.01$) and rT3 concentrations ($P = 0.04$) significant differences were found. Shortly after admission, SS patients had elevated TSH concentrations compared to normal controls (2.6 ± 0.4 vs 1.4 ± 0.2 mU/l; $P = 0.01$), whereas fT3 (2.8 ± 0.5 vs 5.4 ± 0.3 pmol/l; $P = 0.0002$) and fT4 (10.3 ± 1.2 vs 15.4 ± 0.8 pmol/l; $P = 0.007$) were low and rT3 concentrations normal (2.2 ± 0.4 vs 2.4 ± 0.3 nmol/l; $P = \text{NS}$). After 2 and 4 weeks of treatment, elevated TSH concentrations slowly returned to normal. In addition, fT3 and fT4 concentrations increased somewhat, but remained subnormal. However, rT3 concen-

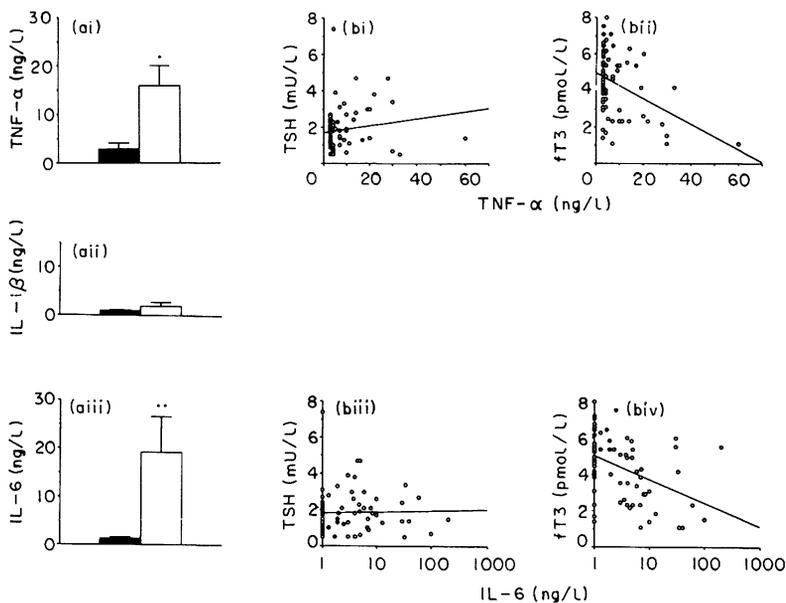


Fig. 2 Mean (\pm SE) plasma cytokine concentrations in African patients with SS and controls studied in parallel. ai, Mean TNF- α ; aii, IL-1 β and aiii, IL-6 levels in \square , newly admitted, unmedicated patients and \blacksquare , controls. * $P=0.003$; ** $P=0.0001$, patients *vs* controls (Mann-Whitney *U*-test). Correlation between baseline bi, TSH and bii, fT3 concentrations and baseline TNF- α , and between baseline biii, TSH and biv, fT3 and IL-6 concentrations in \circ , patients with SS and \bullet , controls. bi, $r=0.18$, $P=0.02$; bii, $r=-0.39$, $P=0.003$; biii, $r=0.05$, $P=NS$; biv, $r=-0.43$, $P=0.0001$.

trations were significantly lower in patients with SS than in controls after 2 and 4 weeks of treatment. After cure, rT3 concentrations remained low in patients with SS, whereas TSH, fT3 and fT4 concentrations were normal.

Seven of 14 (50%) patients on admission, 4 of 19 (21%) after 2 weeks of treatment, 4 of 18 (22%) after 4 weeks of treatment and none of 14 patients after cure had fT4 concentrations below the normal range of controls (10.0–20.7 pmol/l).

TRH stimulation test

All patients and controls underwent a TRH stimulation test. Stimulated TSH concentrations as well as the TSH increase did not significantly differ between patients with SS and control subjects (Kruskal-Wallis test, $P=0.14$ and 0.13 , respectively). TSH concentrations after TRH in control subjects were 16.8 ± 1.7 , in patients with SS shortly after admission 17.4 ± 2.2 , after 2 weeks of treatment 14.8 ± 1.5 , after 4 weeks of treatment 13.8 ± 2.6 , and after cure 17.3 ± 2.1 mU/l, respectively. The corresponding TSH increase was 15.4 ± 1.6 in controls and 14.8 ± 2.0 , 12.8 ± 1.3 , 12.5 ± 2.2 and 15.8 ± 2.0 mU/l, respectively, in patients with SS during the course of treatment.

Cytokines

In all subjects basal circulating TNF- α , IL-1 β and IL-6 concentrations were determined (Fig. 2a). TNF- α (Kruskal-Wallis test, $P=0.005$) and IL-6 (Kruskal-Wallis test, $P=0.0001$), but not IL-1 β , were substantially elevated in SS.

TNF- α concentrations were high in patients shortly after admission (16.0 ± 4.5 vs 2.9 ± 1.4 ng/l in controls, $P=0.003$) and returned to normal after 2 and 4 weeks of treatment (3.8 ± 1.6 and 6.5 ± 1.7 ng/l, respectively). A weak, but significant, positive correlation was observed between basal TNF- α concentrations and basal TSH concentrations in patients with SS ($r=0.27$, $P=0.02$; Fig. 2b). In addition, TNF- α concentrations were inversely correlated with fT3 concentrations ($r=-0.34$, $P=0.003$) and, to a lesser degree, with fT4 concentrations ($r=-0.23$, $P=0.05$). TNF- α concentrations showed a positive correlation with reverse T3 levels ($r=0.26$, $P=0.02$).

IL-1 β concentrations were undetectable in most of the patients with SS, and mean immunoreactive concentrations did not differ from those of control subjects (0.9 ± 0.2 vs 2.0 ± 0.8 ng/l, $P=NS$).

IL-6 concentrations, on the other hand, were dramatically elevated in SS (19.2 ± 7.3 vs 2.9 ± 1.4 ng/l in controls, $P=0.0001$) and slowly returned to normal (after 2 weeks, 16.3 ± 10.8 ng/l; after 4 weeks, 2.8 ± 1.6 ng/l). TSH concentrations showed no correlation with IL-6 concentrations. Free T3 and fT4 concentrations were negatively correlated with basal IL-6 concentrations ($r=-0.43$, $P=0.0001$; $r=-0.22$, $P=0.05$, respectively). No significant correlation was observed between rT3 and IL-6 ($r=0.21$, $P=0.06$).

Discussion

African trypanosomiasis is associated with extensive mononuclear infiltration of organs invaded by the parasite (Murray, 1974; Morrison *et al.*, 1981). In animals, inflammatory

changes in endocrine tissue have been described in the anterior and posterior pituitary (Ikede & Losos, 1975), the thyroid gland (Mutayoba *et al.*, 1988b), the adrenals (Ikede & Losos, 1975) and gonads (Ikede, 1979; Anosa & Kaneko, 1984). Low fertility rates are a well known phenomenon in African trypanosomiasis and have been described in cattle, goats, sheep and rats. Biochemically, infected goats have low circulating oestradiol (Mutayoba *et al.*, 1988a) and testosterone concentrations (Waindi *et al.*, 1986) and low thyroxine concentrations (Mutayoba *et al.*, 1988b). In humans, endocrine abnormalities in SS have been less extensively investigated. Pituitary fibrosis and thyroid atrophy were described in two fatal cases of cerebral SS (Hawking & Greenfield, 1941). Loss of libido, amenorrhoea and impotence frequently occur during the course of the disease (Ridet, 1953; Noireau *et al.*, 1988). Abnormalities in thyroid (Boersma *et al.*, 1989) and gonadal hormone secretion (Emeh & Nduka, 1983; Hublart *et al.*, 1988) have been demonstrated in these patients, and we recently described a significant impairment of adrenocortical function in patients with SS, with 25% of the patients within the adrenocortical insufficiency range, which was most likely secondary to ACTH deficiency (Reincke *et al.*, 1992). We now show that, in addition to abnormalities in the pituitary–adrenal axis, the hypothalamic–pituitary–thyroid axis is impaired in SS, and this is correlated with circulating concentrations of inflammatory cytokines.

Patients with unmedicated SS had slightly, but significantly, elevated TSH concentrations, lowered fT3 and fT4 concentrations and normal rT3 concentrations. The TSH response to TRH was not different from control subjects. These results are similar to reports by Hublart *et al.* (1988) and Boersma *et al.* (1989), who also described elevated TSH concentrations in the presence of low T3 and T4 concentrations in smaller series of patients with SS. In addition, these authors found normal or low rT3 concentrations. The observed abnormalities in thyroid hormone secretion seem to be rather unusual and cannot be explained by either central hypothyroidism, primary hypothyroidism or the 'euthyroid-sick syndrome'. The last is characterized by very low T3 concentrations, low total T4 and normal fT4 levels, normal baseline TSH with a blunted response to stimulation with TRH and elevated rT3 concentrations due to an inhibition of the 5'-deiodinase which converts T3 to the inactive thyroid hormone 3,3'-triiodothyronine (Wartofsky & Burman, 1982; Wehmann *et al.*, 1985; Hamblin *et al.*, 1986; Faber *et al.*, 1987; Felicetta, 1989). Although some of the thyroid hormone abnormalities observed in patients with SS may be attributed to the 'euthyroid-sick syndrome', elevated baseline TSH concentrations and normal rT3 concentrations do not favour this explanation.

Assuming a normally functioning hypothalamic–pituitary unit, primary hypothyroidism is accompanied by elevated baseline TSH concentrations and an exaggerated TSH response to TRH. Our patients had slightly elevated baseline TSH concentrations and a normal TSH response to TRH, excluding the presence of 'simple' primary hypothyroidism. However, pituitary TSH secretion may be abnormal in SS, because of parasitic infiltration of the pituitary gland, thus impairing the appropriate TSH surge in response to TRH in the background of primary hypothyroidism. Since ACTH (Reincke *et al.*, 1992) and LH/FSH (Emeh & Nduka, 1983; Hublart *et al.*, 1988) secretion is also impaired in African trypanosomiasis, patients with SS may suffer from mild panhypopituitarism. Low fT3 and fT4 concentrations in SS, therefore, are most likely the result of combined pituitary and peripheral hypothyroidism. In addition, hypothalamic hypothyroidism resulting from cerebral trypanosomiasis may contribute to the thyroid hormone abnormalities in SS. This condition is associated with slightly elevated baseline TSH concentrations (Ingbar, 1985) which have been attributed to secretion of a form of TSH that is immunoreactive but has little or no biological activity due to reduced ability to bind to its receptor (Faglia *et al.*, 1983; Beck-Beccoz *et al.*, 1985). Post-translational modifications of the TSH molecule associated with reduced biological activity have also been found in patients with non-thyroidal illness (Lee *et al.*, 1987).

The pathogenesis of the impairment of the HPT axis function observed in SS is not clear. It can be explained in two major ways which may not be mutually exclusive. First, it may be due to parasite infiltration and transient inflammatory dysfunction of the hypothalamic–pituitary unit and/or of the thyroid gland. Animal and human data support this possibility (Hawking & Greenfield, 1941; Murray, 1974; Ikede & Losos, 1975; Morrison *et al.*, 1981; Mutayoba *et al.*, 1988b). Thus, experimental infection with *Trypanosoma brucei* in sheep, resulted in acute coagulative necrosis of the adenohypophysis and leucocytic infiltration of the neurohypophysis, with trypanosomas present in pituitary tissue (Ikede & Losos, 1975). In goats experimentally infected with *Trypanosoma congolense*, chronic thyroiditis and very low T4 concentrations have been described (Mutayoba *et al.*, 1988b). In this paradigm the hypothyroidism was severe and permanent, different from the mild to moderate transient dysfunction that we observed.

Second, elevated cytokine concentrations may suppress TSH and T3/T4 secretion in SS. Subcutaneously or intraperitoneally administered TNF- α and IL-1 β decrease TSH and T3/T4 concentrations in rats (Dubuis *et al.*, 1988; Van Der Poll *et al.*, 1990) while the former causes also a reduction in hypothalamic TRH content (Pang *et al.*, 1989). In addition, TNF- α , a putative mediator of the euthyroid-sick syndrome,

inhibits the 5'-deiodinase of peripheral tissues (Ozawa *et al.*, 1988). IL-6 has been shown to inhibit the TSH-induced thyroid peroxidase gene expression and T3 secretion in a dose-dependant manner (Ahren, 1991; Tominaga *et al.*, 1991). The high circulating TNF- α and IL-6 levels in patients with SS correlated positively with baseline TSH and rT3 concentrations, but negatively with fT3 and fT4 concentrations. These data are compatible with a direct inhibitory effect of chronically elevated TNF- α and/or IL-6 on thyroid hormone secretion in SS, resulting in compensatory, albeit inadequate, elevation of TSH with potentially reduced bioactivity due to post-translational modifications (Faglia *et al.*, 1983; Beck-Beccoz *et al.*, 1985; Lee *et al.*, 1987). High plasma inflammatory cytokine levels combined with the release of thyroid antigens due to parasitic thyroiditis could also provoke an autoimmune response with production of thyroid autoantibodies. However, thyroid antibodies measured in pooled serum samples were not elevated in our patients compared to controls (data not shown) which does not support this attractive hypothesis.

The correlation between plasma cytokine and thyroid hormone concentrations was weak in this study. The interaction between the immune system and the HPT axis in SS may be, therefore, more indirect. For example, elevation of inflammatory cytokines and suppression of the HPT axis in African trypanosomiasis can both be regarded as an index of disease activity. In this model, the observed correlation reflects more an association with the severity of the underlying illness rather than a direct inhibitory effect of TNF- α and/or IL-6 on the HPT axis.

Acknowledgements

We would like to thank the staff of the National Sleeping Sickness Control Program for their skilful technical assistance. MR is supported in part by a grant of the Deutsche Forschungsgemeinschaft and the Gesellschaft für Technische Zusammenarbeit (Re 752/2-1).

References

- Ahren, B. (1991) Regulatory peptides in the thyroid gland: a review on their localization and their function. *Acta Endocrinologica (Copenh.)*, **124**, 225–232.
- Anosa, V.O. & Kaneko, J.J. (1984) Pathogenesis of *Trypanosoma brucei* infection in deer mice. Light and electron microscopy study of testicular lesions. *Veterinary Pathology*, **21**, 238–246.
- Apted, P.I.C. (1953) Clinical manifestations and diagnosis of sleeping sickness. In *The African Trypanosomiasis* (eds H. W. Mulligan & W. H. Pott), pp. 661–683. Allen & Unwin, London.
- Bagni, B., Malavasi, F., Cavallini, A.R., Feggi, L.M., Uberti E.D., Zucchi, F. & Iotti, G.S. (1977) A 3,3',5'-triiodothyronine (reverse T3) radioimmunoassay. *Ricerca Clinica e Laboratorio*, **7**, 387–394.
- Beck-Beccoz, P., Amr, S., Menezes-Ferreira, M.M., Faglia, G. & Weitraub B.D. (1985) Decreased receptor binding of biologically inactive thyrotropin in central hypothyroidism. Effect of treatment with thyrotropin releasing hormone. *New England Journal of Medicine*, **312**, 1085–1090.
- Boersma, A., Hublart M., Boutignon, F., Noireau F., Lemerse J.L., O'Herbomez, M. & Degand, P. (1989) Alterations in thyroid function in patients with *Trypanosoma brucei gambiense* infection. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **83**, 208–209.
- Chrousos, G.P. & Gold, P.W. (1992) The concepts of stress and stress system disorders: overview of behavioral and physical homeostasis. *Journal of the American Medical Association*, **267**, 1244–1252.
- Dubuis, J.M., Dayer, J.M., Siegrist-Kaiser, C.A. & Burger, A.G. (1988) Human recombinant interleukin-1 β decreases plasma thyroid hormone levels in rats. *Endocrinology*, **123**, 2175–2182.
- Emeh, J.K. & Nduka, E.U. (1983) Circulating serum levels of gonadotropins in Gambian sleeping sickness. *IRCS Medical Sciences*, **11**, 411.
- Faber, J., Kirkegaard, C., Rasmussen, B., Westh, H., Busch-Sørensen, M. & Jensen, W. (1987) Pituitary-thyroid axis in critical illness. *Journal of Clinical Endocrinology and Metabolism*, **65**, 315–320.
- Faglia, G., Beck-Peccoz, P., Ballabio, M. & Nava, C. (1983) Excess of β -subunit of thyrotropin in patients with idiopathic central hypothyroidism due to the secretion of TSH with reduced biological activity. *Journal of Clinical Endocrinology and Metabolism*, **56**, 908–914.
- Felicetta, J.V. (1989) Effects of illness on thyroid function tests. *Postgraduate Medicine*, **85**, 213–220.
- Hamblin, P.S., Dyer, S.A., Mohr, V.S., Le Grand B.A., Lim, C.F., Tuxen D.V., Topliss, D.J. & Stockigt, J.R. (1986) Relationship between thyrotropin and thyroxine changes during recovery from severe hypothyroxinemia of critical illness. *Journal of Clinical Endocrinology and Metabolism*, **62**, 717–722.
- Hawking, F. & Greenfield, J.G. (1941) Two autopsies on Rhodesian sleeping sickness; visceral lesions and changes in the cerebrospinal fluid. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **35**, 155–164.
- Hublart, M., Lagouche, L., Racadot, A., Boersma, A., Degand, P., Noireau, F., Lemesre, J.L. & Toudic, A. (1988) Function endocrine et Trypanosomiase Africaine. Bilan de 79 cas. *Bulletin de la Societe Pathologie Exotique*, **81**, 468–476.
- Hunter, G.W. III, Swartzfelder, J.C. & Clyde, D.F. (eds) (1984) *Hunter's Tropical Medicine*. 5th edition, pp. 552–565. W.B. Saunders, Philadelphia.
- Ikede, B.O. (1979) Genital lesions in experimental chronic *Trypanosoma brucei* infection in rams. *Research in Veterinary Science*, **26**, 145–151.
- Ikede, B.O. & Losos, G.J. (1975) Pathogenesis of *Trypanosoma brucei* infection in the sheep. III Hypophyseal and other endocrine lesions. *Journal of Comparative Pathology*, **85**, 37–44.
- Imura, H., Fukata, J. & Mori, T. (1991) Cytokines and endocrine function: an interaction between the immune and neuroendocrine system. *Clinical Endocrinology*, **35**, 107–115.
- Ingbar, S.H. (1985) The thyroid gland. In *Williams' Textbook of Endocrinology*. 7th edition (eds J. D. Wilson & D. W. Foster), p. 786. W. B. Saunders, Philadelphia
- Lee, H.Y., Suhl, J., Pekary, A.E. & Heishmann, J.M. (1987) Secretion of thyrotropin with reduced concavalin-A-binding

- activity in patients with nonthyroidal illness. *Journal of Clinical Endocrinology and Metabolism*, **65**, 942-945.
- Manson-Bahr, P.E.C. & Apted, F.I.C. (eds) (1982) *Manson's Tropical Medicine*. 18th edition, pp. 72-85. Baillière Tindall, East Sussex.
- Morrison, W.I., Murray, M. & Sayer, P.D. (1981) The pathogenesis of experimentally induced *Trypanosoma brucei* infection in the dog. I Tissue and organ damage. *American Journal of Pathology*, **102**, 168-181.
- Murray, M. (1974) The pathology of African trypanosomiasis. In *Progress of Immunology II*, Volume 4, *Clinical Aspects* (eds L. Brent & J. Holborow), pp. 182-192. North-Holland Publishing, Amsterdam, Oxford.
- Mutayoba, B.M., Gombe, S., Waindi, E.N. & Kaaye, G.P. (1988a) Depression of ovarian function and plasma progesterone and estradiol-17 β in female goats chronically infected with *Trypanosoma congolense*. *Acta Endocrinologica (Copenh.)*, **117**, 477-484.
- Mutayoba, B.M., O'hara-Ireri, H.B. & Gombe, S. (1988b) Trypanosome-induced depression of plasma thyroxine levels in prepubertal and adult female goats. *Acta Endocrinologica (Copenh.)*, **119**, 21-26.
- Noireau, F., Apembet, J.D. & Frezil, J.L. (1988) Revue clinique des troubles endocriniens observés chez l'adulte trypanosomé. *Bulletin de la Société Pathologie Exotique*, **81**, 464-467.
- Ozawa, M., Sato, K., Han, D.C., Kawakami, M., Tsushima, T. & Shizume, K. (1988) Effects of tumor necrosis factor- α /cachectin on thyroid hormone metabolism in mice. *Endocrinology*, **123**, 1461-1467.
- Pang, X.P., Hershman, J.M., Mirell, C.J. & Pekary, A.E. (1989) Impairment of hypothalamic-pituitary-thyroid function in rats treated with human recombinant tumor necrosis factor- α (cachectin). *Endocrinology*, **125**, 76-84.
- Reincke, M., Heppner, C., Petzke, F., Mbulameri, D., Allolio, B. & Winkelmann, W. (1992) Combined hypocortisolism and hypogonadism in patients with African sleeping sickness. *Acta Endocrinologica (Copenh.)*, **126 (Suppl. 4)**, 61.
- Ridet, J. (1953) Etude des troubles du cycle menstruel chez la femme trypanosomée à l'aide de frottis vaginaux (étude préliminaire). *Medicine Tropicale*, **13**, 514-519.
- Tominaga, T., Yamashita, S., Nagayama, Y., Morita, S., Yokoyama, N., Izumi, M. & Nagataki, S. (1991) Interleukin 6 inhibits human thyroid peroxidase gene expression. *Acta Endocrinologica (Copenh.)*, **124**, 290-294.
- Van Der Poll, T., Romijn, J., Wiersinga, W.M. & Sauerwein, H.P. (1990) Tumor necrosis factor: a putative mediator of the sick euthyroid syndrome in man. *Journal of Clinical Endocrinology and Metabolism*, **71**, 1567-1572.
- Waindi, E.N., Gombe, S. & Oduor-Okele, D. (1986) Plasma testosterone in *Trypanosoma congolense*-infected Toggenburg goats. *Archives of Andrology*, **17**, 9-17.
- Wartofsky, L. & Burman, K.D. (1982) Alterations in thyroid function in patients with systemic illness. *Endocrine Reviews*, **3**, 164-175.
- Wehmann, R.E., Gregerman, R.I., Burns, W.H., Saral, R. & Santos, G.W. (1985) Suppression of thyrotropin in the low-thyroxine state. *New England Journal of Medicine*, **312**, 546-550.
- World Health Organization (1987) Parasitic diseases. The primary health care approach to the control and prevention of sleeping sickness. *Weekly Epidemiological Record*, **62**, 197-204.
- World Health Organization (1990) Trypanosomiasis. Situation in the OCEAC member states. *Weekly Epidemiological Record*, **65**, 388-391.

Referees

We wish to thank the following who acted as referees during the period 1 January–30 June 1993.

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|---------------------|---------------------|--------------------|--------------------|
| J. E. Adams | I. Doniach | W. J. Jeffcoate | S. Reichlin |
| K. G. M. M. Alberti | P. L. Drury | J. S. Jenkins | C. Ribot |
| S. A. Amiel | A. Dunaif | D. E. Jewitt | B. L. Riggs |
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