# Thyroid Function in Protein-Energy Malnutrition

BY

J. M. VAN DER WESTHUYSEN

*Department Physiology, Godfrey Huggins School of Medicine, University of Rhodesia, Salisbury.*

*Present Address: Department Human and Animal Physiology, University of Stellenbosch, Stellenbosch.*

Protein-energy malnutrition is known to produce a wide variety of metabolic disturbances to which the body attempts to adapt by neural or endocrine mechanisms in order to maintain homeostasis. Endocrine changes have been investigated intensively in the deficiency diseases kwashiorkor and marasmus over the last decade and their roles, causes or effects or relationships to other metabolic changes have been a field of argument. Thyroid hypoplasia have been described in malnourished humans (Stephens, 1940; Tejada, 1958) and experimental animals (Platt and Steward, 1967), while thyroid function tests have been reported as low in malnourished children (Singh, Anderson and Turner, 1971; Beas, Mönckeberg and Horwitz, 1966). Since TSH did not always elevate thyroid function in protein depleted animals subnormal thyroid rather than pituitary function have been reported (Cowan and Margossion, 1966).

On the other hand, some histological evidence has reported the thyroid to be normal (Stirling, 1962) whereas a high basal TSH and a good response to TSHRF implies only minor impairment of thyroid function and normal TSH reserve in protein-energy malnutrition (Pimstone, Becker and Hendricks, 1973). This study was therefore undertaken to investigate concentrations of thyroid hormones in plasma of kwashiorkor and marasmic patients and attempt to relate them to mortality in these diseases.

## Patients and Methods

Thirty-nine malnourished patients admitted to Harare Hospital, Salisbury, during December, 1972, to March, 1973, were studied. These children were classified according to the Wellcome Working Party (1970) into 26 cases of kwashiorkor and 13 cases of marasmus. Within the first 24 hours after admission to hospital a routine blood sample was taken.

This sample, which was immediately placed into crushed ice was used for analysis. Further blood samples were taken following one week of hospital treatment and during the week of discharge from hospital. These samples were analysed for total plasma thyroxine by competitive protein binding (Braverman, Vagenakis, Foster and Ingbar, 1971). $T_3$ uptake was determined by the method of Walther (1970) using Sephadex G 25 and $I^{125}$ liothyronine (Amersham). Multiplication of each total thyroxine determination with its corresponding $T_3$ uptake determination gave the "free thyroxine index", which is highly correlated with the actual free thyroxine concentration (Anderson, 1968; Liewendahl, Totterman and Lambert, 1971). In addition, free thyroxine was estimated from these results using the equation: $Y = 0{,}85 + 17\ X$ (Anderson, 1968).

Where Y is free thyroxine, X the product of thyroxine and $T_3$ uptake. Total triiodothyronine ($T_3$) was determined by radioimmunoassay (Biolab: Belgium). This method was found to be greatly influenced by the level of plasma protein (Van der Westhuysen, 1973). Total plasma protein was determined by the biuret method (Weischelbaum, 1946).

## Results

From Table I it can be seen that on admission to hospital the total plasma thyroxine concentration in all children suffering from protein-energy malnutrition was significantly ($P < 0{,}01$) lower than that of Well Babies. However, due to the reduction in total plasma protein this difference could be attributed to the decrease in the proportion of bound hormone. This is shown by the insignificant changes in the free thyroxine index and the calculated free thyroxine. Although the figures for malnourished children are slightly lower than those of Well Babies, only the children that subsequently died had a significantly ($P < 0{,}05$) lower free thyroxine index or free thyroxine values.

Plasma triiodothyronine ($T_3$) concentration (Table I) was significantly ($P < 0{,}05$) lower in kwashiorkor patients than Well Babies. This difference proved to be greatly influenced by the protein content of the plasma assayed (Van der Westhuysen, 1973), so that samples with low plasma protein gave spuriously low concentrations of triiodothyronine.

During the period of recovery total thyroxine increased significantly ($P < 0{,}05$) in all malnourished children, so that their thyroxine concentration in the week prior to discharge from hospital did not differ significantly from that of Well Babies (Table II). Small but insignificant increases in the free thyroxine index and the calculated free thyroxine occurred, but these figures never differed significantly from those of the Well Babies. The total concentration increased significantly ($P < 0{,}01$) in the first week in hospital and again ($P < 0{,}01$) up to the week of discharge. During their final week in hospital triiodothyronine values of patients with kwashiorkor did not differ significantly from the values of the Well Babies.

## Discussion

There is histological evidence of thyroid hypoplasia in human (Stephens, 1940) and experimental (Platt and Steward, 1967) protein-energy malnutrition, although this has been disputed by Stirling (1962). Protein bound iodine, butanol extractable iodine (Rao *et al*, 1971; Beas *et al*, 1966) and thyroidal radioidodine uptake (Beas *et al*, 1966) has been reported to be considerably decreased when compared with normal children. Results of the present experiment are in agreement with these findings in that the total plasma thyroxine of all children with protein-energy malnutrition is markedly decreased when compared with Well Babies. However, the close relationship of total thyroxine with total plasma protein and the reverse relationship of total thyroxine and the $T_3$ resin uptake indicates that the low level of thyroxine is a result of the decrease in the thyroxine binding proteins during protein-energy malnutrition. During recovery in hospital the rapid increase in plasma proteins is therefore accompanied by an concomitant increase in the total thyroxine and triiodothyronine.

The "Free thyroxine index" ($T_4 \times T_3$ resin uptake) eliminates the effect of a reduction in thyroxine binding globulin. Therefore, the insignificant differences in the "free thyroxine index" between the malnourished and Well Babies indicate only minor impairment of thyroid function in protein-energy malnutrition. In fatal protein-energy malnutrition however, the lower "free thyroxine index" found in this study probably indicates a total collapse of metabolism.

Although there is evidence of decreased thyroid function (Singh, Anderson and Turner, 1971; Beas *et al,* 1966) due to a decrease in the secretion of thyroid stimulating hormone (Beas *et al,* 1966), the present study indicates that the low concentrations of protein bound iodine and butanol extractable iodine (Beas *et al,* 1966) and of thyroxine (Krieger and Good, 1970) found more in most previous studies was due more to a reduction in the thyroxine binding than to a reduction in the "active" free thyroxine. Therefore thyroid function as such probably plays a minor role in the metabolic adaptation to protein-energy malnutrition and in agreement with Pimstone *et al* (1973) this study also suggests only minor impairment.

Acknowledgement

The author wishes to express his sincere appreciation to the Ames Co. for the thyroxine kits used in this experiment.

References

Anderson, B. G. (1968). *J. Amer. med Assoc.* **203,** 135.
Beas, F., Monckeberg, F. and Horwitz, I. (1966). *Pediatrics,* **38,** 1003.
Braverman, L. E., Vagenakis, A. A., Foster, A. E. and Ingbar, S. H. (1971). *J. Clin. Endocr.* 32.
Cowan, J. W. and Margossian, S. (1966). *Endocrin.* **79,** 1023.
Krieger, I. and Good, M. H. (1970). *Am. J. Dis. Child* **120,** 95.
Liewendahl, K., Totterman, J. and Lambert, B.-A. (1971). *Acta Endocrin.* **67,** 793.
Pimstone, B., Becker, D. and Hendricks, S. (1973). *J. Clin. Endocr. Metab.* **36,** 779.
Platt, S. S. and Steward, R. J. C. (1967). *J. Endocr.* **38,** 121.
Rao, K. S. J., Raghuramulu, N. and Srikania, S. G. (1971) *Ind. J. Med. Res.* **59,** 1300.
Singh, D. V., Anderson, R. R. and Turner, C. W. (1971). *J. Endocr.* **50,** 445.
Snedecor, G. W. and Cochrane, W. G. (1967). *Statistical methods.* 6th ed. Ames: Iowa State University Press.
Stephens, D. J. (1940). *Endocrin.* **26,** 485.
Stirling, G. A. (1962). *Arch. Dis. Child.* **37,** 99.
Tejada, C. (1958). *Fed. Proc.* **17,** 66.
Van der Westhuysen, J. M. (1973). *Lancet* **2,** 965.
Walther, W. W. (1971). *J. Pediat.* **78,** 177.
Wellcome Working Party on Infantile Malnutrition, 1970. *Lancet* **2,** 302.

*Table I*

Plasma Thyroxine, Triiodothyronine and Protein Concentrations in Kwashiorkor and Marasmic Patients on Admission to Hospital and in Well Babies.

| | *KWASHIORKOR* | | *MARASMUS* | | *WELL BABIES* |
|---|---|---|---|---|---|
| | *Lived* | *Died* | *Lived* | *Died* | |
| *Number* | 12 | 14 | 9 | 4 | 21 |
| Total plasma protein g/100ml | 4,25 ± 0,16[a] | 4,40 ± 0,17[a] | 5,16 ± 0,22[b] | 5,36 ± 0,76[b] | 7,61 ± 0,10 |
| Total thyroxine ng/100ml | 4,47 ± 0,87[a] | 2,60 ± 0,52[b] | 3,55 ± 0,73[a] | 2,72 ± 0,52[c] | 10,22 ± 0,51[b] |
| Free thyroxine index | 8,97 ± 1,70[ac] | 5,55 ± 0,98[bc] | 8,55 ± 2,26[ac] | 4,70 ± 0,98[bc] | 11,48 ± 0,60[a] |
| Free thyroxine ng/100ml | 1,87 ± 0,20[ab] | 1,41 ± 0,15[a] | 1,79 ± 0,25[ab] | 1,37 ± 0,15[a] | 2,14 ± 0,07[b] |
| Triiodothyronine (Total) (ng/100ml | 12,50 ± 1,54[a] | 8,9 ± 1,24[a] | — | — | 166,0 ± 6,32[b] |

[abc]Within the body of the table, figures having the same superscript are not significantly (P 0,01) different from each other.

PLASMA THYROXINE, TRIIODOTHYRONINE AND PROTEIN CONCENTRATIONS IN KWASHIORKOR AND MARASMUS ON ADMISSION AND DURING RECOVERY IN HOSPITAL AND ALSO IN WELL BABIES.

| | *KWASHIORKOR* | | | *MARASMUS* | | | *WELL BABIES* |
|---|---|---|---|---|---|---|---|
| | *Admission* | *7 Days* | *Discharge* | *Admission* | *7 Days* | *Discharge* | |
| *Number* | 11 | 11 | 11 | 8 | 8 | 8 | 21 |
| Total plasma protein g/100ml | 4,56 ± 0,21[a] | 5,82 ± 0,27[b] | 7,16 ± 0,14[b] | 5,16 ± 0,35[a] | 5,82 ± 0,42[b] | 7,46 ± 0,36[b] | 7,61 ± 0,10[b] |
| Total thyroxine g/100ml | 4,38 ± 1,04[a] | 5,85 ± 0,85[a] | 8,17 ± 1,01[b] | 4,09 ± 0,89[a] | 12,35 ± 4,41[a] | 9,69 ± 0,89[b] | 10,22 ± 0,51[b] |
| Free thyroxine index | 8,80 ± 2,05[a] | 9,25 ± 1,18[a] | 9,47 ± 0,92[a] | 8,53 ± 2,67[a] | 10,79 ± 1,80[a] | 13,16 ± 1,53[a] | 11,48 ± 0,60[a] |
| Free thyroxine ng/100ml | 1,86 ± 0,24[a] | 1,88 ± 0,13[a] | 1,91 ± 0,10[a] | 1,79 ± 0,30[a] | 2,11 ± 0,25[a] | 2,31 ± 0,17[a] | 2,14 ± 0,07[a] |
| Triiodothyronine (Total) (ng/100ml | 12,5 ± 1,69[a] | 83,75 ± 14,75[b] | 160,62 ± 25,28[c] | — | — | — | 166,00 ± 6,32[c] |

[abc]Within the body of the table, figures having the same superscript are not significantly (P 0,05) different from each other.