# Human biology and medicine

## Changes in thyroid hormone status with antarctic residence

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Studies carried out in temperate, mid-latitude regions suggest a winter elevation in blood pressure (Tanaka et al. 1989) and increased incidence of heart attack (Vuori 1987), stroke (Keatinge, Coleshaw, and Holmes 1989), and mood disorder (Sack et al. 1985) compared with summer measurements. At high global latitudes, circumpolar winters are associated with extremes of low temperature, low relative humidity, increased electromagnetic radiation, changing photoperiods, and social isolation. Thyroid hormones help regulate metabolic rate, cardiovascular function, lipid metabolism, and mood, and they are rapidly adjusted to starvation, overfeeding, illness, and cold exposure. Thyroxine ($T_4$) is the prohormone, and triiodothyronine ($T_3$) is considered the active thyroid hormone with nuclear binding capability. Changes in human thyroid hormone function with prolonged polar residence may extend our understanding of circannual changes observed during mid-latitude winters.

A paired design was used to study men in August while in California (34°03'N 118°14'W), after 20–24 weeks of residence at McMurdo Station (77°51'S 166°37'E), and again after 40–44 weeks of antarctic residence. Tests conducted included basal and dynamic thyroid hormone measurement of the pituitary thyrotropin reserve and the serum clearance of both unlabeled (oral dose) and iodine-125 labeled (intravenous dose) $T_3$. *In vitro* studies of hormone binding to serum carrier proteins have also been conducted (Reed et al. in press; Quesada, Reed, and Smith 1989). Climate chambers in Bethesda, Maryland, were used to contrast antarctic findings with changes in human thyroid hormone physiology during experimental cold adaptation (Reed et al. 1990a).

The results of our study can be summarized in five categories:

- Pituitary physiology (figure 1). We found that the pituitary response of thyrotropin to intravenous thyrotropin-releasing hormone increased 50 percent after 5 months of residence in Antarctica and remained elevated after 11 months of residence in Antarctica (Reed et al. 1986; Reed et al. 1988). Basal thyrotropin values do not change over the year (Reed et al. 1986; Reed et al. 1988; Reed et al. 1990b). Inhibition of thyrotropin release by $T_3$ administration is unchanged during residence in Antarctica (Reed et al. 1988).

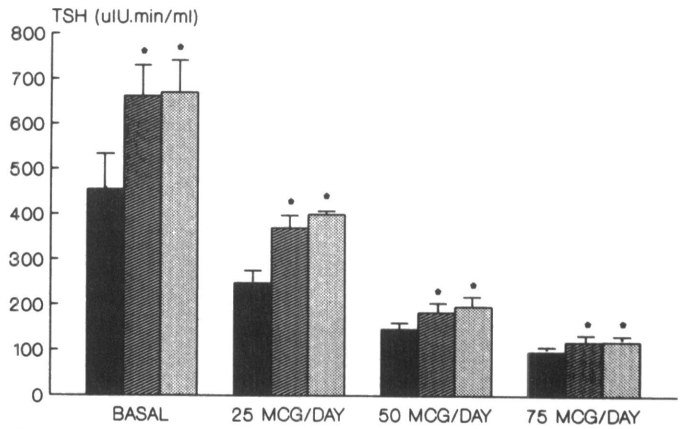


**Figure 1. Integrated thyrotropin (TSH) response to thyrotropin-releasing hormone (mean ± standard error) measured in nine subjects before and after 25, 50, and 75 milligrams per day of $T_3$. This response was measured in a warm control climate (■) and after 20 (■) and 42 weeks (▒) antarctic residence. There was no difference between results obtained after 20 and 42 weeks residence in Antarctica. *$P<0.05$ compared with warm control climate values. (MCG denotes micrograms. μIU.min/ml denotes micro international units times minutes per milliliter.) (Reproduced with permission from Reed et al. 1988.)**

- Serum static values. Serum values of $T_3$ and free $T_3$ had a variable fall with residence in Antarctica. Total and free $T_4$ remained unchanged. The maximum binding capacity to serum carrier proteins was reduced (Quesada et al. 1989). The percentage of the free $T_4$ and $T_3$ hormone at physiological concentrations was also decreased (Reed et al. in press).
- Serum kinetic values (figure 2). Extravascular $T_3$ distribution space increased by 178 percent, production rate by 137 percent, and metabolic clearance rate by 121 percent when measured using tracer iodine-125 $T_3$. Iodine-125 $T_4$ kinetic changes were minor (Reed et al. 1990b).
- Experimental cold adaptation. After 20 to 80 repeated cold-air exposures, humans increased serum $T_3$ production rate and metabolic clearance rate by approximately 20 percent. There was no change in the $T_3$ extravascular $T_3$ distribution space during this same period (Reed et al. 1990a). The cold-associated increase in $T_3$ production was independent of serum $T_4$ and thyrotropin. This dissociation was determined by administering supplemental $T_3$ to one group of cold-exposed individuals.
- Cellular $T_3$ binding capacity. There was a twofold increase in specific nuclear $T_3$ binding capacity of human mononuclear cells in men receiving 20 to 80 repeated cold-air exposures and supplemented with an oral daily dose of $T_3$. Without supplementing $T_3$ during cold exposure, no changes were observed in the number of available receptor sites.

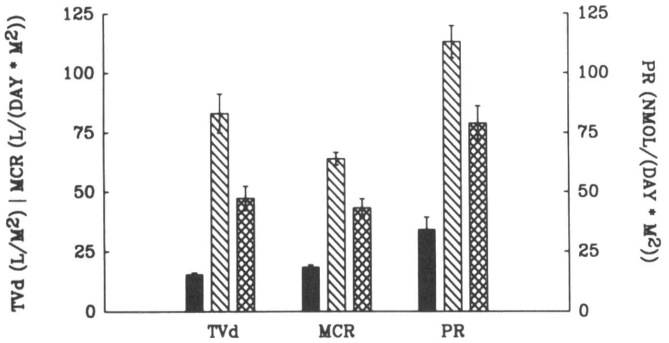


**Figure 2. Mean (± standard error) $T_3$ kinetic parameters of $T_3$ distribution space (TVd) (liter per square meter), metabolic clearance rate (MCR) (in liters per day per square meter), and production rate (PR) (in nanomoles per day per square meter) are shown for measurements made in the control period before leaving for Antarctica (■) and after 20 (▨) and 42 (▩) weeks of antarctic residence. $T_3$ distribution space, metabolic clearance rate, and production rate are increased after 42 weeks compared to control values. ($L/M^2$ denotes liters per square meter.) (Reproduced with permission from Reed et al. 1990b.)**

We describe a major increase in the extravascular binding and the production and clearance of $T_3$ with antarctic residence measured using tracer iodine-125 $T_3$ (Reed et al. 1990b). These men also displayed an unchanged pituitary sensitivity to $T_3$ (Reed et al. 1988), a variable decrease in serum total and free $T_3$ basally and after oral $T_3$ administration, and an increased pituitary response of pituitary thyrotropin release to a standard stimulus of thyrotropin releasing hormone (Reed et al. 1986; Reed et al. 1988; Reed et al. in press). Our data implicate $T_3$ more so than $T_4$ as playing a regulatory role in adaptation to polar life. These observations also suggest that the increased $T_3$ distribution space of $T_3$ with residence in Antarctica is not likely to be similar in all tissues. With an increased pituitary thyrotropin response, the local pituitary $T_3$ concentration would be expected to be low. Kinetic data, however, support that the average $T_3$ distribution space throughout the body is dramatically increased (Reed et al. 1990b), thus establishing a tissue discordance.

Common factors known to change thyroid hormone economy such as fasting, overfeeding, depression, photoperiodicity, and dietary iodine cannot completely explain our findings. In separate cold-adaptation experiments where cold is isolated as a single variable, human $T_3$ production is increased although not as dramatically as in Antarctica (Reed et al. 1990a).

Our findings are consistent with others who have described changes in static serum $T_3$ values in humans working in cold chambers (Solter et al. 1989), cold climates (Nagata et al. 1976), and Antarctica (Vining et al. 1983).

Most of the body's $T_3$ is normally distributed in muscle and skin. These tissues, unlike the central nervous system, are likely to exhibit an increase in $T_3$ content with residence in Antarctica. This discordance of hormone distribution is not uncommon in states of caloric deprivation but has not been described for environmentally associated conditions such as life in Antarctica. Further investigation of this constellation of findings should be carried out with paired human studies. Specific tissue responses, environmental interaction, and the physiological significance of thyroid hormone changes in other high-latitude areas need future exploration.

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