Medicine

Increased energy requirements for humans residing in Antarctica: A proposed model

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Studies currently in progress are designed to identify the mechanism of the presumed 40 percent increase in energy requirement, which occurs in humans living and working at McMurdo Station, Antarctica, for as little as 4 months. Additionally, these studies will attempt to determine the relationship between increased energy requirements and increased thyroid hormone requirements, which are described for this same time period in McMurdo, Antarctica. We have studied members of the 1996–1997 winter-over party before and then monthly during their period of antarctic residence. By using measurements of both the resting oxygen consumption and submaximal exercise capacity, we are able to determine differences in oxygen use and, therefore, energy requirements, which may change during antarctic residence. We have also contrasted these subjects with similar measures in patients suffering from clinical excess thyroid hormone conditions as previously reported by our group (Gibson et al. 1993). By making this clinical comparison, we hope to understand better the relationship between increased physiological energy requirements and increased thyroid hormone tissue content common to both situations.

We have recently reported preliminary observations confirming the presence and suggesting possible mechanisms for the increased energy requirements observed in humans during antarctic residence (Do et al. 1997). Resting oxygen use increases at a rate of nearly 2.5 percent per month during the first 4 months of antarctic residence or approximately 10 percent over the 4-month study. Additionally, we have reported that in this same period the resting metabolic rate derived from a submaximal exercise calculation also increases by about 2.1 percent per month or approximately 8.0 percent over the study. The amount of energy needed to perform a predetermined level of a low workload also increases during this period by approximately 3.8 percent per month or approximately 15 percent over the study (Do et al. 1997).

Patients who are known to have excess thyroid hormone concentrations in serum and tissue also show increases in energy requirements. Interestingly, these patients show similar, although greater, increases in resting oxygen use and declines in submaximal exercise performance compared to those subjects residing for 4 months in Antarctica (Gibson et al. 1993). The energy requirements in the patients decrease with improving thyroid status following therapy, and they seem to reflect circulating thyroid hormone concentrations in that condition. The fall in work carried out at a given level of oxygen use suggests a fall in whole body efficiency and increase in heat production associated with thyroid hormone excess (Martin et al. 1991). We support the hypothesis that the major mechanisms for this change occur in the skeletal muscles and not in the cardiovascular system and, thus, the large skeletal muscle mass provides a ready source of heat generation (Zurol et al. 1990; Martin et al. 1991; Olson et al. 1991). The heterogeneous tissue-specific nature of the thyroid hormone distribution has recently been proposed (Everts et al. 1996), and we feel it may apply directly to this syndrome. For example, with extended polar residence the brain seems to have a fall in thyroid hormone while peripheral tissues, such as skeletal muscle, seem to have an augmented amount of hormone. Symptoms and findings specific to each of these two conditions are being investigated by our group.

If thyroid excess is a physiological model, we propose that the 15 percent fall in work produced for each 400 milliliters per minute per square meter ($ml/min/m^2$) is a source for increased daily energy use and increased peripheral heat production. With the reported lower body temperature in McMurdo (Reed, Brice, et al. 1990), it is possible that some energy is conserved to maintain this lower body temperature. Then, with acute cold exposure, humans may initiate voluntary muscle contraction at low work levels and, thus, generate substantial heat to avoid further body cooling. Resting energy expenditure also appears to increase, but to a lesser degree, than exercise energy use. Perhaps resting thermogenesis is required to replace the loss of shivering thermogenesis, which occurs with hypothermic-cold adaptation found in McMurdo (Reed, Brice, et al. 1990; Do, LeMar, and Reed 1996).

Whatever the mechanism, these data support the observation of increased energy requirements for both indoor and outdoor workers in a sedentary polar camp. Additionally, the nature and direction of the increase, although reduced in magnitude, are similar to previously reported conditions of excess thyroid hormone. Future studies must address the metabolic and cognitive cost of this form of endocrine adaptation, with

specific regard to the apparent shunt or shift of thyroid hormones toward skeletal tissue and away from brain or central nervous system tissues.

This research is supported by National Science Foundation grant OPP 89-22832.

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Association between the Polar T_3 Syndrome and the Winter-Over Syndrome in Antarctica

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The austral winter in Antarctica has long been associated with reports of depression, irritability, aggressive behavior, insomnia, difficulty in concentration and memory, absentmindedness, and the occurrence of mild fugue states known as "long-eye" or the "antarctic stare" (Palmai 1963; Palinkas, Cravalho, and Browner 1995). During the 1989 winter season at McMurdo Station, for instance, 64.1 percent of the winter-over crew members interviewed reported some problem with sleep over the winter; 62.1 percent reported feeling depressed; 47.6 percent reported feeling more irritable than usual; and 51.5 percent reported difficulty with concentration or memory (Palinkas 1992). Collectively, these symptoms are referred to as the "Winter-Over Syndrome" (Strange and Youngman 1971).

Despite decades of research, the etiology of the Winter-Over Syndrome has not been clearly identified. In many instances, these symptoms can be attributed to characteristics of the social environment, including the absence of face-to-face social interaction and support associated with the prolonged isolation from family and friends (Palinkas 1992), the absence of social stimulation and opportunities to disengage from stressful social situations associated with the experience of confinement with the same small group of individuals, and increased work demands at certain times of the winter season (Palinkas et al. in press). On the other hand, the role of certain environmental factors including the lack of environmental stimulation and prolonged exposure to cold temperatures and constant darkness is suggested by the observation that winter-over personnel experience a significant increase in the prevalence of subsyndromal seasonal affective disorder (S-SAD) during the austral winter and that this increase appears to be associated with increasing latitude and, hence, exposure to prolonged darkness (Palinkas, Houseal, and Rosenthal 1996).

Alterations in thyroid hormone functions similar to those reported by Reed and colleagues during the austral winter in Antarctica (Reed et al. 1986) are also known to be associated with increased depressive symptomatology and disruption of cognitive performance (Gold, Pottash, and Extein 1981). Known as the Polar T_3 Syndrome, these alterations share many of the same characteristics of subclinical hypothyroidism (SCH), including elevated thyrotropin-stimulating hormone (TSH) levels and/or enhanced TSH response to thyrotropin-releasing hormone (TRH) stimulation. Subclinical hypothyroidism is found in 8 to 17 percent of depressed patients vs. 5 percent of the general population (Haggerty and Prange 1995).

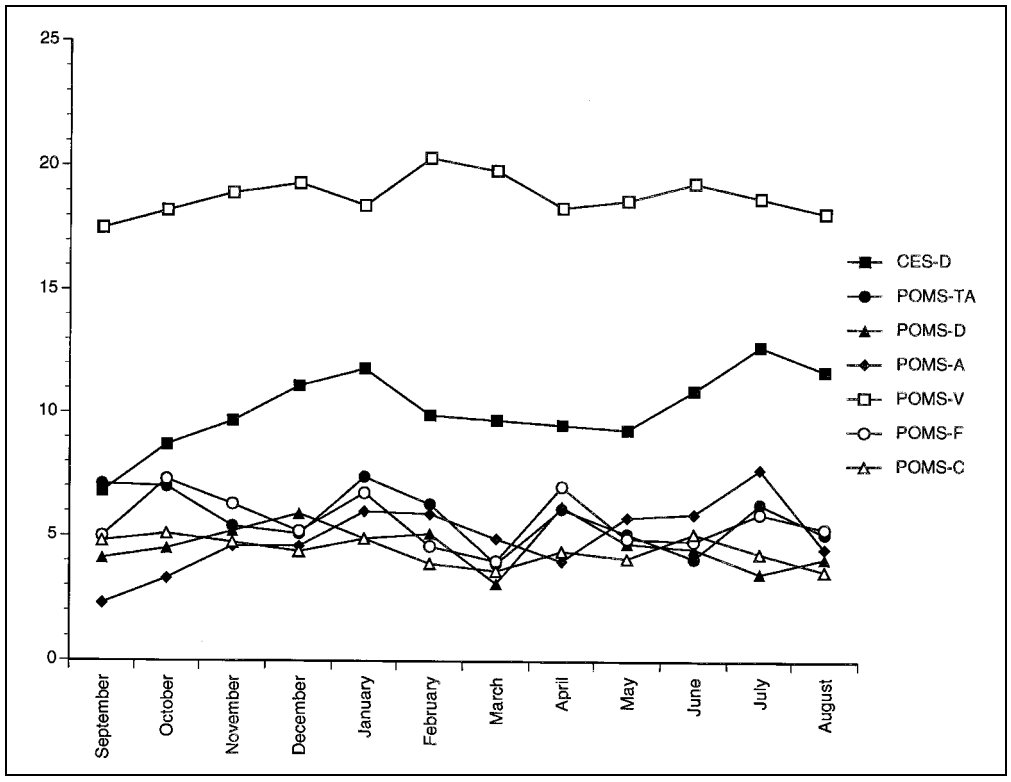
The Polar T_3 Syndrome is also associated with a significant reduction in serum total triiodothyronine (T_3) and free T_3, and a 12 percent reduction in thyroxin (T_4) (Reed et al. 1986). Individuals with low normal T_4 values experience more memory loss than those with high normal T_4 values (Zach and Ackerman 1988). Studies have also found improved memory

in patients with SCH following T_4 treatment (Nystrom et al. 1988). These results support the hypothesis that the cognitive and affective symptoms characteristic of the Winter-Over Syndrome are a state of relative central nervous system hypothyroidism accompanied by systemic euthyroidism (Jackson 1996). The T_3 receptor is widely distributed throughout the central nervous system, suggesting that thyroid hormones are necessary for normal brain function. Some evidence suggests that these hormones may have synaptic as well as nuclear actions (Haggerty and Prange 1995). A reduction in levels of T_3 and T_4 in the brain resulting from the increased energy requirements of the Polar T_3 Syndrome could conceivably affect adrenergic neurotransmission. On the other hand, T_3 in the brain is normally derived by conversion locally from T_4 due to the effect of brain Type II 5'-deiodinase. Any mechanism that inhibits this enzyme, such as an increase in cortisol due to stress, could result in functional brain hypothyroidism (Jackson 1996). A TSH-driven increase of circulating thyroid hormones typically occurs in euthyroid individuals in the face of depression and other stress states; an increase in thyroid hormone favors recovery from depression (Haggerty and Prange 1995).

Longitudinal assessments of thyroid function, cognitive performance, and depressive symptoms are essential to identifying the causal nature of the relationship between the Polar T_3 Syndrome and the Winter-Over Syndrome if, in fact, such an association exists. Over the past year, 16 members of the winter-over crew at McMurdo Station participated in a randomized clinical trial to determine if changes in thyroid function characteristic of the Polar T_3 Syndrome were associated with changes in mood and memory characteristic of the Winter-Over Syndrome. This association was assessed in two ways:

- by comparing changes in serum thyroid hormone levels, plasma lipids, and metabolic regulation with changes in depressive symptoms and mood states and
- by comparing differences in changes of mood and memory measures between two groups, one taking an oral thyroxine supplement and one taking a placebo.

A preliminary analysis of the data collected during the past year and presented in the figure suggests an increase in Center for Epidemiologic Studies-Depression (CES-D) scores in the 1996–1997 study cohort from baseline (September) to mid-January, followed by a gradual decline through May and a second increase in midwinter (June and July). This second increase was not observed in the Profile of Mood States (POMS) depression (D) scores. Mean POMS scores of tension-anxiety (TA) and fatigue (F) declined during the austral summer and most of the winter, followed by an increase during the last two months of winter. Mean POMS anger (A) scores increased during the austral summer, decreased during the first few months of winter, and increased again at the end of winter. Mean POMS confusion (C) and vigor (V) scores remained relatively stable throughout the study period. Analyses are underway to determine if these patterns correspond to changes in thyroid function and metabolic regulation and if they are affected by thyroxine supplementation.



Changes in Centers for Epidemiological Studies-Depression and Profile of Mood scores by month, Polar T_3 Study Cohort, 1997.

This work was supported by National Science Foundation grant OPP 94-18466. The author wishes to acknowledge the contributions of Kathleen Reedy, Sam Case, Mark Staudacher, and Nancy Finney to this study.

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Measuring metabolic change in humans residing in Antarctica: A thyroxine supplement placebo control trial

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McMurdo Station, Antarctica, has a year-round population of science support staff from which 17 people have volunteered to participate in this year's (October 1997 to August 1998) study of the metabolic changes that occur in humans in response to the polar environment. This study is designed to identify the mechanism of these changes and follows the report of 16 subjects who participated in a study the previous year (October 1996 to August 1997) at McMurdo (Do et al. 1997).

The 17 subjects are randomized into two groups, closely matched in age, weight, height, body surface area, body mass index, body temperature, resting heart rate, maximum capacity of oxygen use, with gender balance. This subject pool is representative of typical antarctic residents: indoor and outdoor workers, day and night workers, and a wide age range. This study is a double blind, in which one group will receive placebo, the other a daily 50-microgram thyroxine supplement. In contrast, last year's study group was randomized to two well-matched groups, both of which received placebo for the first 4 months, single blind, and for the remaining 7 months of antarctic residence, double blind; one group continued to receive placebo, and the other group received a daily supplement of 50 micrograms of thyroxine. We were able to observe the early stages (Do, Lemar, and Reed 1996) of cold-adaptation mechanisms in all subjects, then see differences in the two groups after intervention.

Among other things, thyroid hormones, which include triiodothyronine (T_3) and thyroxine (T_4), regulate energy expenditure. Production and tissue uptake of T_3 are dramatically increased during antarctic residence (Reed et al. 1990). These increases are not consistent for all tissues and appear to be greatly increased in skeletal muscle, while in tissues such as brain and central nervous system sites the level may decrease (Reed et al. 1988; Harford et al. 1993). We interpret this change in relative thyroid content as a shift in distribution function, which results in a phenomenon we call the "Polar T_3 Syndrome" (Harford et al. 1993).

For this year's project, each subject will complete a monthly measure of body temperature with an aural thermometer, resting metabolic rate (RMR), and energy requirement for a fixed submaximal work task on a cycle ergometer measured by oxygen uptake with a metabolic cart (Gibson et al. 1993; Do et al. 1997). Short-term memory is measured with a "matching to sample" exercise on a computer screen.

A small tissue sample from the anterior thigh will be examined to determine fiber typing and the level of T_3 in the skeletal muscle. Samples at the beginning and end of the year of antarctic residence will be compared to determine changes in muscle T_3 level during extreme cold adaptation and between the placebo and thyroxine supplemented treatment groups.

Employing these 17 volunteer subjects, we will execute thyroid hormone kinetics studies at the beginning, midway, and the end of their winter-over year. TSH, bound and free T_3 and T_4 levels, T_3 production and distribution (Reed et al. 1990) will be measured and the progress tracked by introducing a bolus of T_3 into the venous system of each subject and withdrawing small (3-milliliter) samples of blood several times the first hour, twice an hour for 4 hours, then hourly to 12 hours and each 12 hours to 72 hours. These kinetic studies will help

define the stage of adaptation (Do et al. 1996), the mechanism of change affected by length of antarctic residence, and the effect of thyroxine supplementation.

This is acknowledgment of the collaborating scientists participating in the execution of these protocols: Nhan Van Do, Lawrence Palinkas, John Thomas, Nancy Finney, Rick Seip, Samuel Case, and Liz Mino.

This research is supported by National Science Foundation grant OPP 89-22832.

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