

UNCLASSIFIED

NMRI-02

Technical Report
distributed by



NAV1.954605.002

DEFENSE
TECHNICAL
INFORMATION
CENTER

DTIC / *Acquiring Information—
Imparting Knowledge*

Cameron Station
Alexandria, Virginia 22304-6145

UNCLASSIFIED

REPORT DOCUMENTATION PAGE

2025 FILE COPY

2

1a. REPORT SECURITY CLASSIFICATION	1b. RESTRICTIVE MARKINGS
------------------------------------	--------------------------

AD-A230 347

TITLE

AUTHOR(S)

NMRI 90-113

3. DISTRIBUTION/AVAILABILITY OF REPORT

Approved for public release; distribution is unlimited

5. MONITORING ORGANIZATION REPORT NUMBER(S)

6a. NAME OF PERFORMING ORGANIZATION Naval Medical Research	6b. OFFICE SYMBOL (if applicable)	7a. NAME OF MONITORING ORGANIZATION Naval Medical Command
---	--------------------------------------	--

6c. ADDRESS (City, State, and ZIP Code) Bethesda, Maryland 20814-5055	7b. ADDRESS (City, State, and ZIP Code) Department of the Navy Washington, D.C. 20372-5120
--	--

8a. NAME OF FUNDING/SPONSORING ORGANIZATION Naval Medical Research and Development Command	8b. OFFICE SYMBOL (if applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER
---	--------------------------------------	---

8c. ADDRESS (City, State, and ZIP Code) Bethesda, Maryland 20814-5055	10. SOURCE OF FUNDING NUMBERS								
	<table border="1"> <tr> <th>PROGRAM ELEMENT NO.</th> <th>PROJECT NO.</th> <th>TASK NO.</th> <th>WORK UNIT ACCESSION NO.</th> </tr> <tr> <td>62233</td> <td>MM33C30.04</td> <td>1002</td> <td>DN247509</td> </tr> </table>	PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT ACCESSION NO.	62233	MM33C30.04	1002	DN247509
PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT ACCESSION NO.						
62233	MM33C30.04	1002	DN247509						

11. TITLE (Include Security Classification)
Decreased free fraction of thyroid hormones after prolonged Antarctic residence

12. PERSONAL AUTHOR(S) Reed HL, Brice D, ShaKir KM, Burman KD, D'Alesandro MM, O'Brian JT

13a. TYPE OF REPORT journal article	13b. TIME COVERED FROM TO	14. DATE OF REPORT (Year, Month, Day) 1990	15. PAGE COUNT 6
--	------------------------------	---	---------------------

16. SUPPLEMENTARY NOTATION
Reprinted from: Journal of Applied Physiology 1990 Vol.69 No.4 pp. 1467-1472

17. COSATI CODES	18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)						
<table border="1"> <tr> <th>FIELD</th> <th>GROUP</th> <th>SUB-GROUP</th> </tr> <tr> <td></td> <td></td> <td></td> </tr> </table>	FIELD	GROUP	SUB-GROUP				cold adaptation, blood pressure, temperature, thyroxine, triiodothyronine
FIELD	GROUP	SUB-GROUP					

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

DTIC
SELECTED
S D D
JAN 03 1991

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT <input checked="" type="checkbox"/> UNCLASSIFIED/UNLIMITED <input type="checkbox"/> SAME AS RPT. <input type="checkbox"/> DTIC USERS	21. ABSTRACT SECURITY CLASSIFICATION Unclassified
---	--

22a. NAME OF RESPONSIBLE INDIVIDUAL Phyllis Blum, Information Services Division	22b. TELEPHONE (Include Area Code) 202-295-2188	22c. OFFICE SYMBOL ISD/ADMIN/NMRI
--	--	--------------------------------------

September 1984, with each subject serving as his own control. The protocol was approved by our Institutional Review Board, and all participants provided signed informed consent. The men were similar with respect to age [24.5 ± 0.9 (SE) yr] and body weight (81.3 ± 2.7 kg).

Acute Cold Air Exposure

Three standardized 60-min SCATs ($0 \pm 2^\circ\text{C}$) were performed with each subject seated in an environmental chamber (wind speed ~ 4.5 m/s) (2, 11, 21). One SCAT was carried out in California (control) initially and then repeated after 24 and 44 wk AR. SCATs were performed between 0800 and 1100 h local time in an identical fashion for each testing period. Subjects, wearing a cotton T-shirt, shorts, socks, and shoes, had a Teflon catheter inserted into the brachial vein for free-flowing blood sampling. Pre-SCAT blood samples were obtained in the postabsorptive state 20 min after catheter placement while the subject was seated in a warmed laboratory (22°C) before entering the climatic chamber. Post-SCAT blood samples were obtained from the same catheter after 60 min of cold air exposure. Subjects were quiet during the cold air exposure and were not allowed to smoke, eat, or move excessively. The sublingual oral temperature (T_{sl}) was recorded with a digital display analog input circuit thermocouple (IVAC, San Diego, CA) after local oral thermal equilibrium. All subjects were asked to breathe through the nares with mouth closed while the T_{sl} was recorded. Changes in respiratory rate were not clearly evident. The subjects were not allowed to eat or drink for 20 min before temperature measurements, thus minimizing variables that might affect T_{sl} . Auscultatory blood pressure and pulse from the brachial artery were measured by the same investigator pre-SCAT and after 15, 30, 45, and 60 min of each cold air exposure. Mean arterial pressure (MAP) was calculated as [diastolic pressure + (pulse pressure/3)]. Serum from blood coagulated at room temperature was frozen at -30°C , and all samples were transported to Bethesda, MD, for processing and then analyzed together at the completion of the 1-yr study.

Extended Antarctic Residence

The men were studied in August 1983 while in Port Hueneme, CA (latitude $34^\circ 07'$ N, longitude $119^\circ 07'$ W), before departing for Antarctica, in April 1984 after 24 wk, and in September after 44 wk in McMurdo Sound, Antarctica ($77^\circ 51'$ S, $166^\circ 37'$ E). The 24- and 44-wk time points are similar to previous reports (24, 25). The mean monthly ambient temperatures for California in August (22.7°C) and McMurdo Sound, Antarctica, in April (-23.6°C) and September (-29.2°C) were similar to those of past reports (24, 25, 27). An internationally utilized US Navy diet as previously described (24, 25) was consumed, with calories distributed as $\sim 40\%$ carbohydrate, 35% protein, and 25% fat. Energy intake increases with AR at this base from $\sim 2,000$ – $2,500$ to $3,000$ – $3,500$ kcal/day (24, 25, 27). Each subject wore standard military polar clothing while in McMurdo Sound; the face and hands are commonly exposed during outdoor activity. Subjects were exposed to outdoor temperatures

for an average of 4.3 ± 0.7 h/day. Indoor fluorescent lighting was used during the austral winter months. Indoor temperatures ranged from 19 to 27°C . All subjects maintained routine sleep cycles of 8 h/day. Blood samples and physiological measurements were taken just before each SCAT as described.

Blood Analysis

Serum TT_4 and TT_3 were measured by RIA (Nichols Institute, San Juan Capistrano, CA). The percent free fraction of T_4 and T_3 ($\%FT_4$ and $\%FT_3$) were measured by equilibrium dialysis (Nichols Institute) by use of a modified method of Sterling and Brenner (32). After dialysis, contaminating free iodine was removed by antibody precipitation. The percent dialyzable fraction of total hormone is referred to as the percent free fraction (normal $\%FT_4 \sim 0.03\%$ and $\%FT_3 \sim 0.3\%$) (19). The free hormone concentrations were calculated as the product of the total hormone concentration and the percent free fraction of the hormone. We tested the effect of freezer storage on this assay of thyroid hormone binding. The sera of 10 subjects different from those in the present study were analyzed for $\%FT_3$ before and after 21 mo of storage at -30°C . We did not find an increase in the $\%FT_3$ with this duration of storage. Serum TSH was measured by a sensitive and specific enzyme-linked immunosorbent assay technique (34). Serum cortisol and prolactin responses in the SCAT were measured as standard markers of cold exposure (11, 13). Serum cortisol levels were measured using a commercially available RIA kit (Clinical Assays, Cambridge, MA). SI unit conversion for cortisol is $\text{nmol} = 2.759 \times \mu\text{g}$. Serum prolactin was measured by a commercially available RIA kit (Organon Teknika, Irving, TX) with an assay detection limit of $4 \mu\text{g/l}$. We analyzed TT_4 , TT_3 , $\%FT_4$, and $\%FT_3$ with a well-known model of thyroid hormone binding to predict whether the observed changes were primarily due to increases in receptor number or affinity (28). The serum total protein of six subjects was measured pre-SCAT by spectrophotometry to test for hemoconcentration (bicinchoninic acid protein assay, Pierce, Rockford, IL).

Data Analysis

Statistical analysis was performed by using a randomized block design ($n = 15$) with one- and two-way (date and time = treatments) analysis of variance (ANOVA), general linear model (GLM), and Dunnett's test for differences between the one-way ANOVA means (SAS, SAS Institute, Cary, NC, and STAT PAK version 4.1, Northwest Analytical, Portland, OR). The data are expressed as means \pm SE. Significance was determined as $P < 0.05$.

RESULTS

Acute Cold Air Exposure (SCAT)

Thyroid hormones. The SCAT did not induce any differences in serum TT_4 , FT_4 , TT_3 , FT_3 , and TSH (Table 1) or in serum $\%FT_4$ or $\%FT_3$ (Tables 2 and 3). Serum TT_3 increased, although not significantly, during the control SCAT and did not change with the SCATs in Antarctica (Table 1).

The opinions and assertions expressed herein are those of the authors and are not to be construed as official or reflecting the views of the Department of the Navy, Department of the Army, Department of Defense, or the National Science Foundation.

This work was presented at the 1987 meeting of the Federation of American Societies for Experimental Biology, Washington, DC.

Address for reprint requests: H. L. Reed, Mail Stop 11, Dept. of Environmental Medicine, Naval Medical Research Institute, Bethesda, MD 20814-5055.

Received 14 February 1990; accepted in final form 14 June 1990.

REFERENCES

- ADAMS, R. D. AND G. R. DELONG. The neuromuscular system and brain. In: *Werner's The Thyroid: A Fundamental and Clinical Text* (5th ed.). Philadelphia, PA: Lippincott, 1986, p. 885-894.
- BITTEL, J. H. M. Heat debt as an index for cold adaptation in men. *J. Appl. Physiol.* 62: 1627-1634, 1987.
- BITTEL, J. H. M., G. H. LIVECCHI-GONNOT, A. M. HANNIQUET, C. POULAIN, AND J.-L. ETIENNE. Thermal changes observed before and after J.-L. Etienne's journey to the North Pole: is central nervous system temperature preserved in hypothermia? *Eur. J. Appl. Physiol. Occup. Physiol.* 58: 646-651, 1989.
- BRUCK, K., E. BAUM, AND H. P. SCHWENNICKE. Cold-adaptive modifications in man induced by repeated short-term cold-exposures and during a 10-day and -night cold exposure. *Pfluegers Arch.* 363: 125-133, 1976.
- BUDD, G. M., AND N. WARHAFT. Body temperature, shivering, blood pressure and heart rate during a standard cold stress in Australia and Antarctica. *J. Physiol. Lond.* 186: 216-232, 1966.
- BURGER, A. G., M. O'CONNELL, K. SCHEIDEGGER, R. WOO, AND E. DANFORTH, JR. Monodeiodination of triiodothyronine and reverse triiodothyronine during low and high calorie diets. *J. Clin. Endocrinol. Metab.* 65: 829-835, 1987.
- CHOPRA, I. J., A. J. VAN HERLE, G. N. CHUA TECO, AND A. H. NGUYEN. Serum free thyroxine in thyroidal and nonthyroidal illnesses: a comparison of measurements by radioimmunoassay, equilibrium dialysis, and free thyroxine index. *J. Clin. Endocrinol. Metab.* 51: 135-143, 1980.
- FREGLY, M. J. Activity of the hypothalamic-pituitary-thyroid axis during exposure to cold. *Pharmacol. Ther.* 41: 85-142, 1989.
- GUENTER, C. A., A. T. JOERN, J. T. SHURLEY, AND C. M. PIERCE. Cardiorespiratory and metabolic effects in men on the South Polar Plateau. *Arch. Intern. Med.* 125: 630-637, 1970.
- INGBAR, S. H., C. R. KLEEMAN, M. QUINN, AND D. E. BASS. The effect of prolonged exposure to cold on thyroidal function in man (Abstract). *Clin. Res. Proc.* 2: 86, 1954.
- JESSEN, I. The cortisol fluctuations in plasma in relation to human regulatory nonshivering thermogenesis. *Acta Anaesthesiol. Scand.* 24: 151-154, 1980.
- KEATINGE, W. R., S. R. K. COLESHAW, AND J. HOLMES. Changes in seasonal mortalities with improvement in home heating in England and Wales from 1964 to 1984. *Int. J. Biometeorol.* 33: 71-76, 1989.
- LEPPALUOTO, J., I. KORHONEN, P. HUTTUNEN, AND J. HASSI. Serum levels of thyroid and adrenal hormones, testosterone, TSH, LH, GH and prolactin in men after a 2-h stay in a cold room. *Acta Physiol. Scand.* 132: 543-548, 1988.
- LIVINGSTONE, S. D., J. GRAYSON, J. FRIM, C. L. ALLEN, AND R. E. LIMMER. Effect of cold exposure on various sites of core temperature measurements. *J. Appl. Physiol.* 54: 1025-1031, 1983.
- MAEDA, K., Y. KATO, S. OHGO, K. CHIHARA, Y. YASHIMOTO, N. YAMAGUCHI, S. KUROMARU, AND H. IMURA. Growth hormone and prolactin release after injection of thyrotropin-releasing hormone in patients with depression. *J. Clin. Endocrinol. Metab.* 40: 501-505, 1975.
- MULS, E., M. ROSSENEU, J. BURY, M. STUL, G. LAMBERIGTS, AND P. DE MOOR. Hypertension influences the distribution and apolipoprotein A composition of the high density lipoproteins in man. *J. Clin. Endocrinol. Metab.* 61: 882-889, 1985.
- MUZA, S. R., A. J. YOUNG, M. N. SAWKA, J. E. BOGART, AND K. B. PANDOLF. Respiratory and cardiovascular responses to cold stress following repeated cold water immersion. *Undersea Biomed. Res.* 15: 165-173, 1988.
- NAGATA, H., T. IZUMIYAMA, K. KAMATA, S. KONO, Y. YUKIMURA, M. TAWATA, T. AIZAWA, AND T. YAMADA. An increase of plasma triiodothyronine concentration in man in a cold environment. *J. Clin. Endocrinol. Metab.* 43: 1153-1156, 1976.
- NICOLOFF, J. T. Physiologic and pathophysiologic implications of hormone binding. In: *Werner's The Thyroid. A Fundamental and Clinical Text* (5th ed.). Philadelphia, PA: Lippincott, 1986, p. 128-135.
- O'BRIAN, J. T., D. E. BYBEE, K. D. BURMAN, R. C. OSBURN, M. R. KSIAZEK, L. WARTOFSKY, AND L. P. GEORGES. Thyroid hormone homeostasis in states of relative caloric deprivation. *Metabolism* 29: 721-727, 1980.
- O'MALLEY, B. P., N. COOK, A. RICHARDSON, D. B. BARNETT, AND F. D. ROSENTHAL. Circulating catecholamine, thyrotrophin, thyroid hormone and prolactin responses of normal subjects to acute cold exposure. *Clin. Endocrinol. Oxf.* 21: 285-291, 1984.
- QUESADA, M., H. L. REED, AND D. SMITH. Selective alterations in triiodothyronine (T₃) binding to serum proteins during prolonged Antarctic residence (Abstract). *FASEB J.* 3: A395, 1989.
- RADOMSKI, M. W., AND C. BOUTELIER. Hormone response of normal and intermittent cold-preadapted humans to continuous cold. *J. Appl. Physiol.* 53: 610-616, 1982.
- REED, H. L., K. D. BURMAN, K. M. M. SHAKIR, AND J. T. O'BRIAN. Alterations in the hypothalamic-pituitary-thyroid axis after prolonged residence in Antarctica. *Clin. Endocrinol. Oxf.* 25: 55-65, 1986.
- REED, H. L., J. A. FERREIRO, K. M. M. SHAKIR, K. D. BURMAN, AND J. T. O'BRIAN. Pituitary and peripheral hormone responses to T₃ administration during Antarctic residence. *Am. J. Physiol.* 254 (Endocrinol. Metab. 17): E733-E739, 1988.
- REED, H. L., S. PEPPER, D. ARMSTRONG, F. J. VON TERSCH, AND T. B. LEWIS. Oxygen saturation of brachial venous blood correlates with fingertip temperatures between 11 and 39°C. *Aviat. Space Environ. Med.* 60: 1068-1071, 1989.
- REED, H. L., E. D. SILVERMAN, K. M. M. SHAKIR, R. DONS, K. D. BURMAN, AND J. T. O'BRIAN. Changes in serum triiodothyronine kinetics after prolonged Antarctic residence: the polar T₃ syndrome. *J. Clin. Endocrinol. Metab.* 70: 965-974, 1990.
- ROBBINS, J., AND M. L. JOHNSON. Theoretical considerations in the transport of the thyroid hormones in blood. In: *Free Thyroid Hormones*. Princeton, NJ: Excerpta Med., 1979, p. 1-13.
- SACK, D. A., J. NURNBERGER, N. E. ROSENTHAL, E. ASHBURN, AND T. A. WEHR. Potentiation of antidepressant medications by phase advance of the sleep-wake cycle. *Am. J. Psychiat.* 142: 606-608, 1985.
- SKELTON, C. L., AND E. H. SONNENBLICK. The cardiovascular system. In: *Werner's The Thyroid: A Fundamental and Clinical Text* (5th ed.). Philadelphia, PA: Lippincott, 1986, p. 853-864.
- SOLTER, M., K. BRKIC, M. PETEK, L. POSAVEC, AND M. SEKSO. Thyroid hormone economy in response to extreme cold exposure in healthy factory workers. *J. Clin. Endocrinol. Metab.* 68: 168-172, 1989.
- STERLING, K., AND M. A. BRENNER. Free thyroxine in human serum: simplified measurement with the aid of magnesium precipitation. *J. Clin. Invest.* 45: 153-163, 1966.
- TANAKA, S., A. KONNO, A. HASHIMOTO, A. HAYASE, Y. TAKAGI, S. KONDO, Y. NAKAMURA, AND O. IMURA. The influence of cold temperatures on the progression of hypertension: an epidemiological study. *J. Hypertens.* 7, Suppl. 1: S49-S51, 1989.
- TSENG, Y., K. D. BURMAN, J. R. BAKER, JR., AND L. WARTOFSKY. A rapid, sensitive enzyme-linked immunoassay for human thyrotropin. *Clin. Chem.* 31: 1131-1134, 1985.
- TUOMISTO, J., P. MANNISTO, B.-A. LAMBERG, AND M. LINNOILA. Effect of cold-exposure on serum thyrotrophin levels in man. *Acta Endocrinol.* 83: 522-527, 1976.
- VUORI, I. The heart and the cold. *Ann. Clin. Res.* 19: 156-162, 1987.
- WARTOFSKY, L., AND K. D. BURMAN. Alterations in thyroid function in patients with systemic illness: the "euthyroid sick syndrome." *Endocr. Rev.* 3: 164-217, 1982.
- WELLE, S., M. O'CONNELL, E. DANFORTH, JR., AND R. CAMPBELL. Decreased free fraction of serum thyroid hormones during carbohydrate overfeeding. *Metabolism* 33: 837-839, 1984.