Effect of High Environmental Temperature on Basal Metabolism and Concentrations of Serum Protein-Bound Iodine and Total Cholesterol

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DIFFICULTIES inherent in long term investigations of lipid metabolism of human subjects have sharply limited their number. Moreover, emphasis has been placed on association of abnormalities of lipid metabolism with atherosclerosis rather than on basic mechanisms involved in normal lipid metabolism. Since it has been impossible to obtain data antemortem on the changes which take place in the arterial walls of a given subject, diagnostic predictions, as Kritchevsky pointed out,[1] have been based on trust in the validity of comparisons between single observations and group data on serum lipids and cholesterol in patients with known medical histories. Too little is known concerning the effect of physiologic and environmental factors on individual serum cholesterol values. The extent to which the value for any given patient may be expected to vary with age, sex, body build, stress, diet and environmental temperatures may be extremely important.

A number of recent studies support the concept that the increase in basal metabolism, which is known to result when environmental temperature is lowered, is mediated by increased thyroid secretion.[2–8] Mefferd et al.[9] report that in the rat the incorporation of acetate-1C^{14} into cholesterol increases with cold and decreases with heat (2° to 35°C.). However, the data of Vahouny et al.[10] demonstrate that lowering the environmental temperature of rats results in an increase in only the esterified cholesterol of serum and liver, with an accompanying lipotropic effect on liver triglyceride.

The relatively wide fluctuations in temperature which occur in Tucson, Arizona, offer particularly advantageous conditions for an extended investigation on the effect of climatic changes on thyroid activity (measured by protein-bound iodine and basal metabolism) and associated serum cholesterol changes in healthy, normally active men and women. The present paper reports the data in subjects exposed in their daily work and recreation to minimal temperatures averaging 38°F. (3.3° C.) in January and maximal temperatures of 102°F. (38.9°C.) in July, both with monthly mean diurnal changes up to 32°F. (17.8°C.), and the low humidity characteristic of an altitude of 2,400 feet on the arid Sonoran Desert.

PROCEDURE

A total of eighteen subjects was studied for an experimental period of one year. Seven were student nurses (group I) with an average age of 19.6 years (18.8 to 23.4 years) and eleven were postmen (group II) with an average of 39.7 years (26.1 to 48.8

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years). The subjects in group I lived in the nurses' home, worked in well ventilated but non airconditioned hospital wards and spent weekends participating in such activities as swimming, tennis and hiking. The subjects in group II lived in individual homes, walked daily routes and usually rested indoors on free days.

The eligibility of the subjects as participants in the study was determined from their medical and nutritional histories. Recognition of the presence of any disease or abnormality, or use of drugs, which might affect metabolism was a cause for rejection. Medical examinations, made at the beginning and end of the study, included routine blood and urine tests, and electrocardiograms obtained with the patients at rest and after exercise. Other determining conditions for acceptance were nature of family responsibility, pattern of living and accessibility of home to laboratory.

The indirect closed circuit Benedict-Roth apparatus was used to determine basal metabolism. Average oxygen consumption in cubic centimeters per minute was obtained on the basis of the results of at least two eight to ten minute tests agreeing within 5 per cent completed on different mornings. Each test was made in duplicate. Observations were made from June through August, and from December through February. Pulse rates were obtained after the rest period preceding the first basal metabolism test; blood pressures with the subjects seated (group II) were obtained immediately after the last test. In group II, the hemoglobin and hematocrit were measured monthly.

Protein-bound iodine was determined monthly on duplicate 1 ml. samples of nonfasting venous serum* using the dry ash method of Barker et al.[11]

Fasting serum specimens were obtained weekly from the finger-tip and were analyzed for total cholesterol concentration by Adamson's[14] micromodification of the method of Pearson, Stern and McGavack.[15]

Thirty-day dietaries (group I), freely selected in the hospital cafeteria, were weighed daily during April and May. Three one-week dietaries (group II) recorded during August–September, April–May and January–February, were compared for seasonal effect. These were obtained by means of (1) personal interviews by the same interviewer throughout, (2) daily records in terms of household measures and (3) cross check inquiries using a form similar to that of Burke.[16] Dietaries of both groups were then evaluated by the method of Thompson and Tucker[17] for thirteen nutrients including total lipid, cholesterol and fatty acids (total, saturated, monounsaturated and polyunsaturated). Fatty acid ratios were recorded for polyunsaturated to saturated

TABLE I
Physical Measurements of Subjects, Mean Values

Measurement	Group I	Group II
Age (yr.)	19.6 (18.8–23.4)	39.7 (26.1–48.8)
Height (cm.)	162 (150–172)	173 (161–181)
Weight (kg.)		
Summer	52.6 (48.5–61.3)	70.7 (54.2–91.0)
Winter	53.5 (49.7–64.1)	70.9 (55.3–90.3)
Weight change (± kg.)	1.6 (0.5–3.6)	4.1 (1.4–5.9)
Surface area (M^2.)		
Summer	1.55 (1.40–1.72)	1.84 (1.60–2.05)
Winter	1.56 (1.45–1.76)	1.84 (1.62–2.03)
Pulse (beats/min.)		
Summer	62 (44–76)	63 (43–74)
Winter	60 (45–72)	62 (42–75)
Body temperature (°F.)		
Summer	97.7 (97.0–98.3)	97.2 (96.5–97.7)
Winter	97.9 (97.5–98.4)	97.1 (96.5–97.6)
Basal metabolism (cal./M^2./hr.)		
Summer	29.3 (26.5–33.8)	35.9 (32.4–37.8)
Winter	31.9 (26.9–34.5)	37.2 (32.4–40.0)
% deviation (Mayo Foundation standards[18])		
Summer	−20.5 (−13.1–−27.8)	−5.9 (−14.7–+0.2)
Winter	−13.2 (−6.2–−27.2)	−2.3 (−8.0–+7.1)

NOTE: Figures in parentheses represent the range. Summer, mean maximal monthly temperatures, June through August, 101° to 98°F.; winter, December through February, 70° to 59°F.

* Schatz and Volpé[12] reported a lack of diurnal variation in the level of serum protein-bound iodine on samples drawn from a group of euthyroid subjects during four intervals throughout a twenty-four hour period. In the present study, for protein-bound iodine determinations over a yearly period on nineteen aliquots of the same specimen of pooled serum, iodide values (averages of duplicates) were between 4.4 and 5.9 μg.per 100 ml. (mean ± 4.98, S.D. ± 0.31, S.E. ± 0.07 μg. per 100 ml.) For determinations on 124 serum specimens of the subjects, the sample mean difference between duplicates was 0.21 μg. per 100 ml.; the sample S.D. of the differences 0.34 μg. per 100 ml., and the S.E. of the mean difference 0.05 μg. per 100 ml. These values indicate a probable analytical error of approximately ±0.3 to ±0.4 μg. per 100 ml. This is in agreement with variability due to technical sources as reported by others using similar or somewhat different technics as discussed by Gaffney et al.[13]

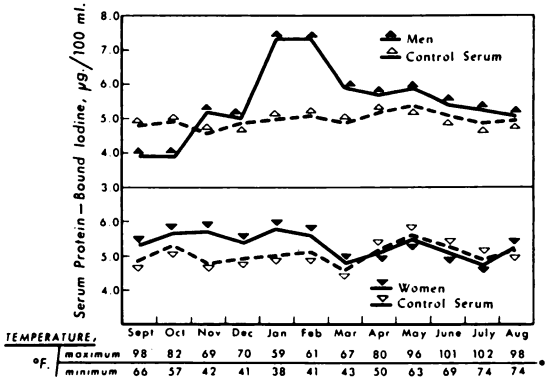

FIG. 1. Monthly concentrations of serum protein-bound iodine in women and men.

(P:S) and for polyunsaturated plus monounsaturated (P + M:S).

Correlations were obtained for (1) environmental temperature and protein-bound iodine, (2) environmental temperature and total cholesterol, and (3) protein-bound iodine and total cholesterol.

OBSERVATIONS ON SEASONAL CHANGES

Physical measurements of the subjects are shown in Table I.

Dietary

In group II the caloric intake averaged 13 per cent more in winter than summer but was compensated by greater outdoor activity. Total lipid calories averaged 38 per cent in summer, 43 per cent in spring and 39 per cent in winter; protein calories were approximately constant. Cholesterol ranged from a daily mean of 530 mg. in summer to 692 mg. in spring. P:S ratio was constant at 0.29, and the P + M:S ratio was 1.18 in summer and 1.37 in spring. The only major change was liberal consumption of cold drinks in summer resulting in a daily increase in ascorbic acid from 60 to 102 mg.

Blood Pressure, Hemoglobin and Hematocrit

In ten subjects (group II) in whom seasonal blood pressures were obtained, systolic pressures in summer ranged between 110 and 120 mm. Hg in four, below this level in four and above this level in two; in winter, the systolic pressures ranged between 110 and 120 mm. Hg in only one subject, below this level in three and above this in six. Diastolic pressures in summer ranged between 65 and 80 mm. Hg in nine subjects and above this level in one; in winter, diastolic pressures ranged between 65 and 80 mm. Hg in three subjects, below this level in two and above this level in five.

Hemoglobin averaged 13.8 gm. per cent (13.1 to 14.5 gm. per cent) from June through August, and 14.3 gm. per cent (12.9 to 15.0 gm. per cent) in January and February, nine of the ten subjects having shown gradual decreases between 0.4 and 1.3 gm. per cent in summer. Hematocrit readings showed similar diminishing values in summer.

Basal Metabolism, Protein-Bound Iodine

In most cases basal metabolism (Table I) was lowest in summer being 8.2 per cent below that in winter in group I and 3.5 per cent below in group II. Deviation from Mayo Foundation Standards in summer was 7.3 per cent below that in winter in group I and 3.6 per cent below in group II.

There was no seasonal change in protein-bound iodine in group I, the mean being 5.2 μg. per 100 ml. in summer and 5.7 μg. per 100 ml. in winter. Monthly differences for any one subject were within the range of 1.5 to 2.1 μg. per 100 ml. However, in group II, there were significant differences (Table II and Fig. 1), the mean being 4.9 μg. per 100 ml. in summer and 7.3 μg. per 100 ml. in winter. From June through October, when monthly mean maximal temperatures were 101°, 102°, 98°, 98° and 82°F., respectively, and minimal temperatures were 69°, 74°, 74°, 66° and 57°F., respectively, protein-bound iodine values for this group were 5.4, 5.3, 5.5, 3.8 and 3.9 μg. per 100 ml., respectively. In January and February, when mean maximal temperatures were 59° and 61°F., respectively, and minimal temperatures, 38° and 41°F., respectively, values were 7.3 μg. per 100 ml., values having increased in all cases.

Serum Cholesterol

No seasonal change was observed in total cholesterol levels in group I (Table II), the mean being 204 mg. per 100 ml. in summer and 209 mg. per 100 ml. in winter. In group II, however, the total cholesterol in summer was 9 per cent below that in winter (233 and

TABLE II

Concentrations of Serum Protein-Bound Iodine and Total Cholesterol During Summer and Winter and Yearly Average*

Case No.	Protein-Bound Iodine (μg. per 100 ml.)						Total Cholesterol (mg./100 ml.)							
	Yearly		Summer		Winter		Yearly Average	Standard Deviation	Standard Error†	Range	Summer		Winter	
	Average	Range	Average	Range	Average	Range					Average	Range	Average	Range
Group I														
1	4.1	3.4– 4.9	4.1	4.0–4.3	4.6	4.7– 4.4	182	12.0	1.8	158–220	185	160–210	183	168–206
2	5.0	4.5– 5.7	5.0	4.7–5.4	5.2	5.7– 4.6	166	9.6	1.2	134–194	171	152–194	164	148–184
3	7.0	6.2– 7.8	6.6	6.2–6.8	7.6	7.8– 7.4	167	12.3	1.5	140–201	170	166–179	164	140–177
4	5.5	4.9– 6.8	5.7	4.9–6.8	5.3	5.5– 5.1	179	11.5	1.5	144–220	172	160–183	184	168–214
5	5.9	4.9– 7.0	5.7	4.9–5.8	6.6	6.3– 6.8	175	13.2	1.8	139–213	167	151–196	171	137–199
6	4.8	3.8– 5.9	4.6	4.0–5.1	5.3	5.0– 5.5	403	26.8	3.3	307–480	396	356–424	424	384–467
7	4.9	4.4– 5.9	4.6	4.4–5.0	5.3	5.5– 5.1	177	12.9	1.9	123–220	164	133–184	174	161–195
Group II														
8	6.0	4.4– 7.4	5.4	4.4–6.4	7.3	7.1– 7.4	222	21.8	2.7	134–270	214	190–235	233	212–248
9	5.0	2.8– 6.2	5.0	3.6–6.1	6.2	6.2– 6.2	271	27.6	3.6	199–323	241	151–308	289	278–304
10	7.5	2.8–10.4	4.3	2.8–5.8	9.9	9.4–10.4	288	30.3	4.9	189–362	277	237–310	291	245–326
11	5.5	3.4– 7.3	5.4	3.9–6.3	7.0	7.2– 6.8	279	22.1	2.9	230–360	259	256–265	296	257–327
12	5.4	3.2– 7.4	4.7	3.8–5.4	6.9	7.4– 6.3	266	17.9	2.5	219–326	250	219–282	276	235–305
13	5.1	2.9– 7.4	4.7	3.2–5.6	6.9	6.3– 7.4	179	13.7	1.7	147–211	177	156–210	191	173–204
14	5.5	3.4– 7.4	5.5	5.0–5.8	6.9	6.3– 7.4	289	23.1	3.0	217–360	275	258–293	303	233–341
15	5.2	2.7– 7.4	4.6	2.7–5.8	7.0	7.4– 6.6	220	20.1	2.6	147–273	202	147–227	243	210–268
16	5.1	3.1– 7.6	4.6	3.1–6.0	7.1	6.6– 7.6	260	26.0	3.3	163–352	257	180–293	267	218–283
17	5.6	4.2– 7.3	5.0	4.2–5.8	6.4	6.2– 6.5	235	24.8	3.1	179–298	231	179–298	243	192–283
18	5.3	3.7– 8.6	4.7	3.7–5.8	8.6	8.6– 8.6	180	13.1	1.7	146–220	182	160–217	175	149–199

* Summer, June through September; winter, January and February.

† S.E. $= \sqrt{\frac{\Sigma[\text{weekly values in each month} - \text{monthly mean}]^2}{N \text{ (total weeks} - \text{total months)}}}$.

255 mg. per 100 ml., respectively). In all but one subject the total cholesterol levels diminished from 10 to 48 mg. per 100 ml. (4 to 17 per cent of the respective means).

During the investigation, difference in variability between the two groups due to hormonal effect became of interest as a potential factor in response to climatic stress. Therefore, total cholesterol concentrations were determined daily in three women, twenty-seven to thirty years of age, over three menstrual cycles.

Patterns of variation (Fig. 2) showed that the values tended to be low within a few days before, during or after menstruation. In two cases values were high between the ninth and fourteenth days, approximating the period of ovulation; in the third case, values were high shortly after the midpoint of each cycle. These data confirm the results of Okey and Boyden[19] and support their suggestion that retrogression of corpus luteum and simultaneous withdrawal of estrogen and progesterone, which occurs during and following the menstrual period, may correspond to that of the drop in blood cholesterol. Although cycle variation presented a pattern which was characteristic of the individual, measures of variability were similar whether for individual cycles or any selected thirty-day period (S.D., ±17.8 mg. per 100 ml.; S.E., ±2.6 mg. per 100 ml. or less). Measures of variability of weekly values of the men were similar.

No correlations were observed between serum total cholesterol and basal metabolism (except Case 6), or dietary calories, protein, cholesterol, total lipid, fatty acids (total, saturated, polyunsaturated or unsaturated) or ratios. One subject (Case 6) was representative of the hypothyroid state in which an in-

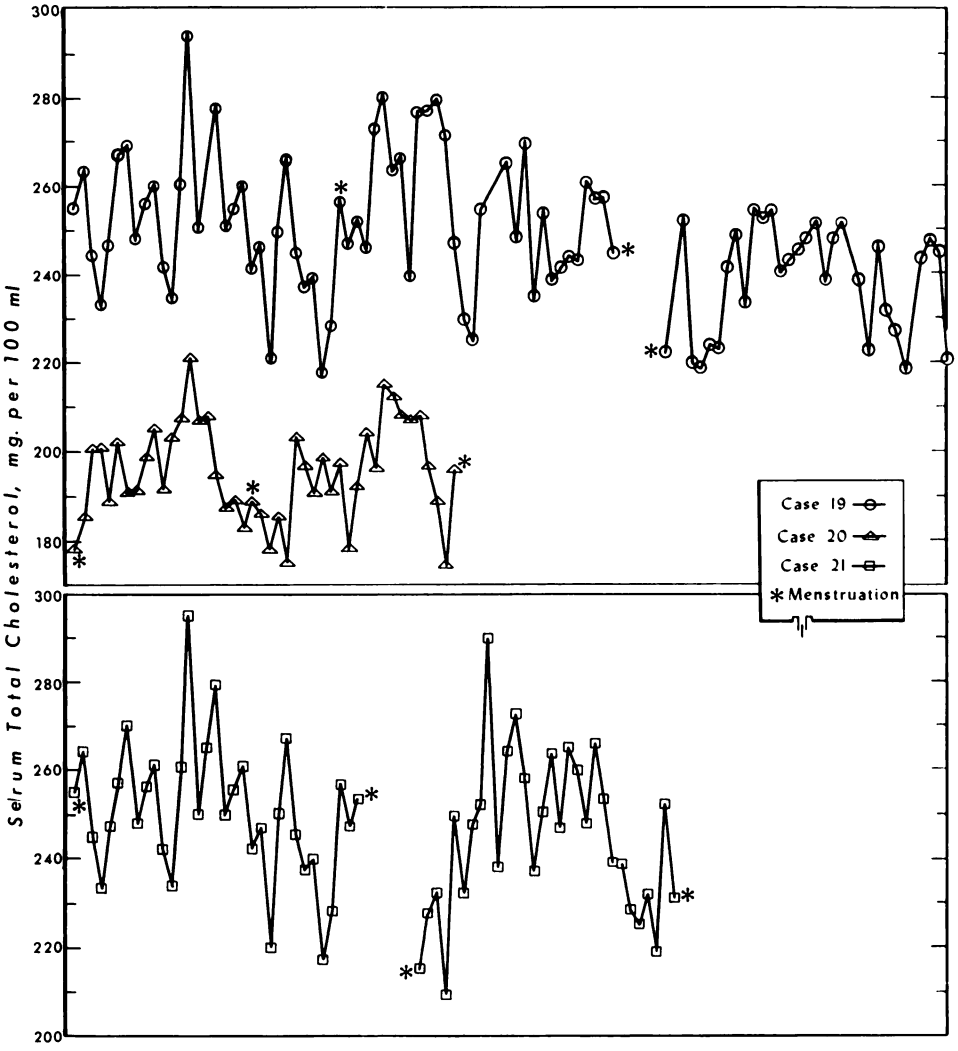

FIG. 2. Daily concentrations of serum total cholesterol in women.

verse relation exists between serum total cholesterol and basal metabolism. This subject's normal protein-bound iodine level indicated the presence of a normal amount of hormonal iodine in transit and would seem to demonstrate the conclusion of DeMowbray and Tickner[20] that basal metabolism is more closely related to severity of thyrotoxicosis than serum protein-bound iodine.

Hemoconcentration

We suggest that the diminished levels of total cholesterol and protein-bound iodine which occurred in summer may be related to changes in hemoconcentration or intercellular and intracellular water distribution as observed by others in studies on thermal stress in cattle.[21–23]

COMMENTS

Yearly correlations of protein-bound iodine to temperature and total cholesterol, and total cholesterol to temperature, varied among subjects, showing no general trends within a group. In group II hemoglobin levels average 13.9 gm. per cent (range 13.0 to 14.7 gm. per cent). Protein-bound iodine values were within the normal range of 4 to 8 μg. per 100 ml. in all

subjects. Total cholesterol monthly means in group I (omitting Case 6) were in close agreement, averaging 174 mg. per 100 ml. (S.D. ± 14.0 mg. per 100 ml., S.E. ± 1.9 mg. per 100 ml.), and in group II 244 mg. per 100 ml. (S.D. ± 21.9 mg. per 100 ml., S.E. ± 2.9 mg. per 100 ml.). Four subjects (Cases 9, 11, 12 and 16), who were 6 to 30 per cent overweight with 2.40 to 2.93 pounds per inch, had total cholesterol levels of 260 to 279 mg. per 100 ml. Two subjects (Cases 10 and 14), whose weight was normal with 2.19 and 2.29 pounds per inch, respectively, had high total cholesterol levels (288 and 289 mg. per 100 ml., respectively). Others, normal or underweight 7 to 28 per cent with 1.85 to 2.27 pounds per inch, had total cholesterol levels of 179 to 235 mg. per 100 ml.

CONCLUSION

Basal metabolism of women, but not of men, diminished significantly in summer. Serum protein-bound iodine and total cholestrol in women remained unchanged; in men, protein-bound iodine levels diminished in summer from high normal to low normal levels and total cholesterol levels diminished 9 per cent. These observations may have been influenced in some measure by differences in daily routine, stresses due to exposure to open sunshine and extremes in weather, and inability of men to adjust to lower levels of basal energy exchange such as occurs in women. These inverse relations to temperature may have resulted from changes in hemoconcentration or intercellular and intracellular water distribution.

Because of the relatively large variations in blood serum cholesterol, levels observed from day to day, we believe it is important to recognize that diagnoses based on single observations may be wholly unreliable.

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