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Body Temperature Variability (Part 2): Masking Influences of Body Temperature Variability and a Review of Body Temperature Variability in Disease

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Abstract

This is the second of a two-part review on body temperature variability. Part 1 discussed historical and modern findings on average body temperatures. It also discussed endogenous sources of temperature variability, including variations caused by site of measurement; circadian, menstrual, and annual biological rhythms; fitness; and aging. Part 2 reviews the effects of exogenous "masking" agents – external factors in the environment, diet, or lifestyle that can be a significant source of body temperature variability. Body temperature variability findings in disease states are also reviewed. (*Altern Med Rev* 2007;12(1):49-62)

Introduction

Body temperature is a complex, non-linear function that is subject to many sources of endogenous and exogenous variation. It also appears to vary in several clinical situations. Part 1 of this review discussed endogenous sources of temperature variability, including variations caused by site of measurement; circadian, menstrual, and annual biological rhythms; fitness; and aging. In this second part of the review of body temperature variability, exogenous sources of variability and variability that might be expected in certain disease states are discussed. Exogenous variability is caused by "masking" agents – external factors in the environment, diet, or lifestyle that influence body temperature. Known sources of exogenous variability are described. Body temperature has been studied in several specific disease states or health conditions and the reported observations on body temperatures in these clinical situations are reviewed.

Variations Due to Miscellaneous Masking Effects

Temperature ranges are complex and adjustable, influenced by many factors both internal (endogenous) and external (exogenous) to the organism. Circadian, circamensal, and circannual rhythms, as well as fitness and age, are examples of endogenous factors that influence body temperature values and variability. The effects these factors can have on body temperature variability can be found in part 1 of this review (*Altern Med Rev* 2006;11(4):278-293).

Many exogenous influences also influence body temperature. Within circadian research these exogenous influences are categorized as masking effects since they mask the actual endogenous temperature rhythms and the activity of biological pacemakers.[1]

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Definitions

*Note: Acrophase, Amplitude, and MESOR are standardized terms used to describe chronobiological rhythms. These terms are defined as:

ACROPHASE: Measure of the crest time of a rhythm from the cosine curve best fitting the data. It provides the timing of a rhythm in relation to a defined reference point of time. Local midnight is often used for a time point for circadian rhythms. It can be expressed in degrees (360°=1 period) or time units (hours and minutes for circadian rhythms, days or months for longer rhythms).

AMPLITUDE: One half of the extent of the change in height of a wave (the difference between the maximum height of the wave and the rhythm-adjusted mean [MESOR] of the wave form).

Midline Estimating Statistic of Rhythm (MESOR): The value midway between the highest and lowest values of the (cosine) function best fitting to the data.

Hormonal Effects

As noted in part 1 of this review, the use of oral contraceptives significantly changes daily temperature minimums, maximums, and amplitudes, shifting the entire curve upward by approximately 1.08° F/0.6° C. Oral contraceptives also blunt or abolish the circamensal rhythm.[2] This is an example of an exogenous influence masking both body temperature daily and menstrual rhythms, causing higher daily readings and more stable monthly rhythms than would be expected in the absence of oral contraceptives. Estrogen replacement therapy (ERT) is another example of a masking effect by a hormonal medication. ERT shifts the daily temperature curve 0.18° F/0.1° C lower, resulting in a lower minimum, maximum, and mean temperature than prior to ERT.[3]

Melatonin administration appears to act as a masking agent, although available evidence suggests this effect is minimal (or non-existent) in young adults and more pronounced in elderly individuals. In older adults, melatonin taken just prior to bedtime decreases the mesor 0.18° F/0.1° C and increases the amplitude to a value much more similar to that found in young adults.[4-6] Melatonin also appears to improve the daily rhythm stability of body temperature, decreasing the variability of inter-individual and intra-individual values for acrophase. This means that when melatonin is administered at the same time of the evening to a group of people over several days or more, it produces a circadian rhythm of body temperature more similarly timed one day to the next in a given individual and more likely to be similarly timed when one individual is compared to other individuals. The potential for melatonin to decrease the variability of acrophase in this manner is evidence in favor of a synchronizing effect of melatonin on temperature circadian rhythms.[6]

Effects of Beverage Consumption, Smoking, and Chewing

Oral temperatures are subject to masking effects from hot and cold beverages, smoking, and chewing of any type (including gum chewing). Drinking a hot or cold beverage can cause an immediate oral temperature increase or decrease for 5-10 minutes after drinking a hot beverage and 10-30 minutes after drinking a cold beverage. Mastication and smoking both cause significant increases in oral temperature that persist for greater than 20 minutes. Gum chewing typically causes minimal oral temperature elevation; however, it can still mask actual temperature when temperatures are being monitored at this site.[7-10] These oral masking agents would not be expected to produce any significant effect on core body temperature monitored at the other sites.

Alcohol consumption might have a significant masking effect on temperature. Alcohol appears to have an overall lowering effect on daytime and early evening body temperature, combined with a pronounced elevating effect on sleep body temperature. In a study investigating the effects of blood alcohol levels designed to mimic chronic alcohol consumption, the circadian amplitude of core body temperature was reduced 43 percent, primarily because of the significant increase in value of the temperature minimum.[11]

Effect of Clothing

Clothing can exert a significant masking effect on temperature. Jeong et al dressed participants in clothing that either covered the whole body area except for the head, hands, and feet, or clothing that covered only the trunk, upper arms, and thighs. Late evening decreases in rectal temperature rhythm after retiring and morning increases in rectal temperature rhythm after rising occurred significantly more rapidly in individuals whose trunk, upper arms, and thighs were covered. And the amplitude of the daily temperature was significantly greater in these subjects compared to participants who clothed more of the body.[12]

Park et al reported similar findings. Rectal temperatures were lower from bedtime until noon when women wore short-sleeved shirts and knee-length pants compared to long-sleeved clothing and full-length pants. It was also observed that the amplitude of rectal temperature was significantly greater when short-sleeved shirts and knee-length pants were worn.[13] Park et al estimated that 27- and 12.4 percent of the circadian amplitude might be influenced by type of clothing worn during daytime and nighttime, respectively.[14]

Wearing foundation garments (girdle and brassiere) over a 24-hour period has also been reported to influence circadian rhythms of core body temperature. Rectal temperatures were shifted significantly higher throughout the day and night when foundation garments were worn compared with periods when they were not worn.[15]

Effect of Heat from Bathing or Electric Blankets

Body heating by a late night bath or using an electric blanket can exert masking effects. Taking a hot bath 1.5-2 hours before bedtime results in a significant delay in the phase of core body temperature rhythm compared to baseline nights, with temperature minimums occurring later in the sleep period.[16] Use of an electric blanket is reported to raise rectal temperature during sleep.[17]

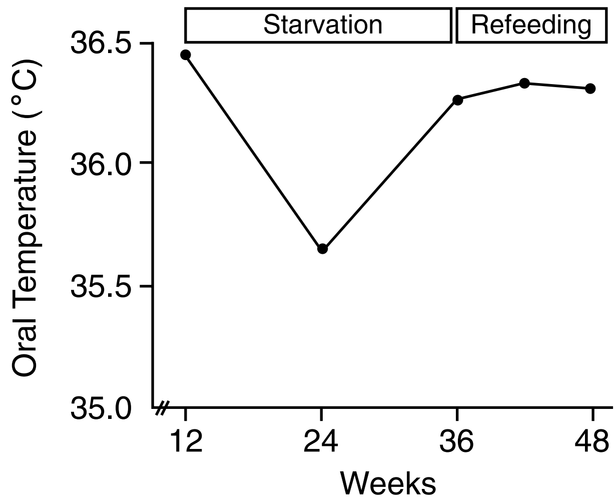
Effect of Meal Timing or Caloric Restriction

Meal timing is an accepted zeitgeber (external time-giving cue) capable of influencing and synchronizing some circadian rhythms to a 24-hour day. An excellent example of changes in meal timing that can impact temperature arises from observations made of Muslims during the month of Ramadan. Ramadan requires that Muslims abstain from drinking and eating between sunrise and sunset for 30 days. This significant shift in meal timing produces a several-hour delay in the acrophase of oral and rectal temperatures, a decrease in daytime oral and rectal temperatures, and an increase in nocturnal oral and rectal temperatures. However, the daily mesor of rectal temperature does not vary significantly. The amplitude of the daily rectal temperature decreases during Ramadan, primarily because minimum temperature levels are higher during, compared to before or after, Ramadan. Temperature patterns resume baseline values after Ramadan ends and subjects resume normal eating patterns.[18,19] This information suggests that shifting meal timing is capable of influencing the timing and amplitude of the circadian rhythm for body temperature.

Caloric restriction exerts a masking effect on temperature. Body temperature decreases subsequent to chronic caloric restriction and rebounds to approximately pre-caloric restriction levels once the weight, lost through caloric restriction, has been regained. Medical screening of participants who entered Biosphere 2 revealed an average pre-entry temperature in the range of 98.6° F/37° C. While individuals were inside Biosphere 2 and subject to chronic caloric restriction and weight loss, temperatures were often in the range of 96-97° F/35.5-36.1° C, and were sometimes below 96° F/35.5° C. Following exit from Biosphere 2 and regain of weight that occurred when calories were freely available, average temperatures returned to a range of 98.6° F/37° C. These temperature changes mirrored changes in thyroid hormone levels, which declined subsequent to inadequate caloric consumption and accompanying weight loss. Normal thyroid function resumed when weight was regained.[20]

Similar findings were observed in the Minnesota Semi-Starvation Study. Compared with temperatures under conditions of weight maintenance, oral temperatures decreased significantly during semi-starvation, especially during the first 12 weeks of calorie restriction, and rebounded to normal with refeeding.[21] Figure 1 shows changes in mean temperatures that occurred during this study for the four men with the highest and lowest oral temperatures. Karklin et al also reported a significant decrease in core body temperature and thyroid hormone levels after several weeks of dieting.[22] It appears caloric restriction results in a hypometabolic state and the declines in temperature and thyroid hormones that occur are effects that self-correct when sufficient calories are made available to promote weight regain.

Figure 1. Effect of Semi-starvation on Oral Temperatures



Oral temperature means for four men after 12 weeks of weight maintenance diet, following 12 and 24 weeks of semi-starvation, followed by 6 and 12 weeks of re-feeding.

Adapted from: Rising R, Keys A, Ravussin E, Bogardus C. Concomitant interindividual variation in body temperature and metabolic rate. *Am J Physiol* 1992;263:E730-E734.

Effect of Light Exposure

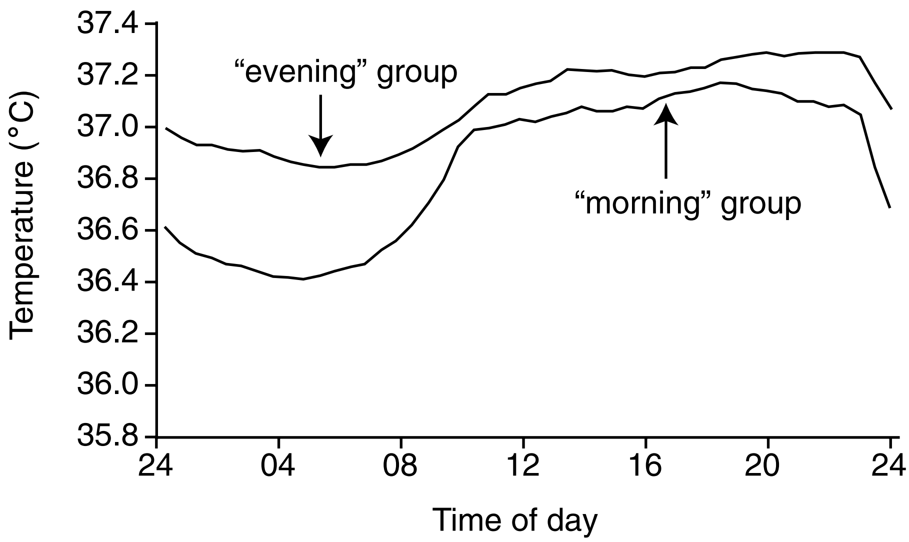
Light exposure influences body temperature in many organisms. Evidence suggests the acrophase of human body temperature rhythms can be shifted by exposure to bright light and is dependent to a degree on the timing of light exposure. As an example, exposure to bright light (as opposed to dimmer light) in the evening hours tends to shift the entire temperature curve several hours later.[23-25]

Effect of Waking Time

The time of day when the first morning temperature is monitored is an important masking effect. The so-called "weekend effect" is well recognized; that is, the phenomenon whereby waking temperatures are significantly higher on Saturday and Sunday than temperatures obtained on Friday or Monday. Evidence indicates this effect is largely a result of waking later on weekend mornings than on workdays. Evidence also indicates that waking earlier than usual will result in lower recorded waking temperatures.[26,27] The reason for this variation in waking temperature is likely due to temperatures being recorded at different points in the circadian temperature rhythmic phase, with earlier waking times capturing temperatures closer to 24-hour minimums and later rising capturing temperatures in the upward curve of this rhythm. As a general rule, temperatures would be expected to increase approximately 0.18° F/0.1° C for every hour later a person wakes compared with typical waking times. A similar adjustment to a lower temperature might be expected when a person wakes an hour or more earlier than typical.[26] Since minimum temperature normally occurs several hours prior to waking (between 03:00-06:00) and can demonstrate individual-to-individual variation, whether an individual wakes earlier or later relative to his or her individual nadir of daily body temperature can confound the results obtained.

The importance of normal waking times on body temperature rhythms is evident when individuals are categorized by chronotype. Within circadian research, three different chronotypes are defined: morning, evening, and intermediate types. Individuals are categorized into these groupings based on responses to a morningness-eveningness questionnaire. Morning types prefer to get up early, engage in the most mentally and physically demanding activities early in the day, and spend a quiet and relaxing time in the evening before retiring early. Evening types prefer to rise late in the day, delay involvement in demanding activities

Figure 2. Differences in Rectal Temperatures in Persons Categorized as Morning and Evening Chronotypes



Adapted from: Waterhouse J, Folkard S, Van Dongen H, et al. Temperature profiles, and the effect of sleep on them, in relation to morningness-eveningness in healthy female subjects. *Chronobiol Int* 2001;18:227-247.

until later in the day, and retire late at night; intermediate types fall between these two extremes. Persons categorized as "morning types" have significantly earlier nadir and peak times for temperatures than do "evening types."[27] As an example, Baehr et al reported that temperature minimums in a group of morning-type subjects occurred at 03:50. For evening types, temperature minimum was at 06:01, while for intermediate types nadir occurred at 05:02. Morning types were also more likely to wake several hours after their temperature minimum, while evening types often demonstrated a wake time much closer to the clock time of their temperature minimums.[28]

The post-peak fall in temperatures also occurs much earlier in morning types, with a downward trend in temperature occurring as early as 18:00. In contrast, evening types do not usually experience the downward trend in temperature until at least 22:00. In other words, a morning type has a much earlier biological day relative to the actual clock time than does an evening type. Morning types also tend to have higher daytime temperatures and lower temperature minimums, resulting in higher daily temperature amplitudes. Individuals categorized as intermediate types have temperatures between those of the other groups.[28,29] Figure 2 shows temperature differences between people categorized as morning and evening chronotypes.

Effect of Sleep Deprivation

Sleep deprivation appears to significantly impact body temperature. Launay et al monitored rectal temperatures in six men before and after 62 hours of sustained waking. Whereas mean rectal temperature maximums were 98.42° F/36.9° C before and after sleep deprivation, sleep deprivation resulted in a significant increase in temperature minimums, with nadirs increasing from 97.0° F/36.1° C prior to the experiment to 97.7° F/36.5° C after 62 hours without sleep. When the data was expressed using circadian parameters, sleep deprivation increased the mesor from 97.75° F/36.53° C to 97.93° F/36.63° C and reduced the amplitude from 0.76° F/0.42° C to 0.43° F/0.24° C, a reduction in amplitude of approximately 40 percent. Acrophase did not change and occurred between 17:00-18:00 under both conditions.[30]

Benoit et al also reported an increase in morning waking temperatures following a night of sleep deprivation; however, this was only observed in persons who habitually slept nine hours or more and was not observed in participants whose habitual sleep duration was less than or equal to 6.5 hours.[31] Murray et al recorded oral temperatures 10 times during each 24-hour period while subjecting participants to 98 hours of sleep deprivation. While a diurnal rhythm remained evident throughout the sleep deprivation study, temperature minimums and maximums were shifted progressively lower and had an inverse relationship with self-ratings of increases in fatigue and sleepiness.[32]

Acute sleep deprivation appears to initially blunt amplitude and increase the temperatures observed at waking and during the day. However, the evidence from Murray et al suggests that several nights of sleep deprivation might produce changes in temperature very similar to those observed in chronic calorie deprivation, with a downward shift of the entire daily temperature rhythm. The effect of chronic partial sleep deprivation on temperature has not been investigated.

The Effect of Removal of External Entraining Agents or Sudden Changes in Schedule

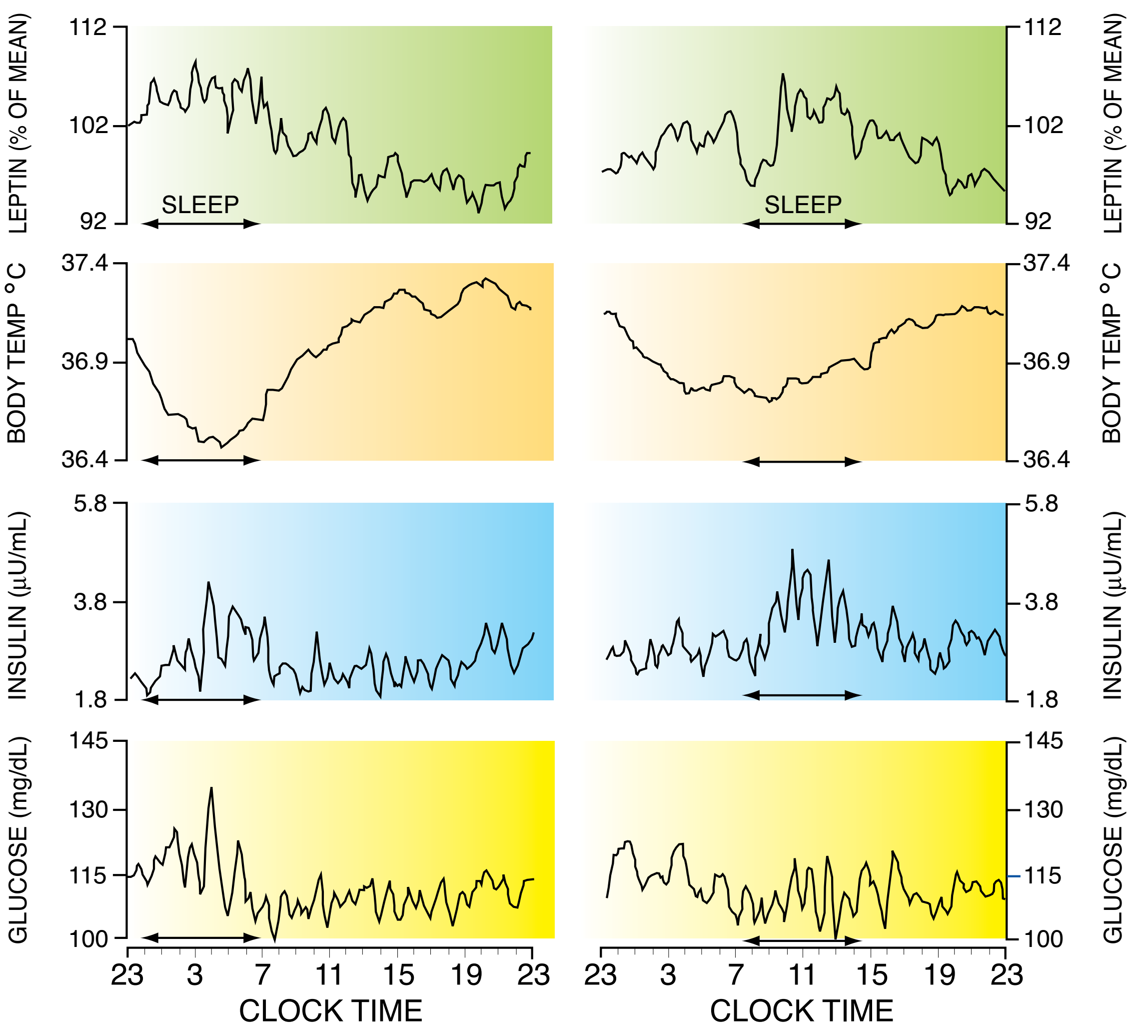
As noted in part 1 of this review, daily body temperature rhythm is considered a "marker rhythm." It is used to tell time on an individual's body clock and determine whether other rhythms are synchronized or desynchronized. Under stable 24-hour, day-night lighting conditions, temperature has a period of 24 hours and the acrophase of temperature will occur in a predictable relationship with day-night cycles and with other biological rhythms that have circadian periods. Body rhythms are said to be synchronized when timed correctly with respect to each other. However, when exposure to external entraining agents (zeitgebers) is removed or abruptly changed, the period of temperature can slightly exceed 24 hours or shift to become temporarily out of phase with other biological rhythms. In order to remain synchronized, all rhythms must shift simultaneously. Evidence indicates that different rhythms shift at different rates, so this does not typically occur. The resulting state is described as a temporary state of internal desynchronization. Shift work, travel across time zones, abrupt shifts in sleep-wake cycles, or changes in light-dark exposure can profoundly influence temperatures, as well as the relationship temperature rhythms have to other biological rhythms, resulting in at least temporary internal desynchronization of circadian rhythms. As a general trend, the acrophase of temperature shifts and amplitude decreases when exogenous influences cause temporary internal desynchronization and while the system is readjusting or coming back into synchronization.

Temporary internal desynchronization is evident in Figure 3. Simon et al monitored the daily rhythms of temperature, as well as plasma leptin, insulin, and glucose before and after shifting sleep-wake schedules by eight hours. Temperature amplitude decreased and acrophase was shifted. Of equal importance, the relationship of temperature acrophase with the other biological rhythms became dissociated from each other (desynchronized).[33]

Travel by airplane across several time zones desynchronizes an individual's circadian rhythms. Upon arrival at a new location, the traveler's temperature (and other circadian) rhythms will no longer correspond to day-night cycles in the local environment and they will temporarily be out of synch with the natural environment in the destination time zone. Since biological rhythms do not shift at the same pace, they will likely experience internal desynchronization, with different biological events temporarily occurring out of phase with each other. Temperature acrophase would be expected to be earlier or later than that normally found among individuals in that location, depending on whether the direction of travel was westward or eastward, respectively. Temperature maximums typically remain unchanged; however, minimum temperatures can increase substantially, resulting in an initial dampening of amplitude by as much as 40-50 percent. Resynchronization of rhythms is estimated to take approximately one day for each time zone change.[34-36]

Desynchronization of circadian rhythms is commonly observed in shift workers.[37-39] Gupta et al studied several different circadian rhythms, including temperature, in senior and junior shift-working nurses compared to controls. They detected circadian rhythms

Figure 3. Mean 24-hour Profiles of Plasma Leptin, Body Temperature, Plasma Insulin, and Glucose with Normal Nocturnal Sleep (left) and after an Eight-hour Shift in Sleep (right)



Adapted from: Simon C, Gronfier C, Schlienger JL, Brandenberger G. Circadian and ultradian variations of leptin in normal man under continuous enteral nutrition: relationship to sleep and body temperature. J Clin Endocr Metab 1998;83:1893-1899.

of the observed variables in 100 percent of the control subjects but in only 38- and 21-percent of the senior and junior nurses, respectively, suggesting a much higher prevalence of desynchronization in shift workers.[39]

Shift work, especially rotating shift work, also causes significant changes in temperature rhythms. The result is a shift in acrophase of the rhythm and, in some individuals, a considerable and progressive decline in temperature amplitude.[38,40-42]

Clinical signs of intolerance to shift work include persisting sleep disturbances, fatigue, changes in mood or behavior, and digestive disturbances. While the mesor of tolerant and intolerant shift workers is similar (~97.7° F/36.5° C), individuals who have higher temperature amplitudes, slower and less pronounced shift in acrophase, and 24-hour circadian temperature periods, appear to be significantly more tolerant to shift work. Conversely, shift workers who develop signs of intolerance are much more likely to have lower temperature amplitudes, faster and more pronounced shift in acrophase, and "free running" temperature rhythms (rhythms with periods greater or less than 24 hours).[43-46] As an example, in one study Andlauer et al observed that 16 of 20 shift workers who had a difference in maximum-minimum oral temperatures greater than 1.9° F/1.07° C were tolerant to shift work. However, 18 of the 28 subjects intolerant to shift work had maximum-minimum differences less than 1.9° F/1.07° C.[45]

Reinberg et al observed that 31 of 38 subjects with excellent long-term tolerance to shift work had a period for temperature rhythm equal to 24 hours. In contrast, only five of 27 with poor tolerance to shift work showed a period equal to 24 hours. They also noted that, in the majority of intolerant individuals, activity-rest rhythms maintained 24-hour periodicity; therefore, temperature rhythm was chronically desynchronized from this and possibly other circadian rhythms.[46]

Variations Due to Disease

Temperature has been investigated in a variety of disease states and clinical syndromes. Findings from these investigations are summarized below.

Allergy

Hamilos et al examined the circadian rhythm of core body temperature in individuals with allergies and controls. Recordings were obtained every five minutes for 48 hours using an ingested radio frequency transmitter (RFT) pill. The 24-hour mean core body temperature was higher in the allergy group (98.90° F/37.15° C) than in controls (98.60° F/37.00° C). The mean peak and trough circadian temperatures were not statistically different; however, the moment-to-moment complex variability was significantly greater in controls.[47]

Brain Lesions

In a survey of patients with several different types of acute and chronic brain lesion, 79 percent were found to have flat circadian rhythms of core temperature. The loss of amplitude with brain lesions suggests a complete lack of circadian time structure of temperature in many of these individuals.[48]

Cancer

Bailleul et al monitored oral temperatures in patients with advanced cancer. Individual analyses of temperature data showed large differences in the circadian rhythm of temperature from patient to patient. These differences were accounted for by differences in performance status. Subjects with poor performance status and rapidly progressive disease had very few validated rhythms compared to those patients with good performance status.[49]

Carpenter et al examined core body temperature via an ingested pill (sampled every 10 seconds) in eight breast cancer survivors with a mean time post-completion of primary treatment of 32.1 months. Analysis of core temperature indicated wide variability of the acrophase. The time of acrophase was between 06:00-12:00 in four participants, after 12:00 and before 18:00 in two participants, and between 18:00 and 00:00 in the remaining two participants. The moment-to-moment complex variability was dampened in all eight subjects. Six of eight subjects had diminished amplitudes (below 0.7° F/0.37° C) and mesors were at or below 96.96° F/36.09° C in five of the eight subjects. All eight subjects demonstrated at least one or more abnormality – disruption of acrophase, reduced amplitude, or low mesor – with seven of eight having two or more abnormalities.[50]

Chronic Fatigue Syndrome (CFS)

Hamilos et al examined the circadian rhythm of core body temperature in 10 subjects who met the Centers for Disease Control criteria for CFS and 10 control subjects. Recordings were obtained every five minutes for 48 hours using an ingested RFT pill. The circadian rhythm of core body temperature in the CFS subjects was nearly indistinguishable (similar acrophase and mesors and slightly reduced amplitude) from normal control subjects.[47,51]

Depression

Studies indicate abnormalities in the daily temperature rhythm phase and amplitude of depressed patients. Nikitopoulou et al monitored temperatures in six manic-depressive patients. Temperature rhythm phase was essentially normal during the manic phases (approximating 24 hours with acrophases occurring at expected times). When subjects were experiencing the depression phase, data suggests the period of the rhythm was approximately 12 hours, and the daytime temperatures appeared disorganized, often falling during the morning instead of rising. They also observed that during depression phases average body temperature was 0.18° F/0.1° C higher than normal and during manic episodes body temperature was 0.45° F/0.25° C higher than when depressed.[52] Karger et al also observed that depressed patients had a higher average body temperature than controls. When normalized for age and time-of-day differences, oral temperatures of depressed patients averaged 0.44° F/0.25° C higher than controls.[53]

On the other hand, Tsujimoto et al found no differences in 24-hour average mean body temperature between 64 psychiatric patients (including 47 with affective disorders) and 13 normal controls. However, body temperature of the patients with affective disorders fluctuated more, did not fit well to a sinusoidal curve, and showed phase instability and a reduced circadian amplitude.[54] Souetre et al reported the peak-trough difference in rectal temperature was 1.6° F/0.9° C in healthy controls, but only 0.9° F/0.5° C in depressed patients. After subjects had recovered from the depressed state, amplitude increased to 1.4° F/0.8° C.[55]

Febrile States

Lell et al obtained hourly measurements of the rectal temperature of 66 children with *Plasmodium falciparum* malaria and observed the circadian rhythm of body temperature was maintained; however, the entire curve was shifted upward. Their findings also illustrate the importance of time-of-day when temperature is obtained in diagnosing fever. Thirty-three of the children (50%) had temperatures above 100.4° F/38.0° C at 18:00 on the first day compared with only nine (14%) at 06:00 the next morning. This considerable difference remained when temperatures were obtained during a second day of monitoring.[56]

Human Immunodeficiency Virus (HIV) Infection

Sothern et al reported that temperature acrophases obtained by monitoring oral temperature in individuals infected with HIV were more variable than those of healthy subjects. The acrophase tended to occur earlier or later, suggesting a disruption of circadian timing and possibly desynchronization with other biological rhythms.[57]

Insomnia

A larger decline in body temperature during sleep is associated with improved sleep quality. Conversely, a reduced drop has a relationship with poorer sleep quality,[4,13,16,17] suggesting that larger amplitudes of daily temperature have a relationship with improved sleep quality.

Timing of temperature acrophase also appears to have an important relationship with sleep quality. Morris et al monitored rectal temperatures in 13 subjects with sleep-onset insomnia and in nine good sleepers. Individuals with sleep-onset insomnia had a temperature acrophase approximately 2.5 hours later than that observed in individuals without insomnia, yielding temperature characteristics of sleep-onset insomniacs at their usual bedtime that were consistent with patterns found in good sleepers significantly before their usual bedtime.[58] Kerkhof et al obtained repeated oral temperatures in 80 chronic insomniacs and found insomniacs with an earlier temperature acrophase tended to have shorter and more restless sleep, while insomniacs with a delayed temperature acrophase tended to experience longer sleep latency.[59]

Obesity

Eriksson et al grouped 800 subjects into quintiles based on body mass and monitored oral temperatures from 07:30-09:30. Subjects with higher body mass had higher morning oral temperatures.[60] Adam calculated mean temperature in 60 subjects after monitoring oral temperatures every hour from 07:00-23:00. The mean oral temperature for 42 women was 98.1° F/36.73° C, while for 18 men it was 97.86° F/36.59° C. A statistically significant inverse association was observed for mean daytime oral temperature and body mass; however, there was no statistically significant correlation between body mass index (BMI) and oral temperatures. This suggests relative fatness or thinness, at least in the sense it can be predicted by BMI, was not an important determinant of average daily temperatures; however, overall body mass might be.[61]

Keys et al reported no statistical correlation between morning oral temperatures and body fat in Pima Indians (an ethnic group at high risk for obesity and obesity-related co-morbidities).[21] Rising et al reported that Pima Indians had a lower core body temperature during sleep and a higher daytime temperature than Caucasian subjects.[62]

Vozarova et al also noted temperature differences between Pima Indians and Caucasians. Oral temperatures were repeatedly monitored immediately on waking in 69 male Caucasians and 115 male Pima Indians. The Pima Indians had a higher average body weight (92.8 kg) and body fat percent (28%) than the Caucasian group (81.3 kg and 21%, respectively). Waking oral temperature was significantly higher in Pima Indians (97.52° F/36.4° C) than Caucasians (97.34° F/36.3° C) and correlated with fat-free mass. Insulin sensitivity was also monitored in a subset of the Pima Indian group. The researchers reported that a 0.18° F/0.1° C increase in waking oral temperature was associated with a 36-percent decrease in insulin sensitivity, suggesting a relationship between higher waking temperatures and insulin resistance, at least in members of this ethnic group.[63]

Psoriasis

Radaelli et al recorded oral temperatures (and other biomarkers of circadian rhythms) at three-hour intervals in both psoriatic and control subjects. Mesors and amplitudes were similar between patients and controls; however, subjects with psoriasis had much more variable acrophases. Oral temperatures of control subjects were also synchronized to the circadian rhythms of other recorded biomarkers in the study (blood pressure, pulse rate, uric acid levels, serum potassium, 17-ketosteroids, and 17-hydroxycorticosteroids). In the psoriatic group, only a few of these variables presented a clearly reproducible circadian rhythm and they tended to be desynchronized from body temperature rhythms.[64]

Thyroid Function

Basal body temperature monitoring has been advocated as a method to diagnose hypothyroidism. Barnes hypothesized that waking axillary temperature was a useful diagnostic test for low thyroid function, based on the prevailing belief at that time that the most basic function of the thyroid gland was regulation of metabolism and that a low waking axillary temperature indicated low metabolism and poor thyroid function.[65] Barnes believed a normal waking axillary temperature should be 97.8-98.2° F/36.55-36.77° C, with temperatures below this range suggestive of hypothyroidism; based on these criteria as much as 40 percent of the population was hypothyroid.[66]

Many aspects of Barnes' hypothesis and claims are inconsistent with modern medical knowledge and thermometry findings. Barnes vastly oversimplified the complex regulation of metabolism and body temperature. While thyroid hormones do influence metabolic function and temperature, they are among many hormones and messenger molecules involved in this regulation, including sex hormones, leptin, epinephrine, norepinephrine, and cytokines. As Brooks-Asplund et al commented: "Results support the concept that basal body temperature is regulated by a network of endocrine and immune mediators…."[67]

A number of factors discussed previously bring into question the validity of Barnes' assertions. Part 1 of this review discussed findings that indicate the following: (1) mean axillary temperature ranges are lower than the ranges proposed by Barnes; (2) circadian changes in temperature produce even lower axillary temperature values at waking than observed mean values; (3) axillary temperatures are a poor surrogate for core body temperature; (4) side-to-side differences in axillary temperatures can be substantial; and (5) waking temperatures are higher in sedentary individuals than in physically fit individuals. Furthermore, changes in temperature caused by exogenous influences confound Barnes' theories. Hormonal medications, alcohol consumption, clothing selection, timing of caloric intake, dieting, timing of bright light exposure, habitual wake-up times and deviations from these times, chronotype, sleep deprivation, and abrupt changes in light-darkness exposure can produce changes in aspects of the amplitude, acrophase, or mesor of temperature that would be significant enough to influence waking temperatures.

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Neither Barnes, nor the foundation that bears his name, has published data that can be used to determine the validity of his claims or the sensitivity and specificity of this assessment method. Based on modern findings in clinical thermometry it does not appear that waking temperature, irrespective of site monitored, is a sensitive or specific assessment for hypothyroidism. Waking temperature in isolation is insufficient to accurately characterize the known variation in temperature that occurs because of endogenous biological rhythms and also fails to account for the complex changes in temperature that occur because of many known, and possibly many other yet to be determined, exogenous influences.

Several human studies have measured thyroid hormone levels while assessing body temperature. Ljunggren et al investigated body temperatures and thyroid hormone levels in subjects with fever caused by various non-thyroidal illnesses. An inverse relationship between temperature and serum T3 levels was observed; with increasing body temperatures serum T3 decreased gradually. At a body temperature of 100.4° F/38.0° C, T3 was below normal mean levels. With temperatures above 104° F/40.0° C, T3 levels were comparable to those seen in severe hypothyroidism, while levels of T4 and thyroid stimulating hormone (TSH) remained unchanged and within the normal range. Reverse T3 (rT3) demonstrated an inconsistent relationship with temperature in these subjects – unchanged in some cases and increasing in parallel with temperature in others.[68]

Sehnert and Croft had 66 post-whiplash trauma patients measure axillary temperature each morning before rising, and standard laboratory assessment, including TSH, T4, free T4 index (an indirect method of calculating free T4), and T3 resin uptake, was performed on each individual. The study found 86.4 percent of the subjects had temperatures that would be categorized as below normal based on ranges advocated by Barnes. Thirty percent of these subjects had at least one thyroid value considered abnormal. In the 13 percent of patients who had "normal" temperatures, 33 percent had at least one thyroid parameter considered outside of the normal reference range. Analysis of groups with "normal" and "below normal" temperatures versus normal and abnormal thyroid laboratory tests "failed to reveal any significant differences in these groups."[69]

Conclusion

Body temperature is a complex and variable physiological function that demonstrates variability in a predictable, time-dependent manner. Quoting from a pioneer of chronobiology, Franz Halberg, in reference to rhythms with a known variation of 24 hours: "It is essential that enough information be collected to allow objective characterization of a periodic phenomenon, to wit, an estimate of M (MESOR, a rhythm-adjusted mean) as given for the three statuses in this patient, an estimate of A (circadian amplitude) itself, and finally an estimate of acrophase. In this way, a patient can be compared with himself at another time, or under another treatment, and the patient can be compared with a normal or with another patient."[70]

Based on available evidence, Halberg's emphasis on the essentiality of collecting sufficient data to objectively characterize periodic phenomenon seems warranted for body temperature. Body temperature has a known 24-hour rhythm, and research findings have found associations between characteristics of 24-hour rhythms and health. While additional research is required before conclusions can be drawn, health appears to be characterized by the following circadian rhythm attributes of temperature: (1) greater amplitude, (2) acrophase appropriately timed to day-night cycles, (3) consistency of day-to-day acrophase, (4) period of approximately 24 hours, (5) mesors consistent with those expected in a healthy population, and (6) synchronization of temperature with other circadian rhythms.

Decreased amplitude of daily body temperature has been associated with intolerance to shift work, reported in aging and sedentary subjects, and observed in several disease conditions. Disruptions in timing of the acrophase have been associated with intolerance to shift work, aging, insomnia, and several chronic diseases, including cancer and HIV. A period deviating from 24 hours has been observed more frequently in persons intolerant to shift work. Lower mesors appear to be a part of the aging process and also have associations with some disease conditions. A growing emphasis within circadian research is the use of body temperature as a marker rhythm and its use in determining synchronization of 24-hour bodily functions. Signs and symptoms of jet lag are thought to be due in large part to internal desynchronization of rhythms; insomnia and cancer also have strong associations with rhythm desynchronization.

Body temperature in a given individual at any particular time is the result of numerous interacting sources of variation (both technical and biological). Predictable daily rhythmic oscillations are one consistent source of biological variation. Temperature also responds to the influence of many exogenous influences. For example, a morning chronotype would be expected to have different rhythmic attributes of daily body temperature than would an evening chronotype, and a person who is dieting would be expected to have lower body temperatures, shifting the entire daily wave lower. Shifts in meal timing, sleep habits, and light exposure are among the diet, lifestyle, and environmental factors that can alter rhythmic aspects of temperature. Since diet, lifestyle, and environmental factors have known associations with poorer health outcomes, monitoring body temperature might prove to be a useful tool to objectively monitor positive changes in these areas. Gathering sufficient body temperature data to characterize rhythmic aspects of body temperature appears to be superior to time-insensitive spot checks when using temperature as an objective component of clinical decision making.

Thermometry has been used in clinical medicine for almost 150 years; however, a significant advancement in the understanding of temperature in health and disease has occurred only in the past 10-15 years, largely as a result of growing interest in non-linear variability of physiological function and chronobiology. Despite new understandings of temperature variability that have emerged from modern thermometry research, understanding of the patterns of temperature that occur in health and disease is still in its infancy. Additional research on rhythmic patterns of temperature in health and disease is warranted. Collecting body temperature data, monitoring other independent circadian rhythms (such as sleep-wake cycles, activity rhythms, or periodic hormones), and comparing the results for synchronization in health and disease would likely be a fruitful area of medical observation and research. Since body temperature is characterized by more complex variability than can be described by simply characterizing the periodic aspects of the rhythm, analysis of body temperature data by advanced mathematical techniques, such as are currently being used to assess heart-rate variability, might also advance understanding of body temperature variability in health and disease.

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