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The thermoneutral zone: implications for metabolic studies

Boris Kingma[1], Arjan Frijns[2], Wouter van Marken Lichtenbelt[1]

[1]Department of Human Biology, NUTRIM School for Nutrition, Toxicology and Metabolism of Maastricht University Medical Center, Maastricht, The Netherland, [2]Department of Mechanical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands

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1. ABSTRACT

A thermoneutral environment is important for many human physiological studies. The thermoneutral zone (TNZ) is defined as the range of ambient temperatures without regulatory changes in metabolic heat production or evaporative heat loss. Many factors influence the thermoneutral zone, such as body composition, clothing, energy expenditure, age and gender. These factors have the potential to introduce bias in study results and therefore need to be taken into consideration in many metabolic studies or studies on obesity, medical conditions, thermal comfort or vigilance. Given new developments on the TNZ combined with historical views the aim of this review is to 1) provide insight in how the human TNZ is affected by internal and external factors, 2) indicate how skin blood flow characteristics could be used as an objective criterion for determining whether someone is in the thermoneutral zone, 3) explain implications of the TNZ on metabolic studies and 4) indicate future directions to enhance understanding of the TNZ, especially for the elderly and obese.

2. INTRODUCTION

2.1. Definition of thermoneutral zone

In 1902, Max Rubner was the first to put forward notion of a thermoneutral environment in mammals; he realized that his experiments on energy balance in nutrition could only be reproduced when the environmental conditions were equal (1). The concept was later adopted and applied to humans by Hardy and Dubois (1937) (2). They defined its lower limit as: *"the maximum gradient (Tskin - Tair) over which the body can maintain its temperature without increase in heat production"*. In nude subjects they found a maximum gradient of 4.7°C at the lower limit of the neutral zone. This corresponded to an air temperature of 28.5°C. Below this limit heat loss regulation through vasoconstriction of the skin blood vessels was no longer sufficient to maintain body temperature (2, 3). Hardy and Dubois did not explicitly define an upper limit of the neutral zone, however their results indicated that evaporation was markedly increased at 32˚C (2). An explicit upper limit of the thermoneutral zone was later defined using heat stress (heart rate or increases in evaporative water loss as a criterion (4, 5).

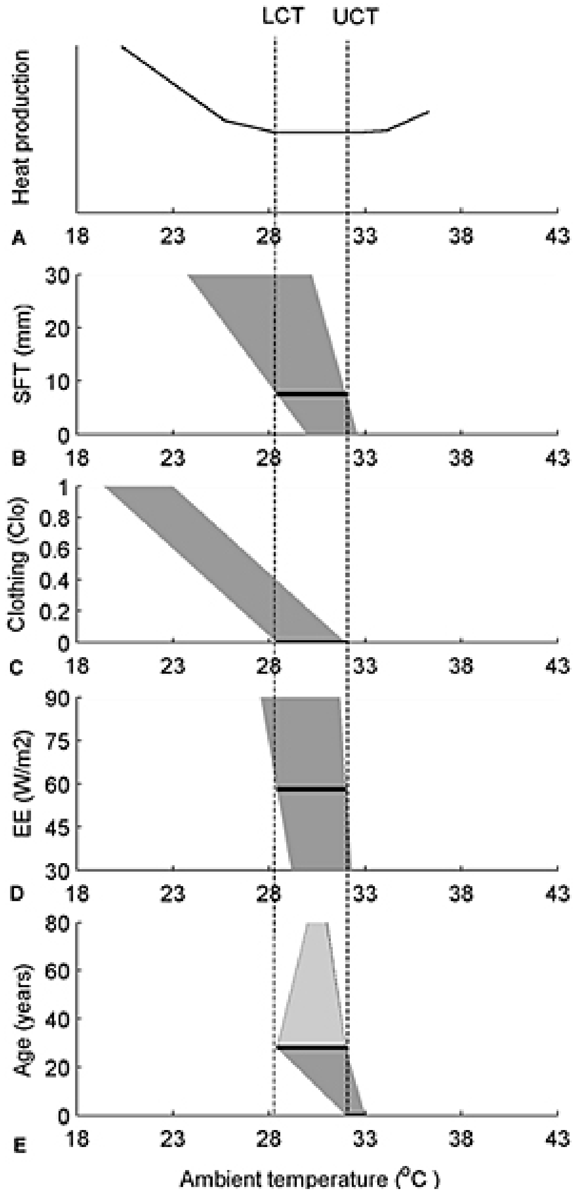

Figure 1. A) Thermoneutral zone (TNZ). The lower critical temperature (LCT) defines the lower bound of the TNZ. Below the LCT facultative heat production is increased to maintain thermal balance. The upper critical temperature (UCT) defines the upper bound of the TNZ. Above the UCT thermal balance is maintained by sweating. The solid horizontal line in subplots B through E indicates a reference TNZ as observed in experiments. B) Theoretical TNZ (gray area) over a range of subcutaneous fat thickness (SFT). C) TNZ (gray area) over a range clothing insulation. D) TNZ (gray area) over a range of energy expenditure. E) TNZ (gray area) over a range of age. Above 28 years (light gray area) the narrowing of the TNZ is not yet confirmed with experiments.

Nowadays the definition of the thermoneutral zone is reformulated to: *"the range of ambient temperature at which temperature regulation is achieved only by control of sensible (dry) heat loss, i.e. without regulatory changes in metabolic heat production or evaporative heat loss. The thermoneutral zone (TNZ) will therefore be different when insulation, posture or basal metabolism vary"* (6). Here regulation of sensible heat loss refers to heat loss by conduction, convection or radiation (7). This means that thermoregulation in the thermoneutral zone only occurs through vasomotor control (8-10).

The concept of the thermoneutral zone is shown in Figure 1A. Below the lower critical temperature (LCT) of the TNZ heat balance can be achieved by up regulation of metabolic heat production (non-shivering thermogenesis and/or shivering). Above the upper critical temperature (UCT) heat balance can be achieved by increases in evaporation (sweating). In humans, the onset of sweating is accompanied with active vasodilation, which also contributes to the maintenance of heat balance by increasing heat transport from the body to the skin (11). Above the UCT heat production also increases due to increased blood circulation, activity of sweat glands and to increased body temperature (12).

For this review we only focus on the thermoneutral zone. Note that there is a clear distinction between the *thermoneutral zone* and the *core interthreshold zone (CIZ)*. Both zones refer to a temperature range in which temperature regulation is achieved without increasing energy expenditure and without sweating. The difference between both zones is that the TNZ refers to the ambient temperature range, whereas the CIZ refers to the internal body temperature range (8).

2.2. Thermoneutral zone across studies

The TNZ has mainly been studied in animals (1, 13-17). However, some studies exist that focus on the human TNZ (2, 4, 5, 9, 18). Hardy and Dubois are the first to describe the TNZ in men and women (2, 18). Craig and Dvorak defined a TNZ in water (4). Hey and Katz studied the TNZ in newborns and Savage and Brengelmann studied skin blood flow in the TNZ (5, 9).

Research fields differ in defining the ambient temperature related to the TNZ. For instance, in the built environment operative temperature is used, which is a weighted combination of air temperature and radiative temperature (19-21). Others use air (dry bulb) temperature or control skin temperature directly by water immersion, or a water-perfused suit (22-34). Due to differences in thermal properties (mainly conduction) the thermoneutral zone in water is shifted upward compared to air (33˚C to 35.5˚C in water vs. 28.5˚C to 32˚C in air) (2, 4, 9, 10). In this review air temperature (i.e. dry bulb temperature) is used as the default TNZ medium.

2.3. Heat balance in the thermoneutral zone

In a steady state environment a subject can only be in the thermoneutral zone when heat production and heat loss are balanced. In classic textbooks on human thermoregulation heat balance is presented by the heat balance equation (35-37): $S = (M - W) - (E + C + R + B)$, where heat storage (S) is defined as the difference between heat production (metabolism M corrected for work W) and heat loss (evaporation E, convection and conduction C, radiation R and respiration B).

2.3.1. Heat production

Total heat production can be categorized into obligatory and facultative components (38). Obligatory components include: basal metabolic rate (BMR), the obligatory part of diet-induced thermogenesis (oDIT) and involuntary physical activity (e.g. feeding, posture). Facultative components include: the facultative part of diet induced thermogenesis (fDIT) and voluntary physical activity. Cold-induced thermogenesis is omitted here because it plays no role for subjects within the thermoneutral zone. BMR is the heat produced in an organism in a rested, awake, fasting and thermoneutral state and is needed to keep vital body processes functioning (6). In a resting sedentary male the energy expenditure is about $58Wm^{-2}$ (37). For comparison, typical values for energy expenditure in a reclining position or during sedentary activity are $46Wm^{-2}$ and $70Wm^{-2}$ respectively (21). Next, the obligatory part of DIT is necessary to process the food ingested. Note that DIT may also consist of a facultative part, i.e. burning excess calories and is the focus of many studies on obesity (39). DIT is typically 10% to 15% of total daily heat production (40). Physical activity thermogenesis (both voluntary and involuntary) occurs when muscles perform work; approximately 65% to 80% of energy associated with work is released as heat (41, 42).

2.3.2. Heat loss

Body heat is lost at the skin surface and by respiration. Heat produced within the body is transported to the skin by conduction through tissues and by blood perfusion (convection) (43, 44). At skin in distal areas (hands and feet) the primary heat influx comes from blood flow, whereas at more proximal sites (torso) heat is also delivered through conduction from underlying metabolically active tissues (liver, gut, etc) (45). In the thermoneutral zone the regulation of skin blood flow is crucial to maintain thermal balance.

2.3.2.1. Skin blood flow

Total skin blood flow can vary from close to 0 L min^{-1} in a cool environment to as high as 7.8 L min^{-1} in a hot environment (46, 47). In the thermoneutral zone, the amount of heat transported from core to skin by blood flow is estimated between $19Wm^{-2}$ (near the LCT) and $218Wm^{-2}$ (near the UCT) (9, 48).

The majority of skin blood flow studies have been performed on the forearm. Extrapolation of blood flow data to whole body skin has to be performed with caution because of large regional differences (45, 49-51). For instance, skin of the head and hands only comprises 7% of the total skin surface, yet between 25% and 27% of total skin blood flow occurs in these areas (52). Blood flow changes to environmental temperature variations are also dependent on the skin region. For example total hand blood flow increased 29-fold during body heating of cooled subjects, whereas forearm blood flow increased 3-fold (50). With respect to reduction in heat loss through vasoconstriction, regional differences reported are about –17% at the head and trunk, –25% at the arms and legs and about –50% at the hands and feet (53). These regional differences in skin blood flow and heat transport are attributed to arterio venous anastomoses (AVAs). AVAs are only present in glabrous skin (palms, ventral region of fingers, soles, forehead and lips) (45, 48). When these AVAs are opened, they form a bypass for blood from arterioles to venules, whereas the blood otherwise would only flow through high resistance capillaries at the skin surface. Hence, opening of AVAs greatly increases heat transport to the skin (45, 54, 55). In a thermoneutral environment blood flow in AVA rich glabrous skin has a characteristic fluctuation with 2 to 3 vasoconstrictions per minute (56). This property, which is found in glabrous skin alone, can be used to measure whether a subject is within the TNZ (see practical considerations) (57).

Overall, the ability of skin to control heat loss is influenced by the vascular anatomy, flow rate, regulation of skin blood flow and the exposure to the environment. See for reviews on skin blood flow regulation Kellogg (2006) and Johnson and Kellogg (2010) (11, 58). Although the area of glabrous skin is small relative to the entire body surface, its importance for heat loss regulation is large. This is due to the above-mentioned AVA's and because glabrous skin areas are normally the skin areas that are actually exposed to the environment. Clothing covers most other parts of the skin. Therefore, in clothed humans, glabrous skin areas are considered as major contributors to heat regulation in the thermoneutral zone (59).

3. MODULATING FACTORS

The thermoneutral zone is influenced by several internal and external factors. Here we address the modulating effect of body composition, clothing, energy expenditure, age and gender on the TNZ. In Figure 1 the influences of these factors on the TNZ are shown. For comparisons the standard TNZ (LCT_0 = 28.6˚C and UCT_0 = 32.0˚C) was taken from a 28 years old nude male subject with standard basal metabolic rate ($BMR_0=58W/m^2$) and subcutaneous fat thickness (SFT_0=7.5mm). The subscript “0” was used to denote the value of the standard, or reference subject. Where possible temperature data from literature was used, otherwise the theoretical influence was calculated as described in the corresponding sections.

3.1. Body composition

Insulation of tissues can be viewed as a series of thermal resistances (inverse of conductivity) of muscle and subcutaneous fat (60). The thermal resistance of tissues is a function of both the conductivity and blood perfusion (see for an overview of heat conductivities of tissues refs. (61, 62)). In general fat mass is positively related to tissue insulation (63). For limb muscle the story is more complicated. In resting conditions, limb muscle tissue is a major factor of the insulative capacity of the body explaining up to 70% of the total insulation (28, 60, 64). However, the insulative effect of limb muscle is only present with reduction of blood flow. During exercise in cold conditions blood flow is maintained in limb muscle, which prevents insulation (60). Under resting conditions, subjects with higher limb muscle mass also have a higher volume of blood -and corresponding heat transport-flowing from the body to the limbs. Therefore, limb muscle mass is negatively associated with tissue insulation (63).

Tissue insulation is also influenced by the subcutaneous fat layer, which serves as an insulating layer between muscle and skin (25, 63-65). The thickness of the subcutaneous fat layer is by far the most important factor for the lower critical temperature when subjects are immersed in water (60). For reviews on the influence of tissue type on tissue insulation and temperature regulation see Rennie (1988) and Anderson (1999) (60, 64).

Rennie (1988) showed that the lower critical *water* temperature of the TNZ can be expressed as a function of the thickness of the subcutaneous fat + skin layer (SFT) (i.e. for subjects with equal heat production and muscle mass) (60). Here we use the same approach to show the influence of sub cutaneous fat thickness on the *air* TNZ (Figure 1B). It is assumed that all heat produced by the body is lost to the environment (windspeed≤0.05m/s), without the need for regulatory increases in evaporation. The LCT and UCT were calculated relative to the standard subject as follows: $\mathrm{LCT} = \mathrm{LCT}_0 + 0.92\cdot\mathrm{BMR0}\cdot((\mathrm{SFT0}\text{-}\mathrm{SFT})/k_{\mathrm{LCT}})$ and $\mathrm{UCT} = \mathrm{UCT0} + 0.92\cdot\mathrm{BMR0}\cdot((\mathrm{SFT0}\text{-}\mathrm{SFT})/k_{\mathrm{UCT}})$, where, k ($\mathrm{Wm}^{-1\circ}\mathrm{C}$) is the conductivity of the subcutaneous fat + skin layer. The factor 0.92 is used to correct for respiratory heat loss, i.e. 8% of total heat production (60). Near the LCT the thermal conductivity of subcutaneous fat and skin is lowest due to vasoconstriction (k_{LCT} = 0.28 $\mathrm{Wm}^{-1\circ}\mathrm{C}^{-1}$ from (28)). Near the UCT the thermal conductivity of subcutaneous fat and skin is higher due increased blood flow (k_{UCT} = 0.73 $\mathrm{Wm}^{-1\circ}\mathrm{C}^{-1}$ from (28)).

Although the calculation above does not account for regional differences in adiposity and other complexities, it does illustrate the impact of the subcutaneous fat layer on the thermoneutral zone. For instance, a subcutaneous fat thickness of 40mm (quite common in obesity (66)) results in a LCT of 22˚C. Note that LCT of 22˚C is for a nude subject. Inclusion of light clothing (0.5clo) lowers the LCT further to about 18˚C. With a lower LCT compared to lean subject, the obese may have a reduced need for cold-induced increases in energy expenditure, which in turn increases the likelihood of sustained overweight (67). Indeed, studies indicate that subjects with increased fat mass (both subcutaneous fat thickness and whole body fat percentage) are capable of enduring lower ambient temperatures without significantly increasing heat production (60, 68), or that the cold induced heat production is negatively related to the thickness of subcutaneous fat (25, 65, 69). In relation to the UCT, no study directly measured the UCT in obese subjects. Yet, it has been suggested that obese may have increased sweat gland activity at normal room temperature (T_{air}=20-22˚C) relative to lean subjects (70).

Body composition also influences the distribution of heat loss. Increased body fat is associated with decreased proximal temperatures (trunk) and increased distal skin temperatures (hands and feet) (71, 72), thereby decreasing heat loss from proximal sites and increasing heat loss from distal sites. This is of special relevance when thermoneutrality is obtained by means of local cooling (e.g. automotive industry). For instance, in obese more body heat can be extracted by hand cooling than in lean subjects.

3.2. Clothing

One of the functions of clothing is to keep the microclimate around the body comfortable for a range of ambient temperatures. Factors that influence the insulation of clothing are: dry resistance, evaporative resistance, compression from wind and movements (37). Extensive databases on the thermal properties of clothing are available (73). The unit used to express the insulation value of clothing is the "Clo" (1 Clo = $0.155\mathrm{m}^{2\circ}\mathrm{CW}^{-1}$ = equivalent to a business suit). A simplified example of the impact of clothing on our thermal environment shows that in a steady state environment of a sedentary resting subject, clothing of 1 Clo lowers required ambient temperature by 9.7˚C ($0.92\mathrm{x}58\mathrm{Wm}^{-2}$ x ($0.155\mathrm{m}^{2\circ}\mathrm{CW}^{-1}$ + ($7.5\mathrm{x}10^{-3}\mathrm{m}$ / $0.28\mathrm{Wm}^{-1\circ}\mathrm{C}^{-1}$)) ≈ 9.7˚C; again the factor 0.92 is used to correct metabolic heat production for respiratory heat loss). Hence, relative to a nude subject, the ambient temperature of the thermoneutral zone is shifted downward by 9.7˚C, which results in a thermoneutral temperature of around 20.3˚C (30.0˚C - 9.7˚C = 20.3˚C). In summary, the ambient temperature of the TNZ is lowered according to the insulation provided by clothing (Figure 1C).

3.3. Energy expenditure

In resting conditions energy expenditure is influenced by factors such as diet, circadian rhythm, posture and acclimatization. These factors may cause a shift in the potential for temperature regulation by sensible heat loss, which may introduce a bias in studies on metabolism, skin blood flow, vigilance and thermal comfort.

Thermal balance can only be maintained when heat production is equal to heat loss. Therefore the TNZ is shifted to lower temperatures when energy expenditure increases (57, 74). Vice versa, the TNZ shifts to higher temperatures when energy expenditure decreases (see Figure 1D). The LCT and UCT were calculated relative to the standard subject as follows: $\mathrm{LCT} = \mathrm{LCT}_0 + 0.92\cdot(\mathrm{BMR}_0\text{-}\mathrm{BMR})\cdot(\mathrm{SFT}_0/k_{\mathrm{LCT}})$ and $\mathrm{UCT} = \mathrm{UCT}_0 + 0.92\cdot(\mathrm{BMR}_0\text{-}\mathrm{BMR})\cdot(\mathrm{SFT}_0/k_{\mathrm{UCT}})$.

Digestion of nutrients is associated with an increase in metabolic rate between +10% to +15% of total daily energy expenditure depending on the nutrients ingested (40, 75). However, the acute thermogenic effect of diet can be much higher (+25%) (76). To maintain thermal balance, heat loss should also increase with 25% and therefore the TNZ shifts to lower temperatures.

With respect to the influence of circadian rhythm on the TNZ: over the course of a day body temperature naturally follows both heat production and heat loss (77-80). Heat production is phase shifted approximately 1.2h ahead of heat loss, with a maximum at noon (+10% of mean 24h heat production) and a minimum at night (-6% of mean 24h heat production) (77, 78). On top of this circadian redistribution of skin blood flow (i.e. from trunk to the extremities) causes minimum internal heat conductance at day (-9% of mean 24h internal heat conduction) and maximum heat conductance at night (+5% of mean 24h internal heat conduction) (79). Therefore, the TNZ is lowest at noon and highest at night.

Posture affects both heat production and heat loss (81-83). In supine position heat production is decreased in muscles that are used during upright position (about -2% heat produced in thermoneutral conditions and about -19% heat produced in cool conditions) (82). As a consequence the TNZ in supine position is shifted upward relative to the TNZ in upright position. Furthermore, arterial baroreceptor reflexes that accompany a supine position cause vasodilatation both in muscle and skin tissue (+57% blood flow in femoral artery), which decreases insulation and contributes to the upward shift of the TNZ in supine vs. upright position (84).

Another factor that influences the TNZ is acclimatization. Relative to non-acclimatized people, those that are acclimatized to cold conditions maintain a significantly greater BMR (i.e. under thermoneutral conditions) (85). As a consequence, the TNZ is shifted downward in cold acclimatized vs. non-acclimatized subjects. The acclimatization can be induced by geography (e.g. tropic vs. arctic regions), altitude and by season (e.g. summer vs. winter in non-equatorial latitudes). With respect to seasonal acclimatization, increased BMR and increased sleeping metabolic rate have been measured in winter (+6% heat production for a 10˚C decrease in air temperature) (86, 87). Thus, depending on the season-induced acclimatization, the TNZ in winter is shifted to lower temperatures relative to the summer TNZ. However, in developed countries there is a continuing trend of increasing indoor temperatures, which reduces seasonal cold acclimatization and may have a causal relation to the increases in obesity prevalence (67). Moreover, obese subjects have a lower LCT due to increased insulation, which may further reduce the need for cold acclimatization and in turn may contribute to sustained overweight.

3.4. Age

In neonates the thermoneutral zone depends greatly on the birth weight and ranges between 35.0˚C to 35.5˚C in 1kg babies and 33.8˚C to 34.5˚C in 2kg babies (5). Within about a month the TNZ ranges from 32.0˚C to 34.0˚C. Until adulthood the TNZ continues to decrease to the range from 28.6˚C to 32.0˚C. With further increasing age, changes occur in various factors that affect thermoregulation. With respect to body composition, lean mass is in general decreased in elderly, whereas fat mass is increased, and subcutaneous fat mass is decreased (88). Secondly, elderly show decreased temperature sensitivity (89, 90) and impaired neural control of vasoconstriction (10, 23, 25, 91-93). On top of that, results suggest that control of skin blood flow in elderly is not able to maintain thermal balance in the same skin temperature range as young adults (10). However, vasoconstriction might not be affected by age in all skin regions (31, 94, 95), and there are indications that the blunting effects of ageing on thermoregulation can partly be compensated for by physical fitness (31, 96, 97). Nevertheless, age is associated with impaired thermoregulation even during mild thermal challenges (23).

Although the majority of studies that describe age effects on thermoregulation relate to the internal temperature range for thermoregulation and not to the ambient temperature range, it does indicate that elderly have an impaired ability to maintain thermal balance in the cold and in the heat compared to young adults (23, 25, 98, 99). Elderly either fail to sense the thermal imbalance and/or they fail to respond appropriately (80). In conclusion, on average, elderly respond slower to slight disturbances in thermal balance and are not able to maintain thermal balance with vasomotor responses in the same temperature range as young adults. Consequently, the thermoneutral zone for elderly is narrower than for young adults, although the exact range has not yet been determined (Figure 1E).

3.5. Gender

Gender differences in thermoregulation are mainly explained by the differences in body characteristics and endocrinal physiology (26, 100). In general, yet with large individual differences, women have a larger surface to mass ratio, which implies that women are more prone to heat loss (100). On the other hand, women have a higher whole body and subcutaneous fat content than men, which in turn increases insulation (26, 64). Interestingly, in men, increased body fat is associated with lower proximal skin (torso and abdomen) temperatures and higher distal (hand and foot) temperatures (71, 72). Women are known to have colder skin at distal areas, despite the increased body fat content relative to men (101). Part of this effect can be attributed to reproductive hormones and the menstrual phase (102). Progesterone levels increase during the luteal phase, and cause an increased internal threshold temperature for vasodilation and sweating (102, 103). As a consequence, the extremities remain colder, more body heat is preserved and core body temperature rises. Vice versa, increased estrogen during the follicular phase decreases the threshold for vasodilatation, which causes increased distal temperature and lowers core temperature.

Unfortunately these shifts in CIZ cannot be directly translated to shifts in the TNZ. A longitudinal study showed that in lightly dressed early pregnant women (i.e. prolonged high threshold for vasodilation) their TNZ was not statistically different from their post-partum follicular-phase (low threshold for vasodilation) TNZ (57). This suggests that there is no shift in the TNZ due to a change in sex hormones. However, during pregnancy, as the metabolic rate of the fetus and mother increased, there was a marked decrease in ambient temperature to reach TNZ (26.64˚C ±0.64˚C at week 8 vs. 22.67˚C ±0.58˚C at week 36).

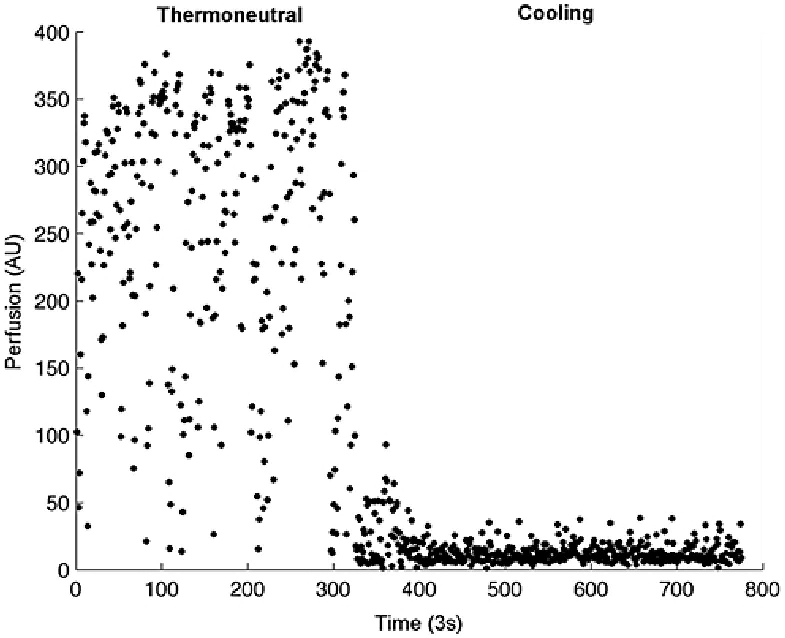

Figure 2. Recording of skin perfusion at glabrous skin of the hand (palm). In thermoneutral conditions perfusion fluctuates between vasoconstriction and vasodilation, yet neither state dominates. In a cool condition vasoconstriction dominates.

Relative to men, thermoregulatory responses to cold and heat are shifted to higher body temperatures (104). Also women are reported to initiate sweating at higher heat loads than males (105, 106). Because of intrinsic gender related differences in body characteristics these internal temperature thresholds cannot be translated directly into changes within the TNZ. Nevertheless, semi-nude women are reported to increase metabolic heat production already when air temperature is decreased below 31˚C, whereas in men the LCT was 28.5˚C (18). Thus in general, relative to men, the thermoneutral zone of women is shifted upward. It is not yet known whether the width of the TNZ is affected.

4. PRACTICAL CONSIDERATIONS AND FUTURE DIRECTIONS

Due to the complex interactions of factors that influence the TNZ it is often difficult to make an *a priori* definition of the thermoneutral zone for any individual subject. When designing an experiment it would be much more practical to define an approximate thermoneutral environment based on the average subject characteristics (e.g. slightly warmer environment for women than for men), and actually measure during a test whether a subject is indeed within the thermoneutral zone. The environmental conditions can then be adjusted to the needs of the individual subject. This concept is used in some human studies (56, 57) and also in animal (rat) thermo-physiology (13, 17). For instance, the study of Hartgill *et al.* (2011) was conducted in a climatic chamber, which allowed for temperature adjustment to each subject. However, most metabolic studies do not use this concept, which might significantly affect the outcome of experiments. For instance, in nutrition it has been reported that resting metabolic rate (while in fasting condition) of clothed female subjects (wearing a thin cotton trouser suit) was higher at 22˚C than at 28˚C (4.329±0.152 kJ min^{-1} vs. 3.899±0.122 kJ min^{-1} respectively). However, after consumption of a meal no difference in resting metabolic rate was observed anymore (107). The author reasoned that before the meal, part of the capacity for diet-induced thermogenesis (DIT) was already used to maintain thermal balance at 22˚C (i.e. cold induced thermogenesis). Further, after the meal, the full capacity for facultative thermogenesis was reached both at 22˚C and 28˚C. Calculation of DIT is performed relative to the baseline resting energy expenditure. Hence, when only measurements at 22˚C would have been observed, there would have been a significant underestimation of the diet-induced thermogenesis. Since most metabolic studies do not incorporate the effects of TNZ-shifts, part of the high variability observed in diet-induced thermogenesis may be attributed to these temperature artifacts.

Relatively simple techniques exist to measure whether a subject is in its TNZ. The basic assumption is that in the TNZ the skin alternates between states of net vasodilation and net vasoconstriction, yet neither state dominates. In a thermoneutral environment blood flow in AVA rich glabrous skin has a characteristic fluctuation with 2 to 3 vasoconstrictions per minute (56). These fluctuations are directly observable by measuring skin blood flow (e.g. by Laser Doppler flowmetry, see Figure 2) or skin surface temperature (13). The major advantage of adopting these criteria for thermoneutrality in humans is that one has an objective criterion to determine whether an individual subject is in the TNZ.

In conclusion, to study temperature-induced responses in different groups (male vs. female; lean vs.

obese), both groups should be relatively equidistant from their thermoneutral zone.

Further research is warranted to measure the effects of age, gender and obesity on the TNZ. The practical impact of these studies can be widespread from individual health to increased productivity and energy conservation in buildings. For instance, in elderly even a mild cold environment can contribute to health problems (108, 109). The same accounts for elderly in warm conditions (110). Precise knowledge of the TNZ is therefore especially important for those elderly that live in care houses.

Although there is some evidence that the lower critical temperature (LCT) of the TNZ is shifted upward in females vs. males, it is not known whether the UCT is also shifted upward. This is important to know, because TNZ differences between males and females could contribute to large variations observed in metabolic or nutritional studies (1, 107).

For obese subjects experimental results showed that the LCT is lowered with increased adiposity (60). Recently it has been suggested that effects of cold exposure on body weight could be studied in context of possible health strategies to tackle obesity (67). For such studies, precise knowledge of the TNZ is warranted. Moreover, since ambient temperature greatly influences the productivity of workers, with an optimum productivity in the TNZ (111), obese subjects might need cooler temperatures for optimal performance relative to their lean counterparts.

5. CONCLUSIONS

For each individual the thermoneutral zone is influenced by factors such as body composition, clothing, energy expenditure, age and gender. Therefore, the thermoneutral zone varies between conditions and between individual subjects. Metabolic studies in which thermoregulatory responses affect the outcome should incorporate individual variations of the thermoneutral zone in study designs. Otherwise, biased study results may cause invalid conclusions. This implies that for sound comparison between subjects, the environmental conditions should be attuned to each individual. Characteristic fluctuations in glabrous skin blood flow can be further explored as an objective criterion to measure whether a subject is within the thermoneutral zone. Already slight deviations from the thermoneutral zone may affect health and productivity. Therefore further research on the thermoneutral zone is warranted, especially for the obese and elderly.

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Abbreviations: AVA: Arterio venous anastomose, BMR: Basal metabolic rate, CIZ: Core interthreshold zone, DIT: Diet induced thermogenesis, LCT: Lower critical temperature, SFT: Subcutaneous fat thickness, TNZ: Thermoneutral zone, UCT: Upper critical temperature

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Send correspondence to: Boris Kingma, Maastricht University, Department of Human Biology, Universiteitssingel 50, P.O. Box 616, NL-6200 MD Maastricht, Tel: 31 043 388 42 60, Fax: 31 0 43 367 09 76, E-mail: B.Kingma@maastrichtuniversity.nl

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