Individualized model of human thermoregulation for the simulation of heat stress response

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Havenith, George. Individualized model of human thermoregulation for the simulation of heat stress response. J Appl Physiol 90: 1943–1954, 2001.—A population-based dynamic model of human thermoregulation was expanded with control equations incorporating the individual person’s characteristics (body surface area, mass, fat%, maximal O2 uptake, acclimation). These affect both the passive (heat capacity, insulation) and active systems (sweating and skin blood flow function). Model parameters were estimated from literature data. Other data, collected for the study of individual differences [working at relative or absolute workloads in hot-dry [45°C, 20% relative humidity (rh)], warm-humid [35°C, 80% rh], and cool [21°C, 50% rh] environments], were used for validation. The individualized model provides an improved prediction [mean core temperature error, \(-0.21 \rightarrow -0.07°C (P<0.001)\); mean squared error, \(0.40 \rightarrow 0.16°C, (P<0.001)\)]. The magnitude of improvement varies substantially with the climate and work type. Relative to an empirical multiple-regression model derived from these specific data sets, the analytical simulation model has between 54 and 89% of its predictive power, except for the cool climate, in which this ratio is zero. In conclusion, individualization of the model allows improved prediction of heat strain, although a substantial error remains.

NUMERICAL MODELS of human responses to heat and cold exposure are widely used to predict the risk of exposures or to evaluate preventive measures [changes to the climate, protective clothing]. Some of these models are empirical (1, 6), others are restricted to heat balance calculations (22) or include a thermoregulatory system with sweating and blood flow regulation (4, 41, 45), and some include detailed physics of clothing (27, 44). The validity of the predictions by these models is dependent on the combination of the climate, clothing, and workload for which they were designed. Most calculate the body core temperature (Tco) for the given conditions and exposure time and use this as an indicator for the risk of the exposure. All models are population based. Hence, they calculate the predicted average response of the population. In the actual use of these models, an important problem became apparent; e.g., when actual work places were evaluated, it was shown that, according to the heat stress assessment model ISO 7933, many conditions in the mining industry were well above the model’s safety limits (25, 24). However, at these workplaces few problems were encountered. One of the possible explanations is that workers at these locations are fitter than average and also acclimated, resulting in a lower strain (i.e., Tco) for the same climatic stress compared to the average population. For a proper assessment of the risks in such a case, an individualized model would be needed. Most models do not have an option to individualize the inputs (5, 22, 27), and in those that have, the possibilities are limited or have received limited validation (41).

The intention of the present paper is to review individual aspects of thermoregulatory response, to incorporate these in an analytical simulation model, and to determine whether this actually improves the prediction of heat stress responses in various conditions. These conditions were chosen to represent the typical experimental paradigms used in thermal physiology, both for climates (cool, hot-dry, warm-humid), which challenge different parts of the thermoregulatory system, and for work (heat production) conditions [workloads relative to maximal O2 consumption (V\(\dot{O}_2\) max) vs. fixed loads]. Model parameters will be estimated based on data from the literature. For validation, data sets not used for the derivation of model parameters will be used.

The value of this model development should be two-fold: it allows for a test of the theories developed over the years regarding relevance of individual characteristics and, if successful, should provide an improved prediction tool.

SELECTION OF A MODEL

It was decided to select an existing analytical model as the starting point for this study. Because the properties of the model itself (number of compartments, solution method) were not the focus of study, but rather the possibility to individualize it, and because the study was limited to heat stress, the choice was made for a readily available two-node model of temperature regulation (5) that had been expanded with a detailed clothing section (27). However, the principles discussed in this paper can be applied to other, more complex, models as well, and the observed effects should be similar.

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THE ORIGINAL MODEL

The model used as a starting point was described by Lotens (27). It comprises a physiological part based on the Gagge model but was introduced by Lotens (27). It consists of a two-node model and a physical model describing the heat transfer characteristics of clothing (27). The physiological model contains a number of control functions for physiological processes as well as the heat transfer properties of the human body. The principle is represented in Fig. 1. Core, skin, and mean body temperatures are used as input for several set-point-defined feedback loops controlling effector responses (skin vasoconstriction/dilation, sweat production, shivering). The effector responses together with metabolic heat production (basal + work) result in a certain heat loss or gain, which then affects the “passive” system (the body), resulting in a new body temperature (i.e., the feedback). The relation between effectors and resulting body temperature is affected by environmental parameters (heat transfer properties) and heat production levels (activity). The passive system itself is defined in terms of heat capacity, mass, and surface area, which are constants in the original model (27).

Two-node model: The nodes represent the body core and the body shell, the core being the compartment with the regulated and defended temperature, the shell being the buffer between core and environment, whose temperature is determined by the heat exchanges with the core and with the environment. Lotens (27) converted this into a five-node model by dividing the skin node into a clothed versus an unclothed part and these into a radiated area and a nonradiated area. Heat transfer may be different in these areas, but control characteristics are identical, and in the current study the distinction is irrelevant.
In performing simulations, the original model expects as inputs a time sequence of the climatic parameters (temperature, humidity or vapor pressure, wind speed, and additional radiation between environment and skin, e.g., fire or sun), the clothing parameters (heat and vapor resistance, ventilation, and radiation properties), and the person's activity level (expressed as the external workload and the metabolic rate, excluding the additional effect due to shivering, which is generated by the model itself). The main model output is the resultant body temperature ($T_{co}$ and skin temperature). Any other variables (skin blood flow, sweat rate, etc.) can also be requested as output. The standard iteration interval used is 1 min.

Considering the above-mentioned input parameters, it is obvious that the model does not discriminate between different individuals when performing a simulation. It will produce the same output, based on parameter estimations on a population level, whether the subject is small or big, fit or unfit, acclimated or not. Individual differences may affect the control system as well as the passive system. Thus, to improve the model's performance for individuals, changes and additions to the model were made.

**THE NEW MODEL**

**General Description**

Starting with the inventory of interindividual differences in heat stress response by Havenith (9) and a survey of more recent literature on this subject, the model makes several additions and changes to the governing equations of both the passive (mass, heat capacity, etc.) and active (effector responses as sweating) components to "individualize" its response. The new model is schematically represented in Fig. 2.

The main change, compared with the original model, is the increased number of input parameters. Apart from the input of climate, clothing, and activity, the following variables (fixed or absent in the old model) were added: body mass ($m$), body fat layer thickness, body surface area ($A_D$), $V\dot{O}_2$ max, and acclimation state. These can either be entered directly, or the model will help to deduce them from other, often more readily

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**Fig. 2.** Schematic representation of the physiological control system in the new model, the inputs [climate, clothing, activity, mass, fat content, acclimation (Acclim), maximal $O_2$ consumption ($V\dot{O}_2$ max), and body surface area ($A_D$)] and the heat exchanges between body core and environment.
available parameters \( (A_D \text{ from mass and height; fat layer thickness from fat percentage, gender, and age; acclimation state from number of acclimation days}) \).

Apart from adding more input parameters and introducing their effects in the governing equations of the model, some changes to the model’s structure were also made. These concern changes in the calculation of the (variable) size of the core and skin compartments, and elimination of mean body temperature as separate parameter from the control functions. These changes are discussed elsewhere (10).

The changes related to the individualization, or the reason for not changing an item, will be discussed in detail in the following paragraphs.

**Anthropometric Characteristics and Adiposity**

The original model mimics a standard man (1.83 m, 75 kg, 15% fat). To enable the user to adjust the simulation to individual anthropometrics, an input option for the values for mass, height, and adiposity of the subject was added. The effects of these variables among subjects on body surface area, body heat capacity, and core-to-skin heat conductance were incorporated in the manner explained below.

**Body surface area.** With increasing \( A_D \), the area for sweat production will increase. For this reason, the amount of sweat produced by the body is made linearly dependent on \( A_D \) by using the standard subject (75 kg, 1.83 m) with an \( A_D \) of 1.97 \( m^2 \) as a reference. The same approach has been chosen for skin blood flow (more skin area = more flow) and for maximal sweat production and maximal skin blood flow. The proposed equations are

\[
\text{sweat rate} = \text{controller output} \cdot \frac{A_D}{A_D\text{-standard}} \tag{1}
\]

\[
= \text{controller output} \cdot \frac{A_D}{1.97}
\]

\[
\text{maximal sweat production} = \text{standard man maximum} \cdot \frac{A_D}{A_D\text{-standard}} \tag{2}
\]

\[
= \text{max}_{\text{standard}} \cdot \frac{A_D}{1.97}
\]

For skin blood flow and maximal skin blood flow, identical equations apply.

**Body heat capacity.** Body heat capacity, relevant for determination of the magnitude of the body temperature change at a certain heat storage rate, is determined by body mass and the specific heat of body tissue. The specific heat of body fat amounts to 2.51 \( J/g \), whereas that of the other tissues (skin, skeleton, muscle, etc., combined) is on average 3.65 \( J/g \) (41). For the calculation of body temperature changes, the following equation for the specific heat of body tissue \( \left( c_b \right) \) is used

\[
c_b = \left( \frac{\text{fat mass}}{\text{body mass}} \right) \cdot 2.51 + \left( \frac{\text{body mass} - \text{fat mass}}{\text{body mass}} \right) \cdot 3.65 \tag{3}
\]

\[
\left( J \cdot g^{-1} \cdot °C^{-1} \right)
\]

Because the distribution of fat over skin and core compartment shows a strong variation among subjects (for which no predictor is available) and over thermal conditions (depending on the change in relative size of the core vs. the skin compartment), this specific heat value is taken as equal for both segments.

**Core-to-skin heat conductance.** The resistance to heat transport from the body core to the skin is formed by the body shell. This consists of muscle, fat, and skin. The muscles are enclosed in the core segment once they become well perfused as in exercise. When the shell is vasoconstricted, the heat flow from core to skin is mainly by conductance. When blood flow through these tissues increases, a convective component is added to the heat flow. In the original model, core-to-skin heat conductance is independent of adiposity and only dependent on thermally regulated skin blood flow. This was deemed to be an oversimplification in respect to the goal of this study. By combining data from different sources (31, 36, 37, 42, 43), a general model for tissue conductance or resistance can be developed.

**FAT LAYER.** Individuals’ shell insulation shows a good correlation with the subcutaneous fat thickness, giving an insulation of 0.0048 \( m^2 \cdot °C \cdot W^{-1} \) per millimeter of fat thickness (43) in addition to an insulation of 0.0022 \( m^2 \cdot °C \cdot W^{-1} \) per millimeter of skin (31, 37, 43). Toner et al. (42) also observed a relation between total body mass and shell conductance, with large, heavy subjects having a lower conductance. Their groups, though having equal fat percentages, differed in mass and total skinfold thickness. The latter parameter, and not the actual mass, may be the cause of the observed effect.

**MUSCLE LAYER.** When vasoconstricted, the muscle layer forms a substantial part of the core-to-skin insulation (60–80%, measured in relatively lean subjects; Ref. 37). When a person becomes active, the perfusion of the working muscle increases strongly, and the muscle contribution to the shell insulation is extremely reduced. Increases in work rates in respective experiments correlated well with reductions in shell insulation (31, 37, 43). At high activity levels (>10 times basal metabolic rate), the shell insulation is between one-fifth and one-tenth of the maximal (0.05 \( m^2 \cdot °C \cdot W^{-1} \)) insulation value (37).

In the old implementation of core-to-skin resistance in the model, as mentioned earlier, no relation with body composition was present. Also, metabolic rate had no direct effect on core-to-skin resistance. In the cold, however, muscle and skin blood flow are not necessarily related. From the literature described above, a different representation can be developed with the following characteristics: 1) Increasing work rate and metabolic rate will increase core-to-skin conductance
through the increase in muscle blood flow. Because this blood flow is mainly axial (extremities), there is a correlation with radial heat flow, rather than an actual radial convective heat transport. 2) Skin blood flow in itself will affect core-to-skin conductance through its convective heat transport, which shortcuts the tissue conductive resistances. This was already present in the model. 3) The subcutaneous fat layer thickness represents a constant conductive heat resistance.

These points are incorporated in the new representation of core-to-skin conductance in the model using the data from the given literature, with an emphasis on the paper by Rennie (37). The essentials of the new description are

\[ R_{\text{core to skin}} = \frac{1}{\left( \frac{1}{R_{\text{skin blood flow}}} + \frac{1}{R_{\text{muscle + fat + skin}}} \right)} \quad (4) \]

with

\[ R_{\text{muscle + fat + skin}} = R_{\text{fat + skin}} + R_{\text{muscle}} \quad (m^2 \cdot °C \cdot W^{-1}) \quad (5) \]

Because muscle blood flow as such is not defined in the model but evidently is related to metabolic rate, this factor can be represented as a function of metabolic rate. Skin blood flow is already a parameter in the model, incorporated as a function of body temperature. The other parameters were deduced from the data in the mentioned papers (31, 37, 43), with the assumption that, because of the experimentation in water at critical water temperature, the tissue insulation was maximal and skin blood flow, even during exercise, was minimal. The equations for the three components of core-to-skin resistance put into the model then read

\[ R_{\text{skin blood flow}} = \frac{1}{(\eta \cdot c_{\text{blood}} \cdot SKBF)} \quad (m^2 \cdot °C \cdot W^{-1}) \quad (6) \]

where \( \eta \) is countercurrent heat exchange efficiency, \( c_{\text{blood}} \) is blood heat capacity (J \cdot l^{-1} \cdot °C), and SKBF is skin blood flow (l \cdot m^{-2} \cdot s^{-1}).

\[ R_{\text{muscle}} = \frac{0.05}{1 + \left( \frac{\text{metabolic rate} - 65}{130} \right)} \quad (m^2 \cdot °C \cdot W^{-1}) \quad (7) \]

with 0.05 as maximal muscle insulation and the denominator relating muscle blood flow to energy consumption.

\[ R_{\text{fat + skin}} = (\text{thickness}_{\text{fat + skin layer}} - 2) \times 0.0048 + 0.0044 \quad (m^2 \cdot °C \cdot W^{-1}) \quad (8) \]

The thickness of skin and fat is readily available to model users when they apply the common method of measuring skinfold thickness (preferably an average of >5 sites) for adiposity assessment

\[ \text{thickness}_{\text{fat + skin layer}} = 0.5 \cdot \text{mean skinfold thickness} \quad (mm) \quad (9) \]

If the skinfold thickness is not available, but instead only the body fat percentage is known, the mean skinfold thickness can be derived by using relations between the two (23). For the model, using gender, age, and body fat percentage as input, the sum of seven skinfolds (SF) was derived with these equations, and from this SF the average superficial fat + skin layer thickness was estimated (10).

**Gender and Age**

The gender and the age of the subjects will not be introduced in the model as factors directly affecting thermoregulation. Enough evidence is present in literature (for a discussion, see Refs. 9, 15, and 12) showing that the main influence of age and gender in exercise heat exposure really acts through concomitant differences in aerobic power, fat content, mass, and \( A_D \). Optionally, the user may be given the choice to select gender and age for an individual subject, but in the model this would be translated in a change in aerobic power, fat content, mass, etc. based on epidemiological data of differences in these parameters between genders and ages.

**Sweating control.**

Individual differences in sweat production can be quite large but are reduced when heat stress increases (20). For the modeling of individual differences in sweat output, major parameters are the training level of the subject (18, 32) as well as the level of acclimation (2, 26, 28). Although most textbooks follow the relations between training, acclimation, and sweat rate as presented by Nadel et al. (32), it was decided to reevaluate the literature on this point because the data of Nadel et al. were not as conclusive as suggested by those citing them. The “typical” graphs presented always are from single subjects, and responses from different individuals within a group were often inconsistent. Also, exposures were very short, so a possible time constant of the system would have a strong impact on the observed relation (9). An overview of those references from which quantitative data could be obtained is presented in Table 1.

**Training vs. acclimation.** Several studies have separated the actual training effect from that of heat acclimation alone or the combination of heat and training. Comparison of quantitative effects is difficult, because the size of effects is strongly related to the training loads used (34, 40). Furthermore, relative loads decrease in the process of training and need adjustment for the proper effects to be present. For the interpretation of data for the “maximal sweat rate,” a problem is that usually heat stress tests before and after the treatment (i.e., acclimation) were identical, and thus the treatment may have resulted in a reduced strain in the second test. Thus, although equal or even lower sweat rates may be observed after treatment, actual maximal sweat capacity may have increased.

**SWEAT THRESHOLD.** Considering the results summarized in Table 1, it seems that heat, exercise, and the
combination of heat and exercise all have an effect on the threshold for sweat appearance at the skin surface. Threshold shifts due to exercise training alone (changes in $V_{O2\text{max}}$ of 12–17%) range between 0.1 and 0.4°C, but, considering the numbers of subjects used in different studies, a shift of 0.1°C seems the best consensus. Heat acclimation after exercise training (32, 38) produces an additional threshold shift of 0.12–0.4°C, but, considering the numbers of subjects used in different studies, a shift of 0.1°C seems the best consensus. Threshold shifts due to exercise training alone are only available from Henane and Bittel (17) and amount 0.27°C. Low exercise during acclimation alone are only available from Henane and Bittel (17) and amount 0.22–0.5°C. Threshold shifts due to heat exposure, the main shift in threshold seems to be caused by the heat exposure.

**GAIN.** With respect to the change in gain of the sweat rate-$T_{co}$ relation, observations (Table 1) range from 36 to 67% increase for exercise training, from 0 to 14% for a subsequent heat with exercise regime, and from 54 to 67% for the total of heat + exercise training acclimation. Heat alone (17) results in increased gain in part of the subjects, but an average number could not be obtained from the data. Heat + low exercise (8, 14) results in 0–47% gain increase. Thus training seems the major factor in the gain increase, but heat by itself also has an effect.

For modeling purposes, training and acclimation need an operational definition, which will be considered below.

**ACCLIMATION.** No quantitative data are available on differences of humid vs. dry heat acclimation on thresholds and gains of the sweat system nor on the effects of different stress levels (e.g., 30°C and 40°C wet bulb globe temperature). The higher the acclimation load, the higher the expected change in thermoregulatory stability is expected to be. In absence of such data, it was chosen to operationalize acclimation in the model as a simple parameter: the number of acclimation days [exposures to a stressful climate (wet bulb globe temperature)]. The equation for this relation ($Eq. \ 10$) was adapted from Givoni and Goldman (7) and Neale et al. (33).

**TRAINING.** For a training effect on the regulation characteristics of sweating (and skin blood flow) to be present, an actual increase in $V_{O2\text{max}}$ has to be observed. Thus the absolute value of $V_{O2\text{max}}$ by itself (a sum of genetic and training influences) does not have to be a valid parameter for the “acclimation-like” effects of exercise training. However, on a population basis, a strong correlation of $V_{O2\text{max}}$ with heat tolerance has been observed (34, 35), and it seems fair to use $V_{O2\text{max}}$ (expressed in ml·kg$^{-1}$·min$^{-1}$ for separa-

### Table 1. Overview of data relating to the effect of training and acclimation on the sweat rate-$T_{co}$ relation

<table>
<thead>
<tr>
<th>Source</th>
<th>n</th>
<th>Condition</th>
<th>Change in $T_{co}$ Rest, °C</th>
<th>$V_{O2\text{max}}$ Subjects, ml·kg$^{-1}$·min$^{-1}$</th>
<th>Change in $V_{O2\text{max}}$</th>
<th>Sweat Threshold, °C</th>
<th>Sweat Gain</th>
<th>Maximum Sweat Rate, g/h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Henane and Bittel (17)</td>
<td>12</td>
<td>Rest + heat</td>
<td>−0.2</td>
<td>?</td>
<td>↓ −0.29</td>
<td>↑ (in 50% subjects)</td>
<td></td>
<td>520 → 800 (+54%)</td>
</tr>
<tr>
<td>Wyndham (47)</td>
<td>13 vs. 353</td>
<td>Exercise + heat</td>
<td></td>
<td>Apprentice miners vs. miners</td>
<td>↓ −0.5 (between groups)</td>
<td>+67%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kobayashi et al. (26)</td>
<td>6</td>
<td>Exercise training (75%$V_{O2\text{max}}$)</td>
<td>38.1 → 44.7 +17%</td>
<td>Heat</td>
<td>↑ +0%</td>
<td>+67%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nadel et al. (32)</td>
<td>6</td>
<td>(50%$V_{O2\text{max}}$) + heat</td>
<td></td>
<td></td>
<td>↓ −0.3</td>
<td>+67%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Henane and Valatx (19)</td>
<td>9</td>
<td>Rest + heat</td>
<td>−0.4</td>
<td>40.9 → 48.3 +18%</td>
<td>↓ −0.1–0.4</td>
<td>+60%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Henane et al. (18)</td>
<td>3</td>
<td>Exercise</td>
<td></td>
<td></td>
<td></td>
<td>+14%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shvartz et al. (40)</td>
<td>10</td>
<td>Exercise (50%$V_{O2\text{max}}$) + heat</td>
<td>41</td>
<td>ns</td>
<td>−0.49</td>
<td>+47%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gonzalez et al. (8)</td>
<td>6</td>
<td>Low exercise</td>
<td></td>
<td></td>
<td>−0.5</td>
<td>+36%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roberts et al. (38)*</td>
<td>8</td>
<td>Exercise training (75%$V_{O2\text{max}}$)</td>
<td>42.7 → 47.7 +12%</td>
<td>Heat only</td>
<td>−1.7%</td>
<td>+14%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heaney et al. (16)</td>
<td>10</td>
<td>Heat + low exercise (33%$V_{O2\text{max}}$)</td>
<td>48</td>
<td>ns</td>
<td>+25% (at lower $T_m$)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Havenith and van Middendorp (14)</td>
<td>4</td>
<td>Heat + low exercise (constant strain)</td>
<td>54</td>
<td>ns</td>
<td>↓ −0.25</td>
<td>=</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$T_{co}$, body core temperature; $n$, no. of subjects; $V_{O2\text{max}}$, maximal O$_2$ consumption; ns, not significant; ↓, decreased; ↑, increased; →, changed to. *Data recalculated to exclude apparent outlier.
tion from the mass effect) as an indicator for training- and aerobic power-induced effects on the sweat rate-Tco relation.

The aerobic power level of the subjects used in the training experiments of Table 1 ranged between 38.1 and 42.7 ml·kg⁻¹·min⁻¹ (below average to average; Ref. 29) before training. The level increased after training to average or above average. Over all experiments, the starting aerobic power level of all subjects ranged from below average to good. When considering the studied effects over a larger population, one may expect a wider distribution in aerobic power levels, and thus the differences in associated thermoregulatory responses are likely to be larger than observed here. Therefore, the model will use this range as a linear scaling factor for changes outside this range of V˙O₂ max values. The practical implementation of the effects of aerobic power and heat acclimation on the model's sweat control function is illustrated in Fig. 3A. The V˙O₂ max range used for having an effect on the sweat rate-Tco relation is arbitrarily chosen to be 20–60 ml·kg⁻¹·min⁻¹.

For the threshold shift related to V˙O₂ max, a number of 0.1°C was derived from Table 1 for a 10 ml·kg⁻¹·min⁻¹ range. For the full range (40 ml·kg⁻¹·min⁻¹), this is extended to 0.4°C. For the gain change, the increase seen in Table 1 of 36–67% for the 10 ml·kg⁻¹·min⁻¹ range was extended to 200% for the full range (double from unfit to fit). Taking the aerobic power average of 40 ml·kg⁻¹·min⁻¹ as a reference (18- to 45-yr average; Ref. 29), this leads to the following training and acclimation based adjustments in the governing equations, which modify threshold and gain

$$acclim = 1 - e^{-0.3 \cdot (\text{number of acclimation days} - 1)} \quad (10)$$

$$fit = VO_2_{max} - VO_2_{max-standard} = VO_2_{max} - 40 \quad (11)$$

$$\text{threshold} = \text{threshold}_{standard} \cdot \left( \frac{\text{fit}}{10} \right) \cdot 0.1 - \text{acclim} \cdot 0.25 \quad (°C)$$

$$\text{gain} = \text{gain}_{standard} \cdot \left( 1 + \frac{\text{fit}}{20} \cdot 0.35 \right) \cdot (1 + \text{acclim} \cdot 0.15) \quad (g \cdot m^{-2} \cdot h^{-1} \cdot °C^{-1}) \quad (13)$$

For maximal sweat rate (MSR), a difference of 100% between unfit, unacclimated, and fit, acclimated was arbitrarily chosen (doubling from unfit, unacclimated to fit acclimated), mainly on the basis of data from methacholine injection studies (21) and studies comparing medium-fit, unacclimated subjects with fit, acclimated subjects (Ref. 47; Table 1)

$$MSR = MSR_{standard} \cdot \left[ 1 + \left( \frac{\text{fit}}{20} \cdot 0.25 + \text{acclim} \cdot 0.25 \right) \right] \quad (g \cdot m^{-2} \cdot h^{-1}) \quad (14)$$

with MSR_{standard} = maximum for unacclimated

$$40 \text{ ml·kg}^{-1} \cdot \text{min}^{-1} \cdot \text{person}$$

### Skin Blood Flow

Regulation of skin blood flow was studied by using data from plethysmography and core-to-skin conductivity. Extremity blood flow is regarded as indicative and representative for total body skin blood flow and provides a more direct measure than core-to-skin conductivity does.

Data on the effect of training and acclimation on skin blood flow are limited and often conflicting. Acclimation results in a reduced core temperature threshold for forearm, hand, chest, and ear vasodilation (8, 38). Also maximal conductance measured at the chest increases (8). Besides increased vasodilation, venoconstrictor tone also increases in the first days of acclimation. Comparisons before and after acclimation do not show changes in skin blood flow, however. This may be due to the same requirement of heat transfer from core to skin, although the actual core and skin temperatures (strain levels) are lower. Also, venous tone is strongly affected by nonthermal influences.

Wyndham (46) studied the effect of acclimation (with exercise) during extreme heat exposure. With this maximal stimulus, forearm blood flow increased from 14 to 26 ml·100 ml⁻¹·min⁻¹. Roberts et al. (38) provided quantitative data on threshold and gain of the forearm blood flow-Tco relation. They observed a reduction in threshold for vasodilation of 0.2°C by exercise (V˙O₂ max: 42.7 → 47.7 ml·kg⁻¹·min⁻¹) and
another reduction of 0.26°C by successive exercise + heat acclimation. The change in gain was less consistent. Exercise training resulted in an average gain increase of 1.3 ml·100 ml⁻¹·min⁻¹°C⁻¹ and subsequent acclimation by heat and exercise in a reduction with 0.8 ml·100 ml⁻¹·min⁻¹°C⁻¹. However, the validity of these gain changes for a generalized model is questionable because different subjects showed very different reactions.

The maximal value of skin blood flow in relation to aerobic power has received little attention in the literature. Because competition exists during heat stress between blood flow for supply of nutrients and oxygen to muscles and skin blood flow for core-to-skin heat transport, it is likely that a high maximal cardiac output is a good indicator for the ability to produce and maintain a high skin blood flow. Maximal cardiac output is strongly related to VO₂ max (3). Thus it seems reasonable to relate maximal skin blood flow in the model to aerobic power. Acclimation will have an effect on maximal skin blood flow because of its stabilizing effect on circulation. However, the size of this effect is smaller than that of aerobic power.

In absolute terms, maximal skin blood flows of ±240 l·m⁻²·h⁻¹ have been observed (39), but this was for passive subjects, with values for exercising subjects being much lower because of competition for blood flow by the muscle. For forearm blood flows, maxima above 30 ml·100 ml⁻¹·min⁻¹ have been observed in exercising supine subjects. For seated or upright subjects, the maxima went down to below 20 ml·100 ml⁻¹·min⁻¹ (30). In the original model, the basal skin blood flow rate is 6.3 l·m⁻²·h⁻¹ with a maximum of 90 l·m⁻²·h⁻¹, the latter seeming quite low. Skin blood flows measured with plethysmographic techniques are ~1 ml·100 ml⁻¹·min⁻¹ at rest and on average 15 ml·100 ml⁻¹·min⁻¹ at maximum during work in the heat. These are similar ratios as in the model. The maximal skin blood flow between subjects of different aerobic power levels usually ranges between 10 and 20 ml·100 ml⁻¹·min⁻¹ (13). Thus, translated to model units, the maximum, assuming working subjects, should range from 60 to 120 l·m⁻²·h⁻¹ for different aerobic power levels, with a mean of 90 l·m⁻²·h⁻¹ at an average aerobic power.

For the model, equations graphically represented in Fig. 3B were used. For the threshold shift, considering the limited amount of data, an analogy with the threshold shift due to training for sweating was chosen, resulting in a relation as described in Eq. 12. For the gain, no effect was introduced because of the inconsistency in the data. For maximal skin blood flow (MSKBF) the effects of aerobic power and acclimation were formulated as follows

\[
\text{MSKBF} = \text{MSKBF}_{\text{standard}} \cdot \left[1 + \frac{\text{fit}}{60} + \text{acclim} \cdot 0.15\right] \quad (\text{l·m}^{-2} \cdot \text{h}^{-1})
\]

with \(\text{MSKBF}_{\text{standard}} = \text{maximum for unacclimated}\)

\[40 \text{ ml·kg}^{-1} \cdot \text{min}^{-1} \cdot \text{person}\]

**DISCUSSION**

When evaluating the present model, one should keep in mind that most parameters were derived from population average-based studies. Typically, studies used would compare subject groups differing only on one parameter, while all other characteristics were matched, whereas subjects in the validation data sets differed on many characteristics at the same time. Also, for the description of some parameters (e.g., VO₂ max effect), inferences were made for differences between subjects that were based on data observed when that parameter changed within a subject (training). Given the available data, there is no alternative available for this at the moment, and the reasoning behind the inferences is presented with the actual data.

**Sensitivity**

Results for the improvement of the model will be presented for the full model, including all aspects of individualization. To provide an indication of the sensitivities of the model to the various individual characteristics, simulations were performed using the 5th and 95th percentile of each of the characteristics of the subject group used for validation (Table 2) and are presented in Table 3. Sensitivities for relative (Rel) vs. absolute (Abs) workloads are, as is to be expected, identical for all parameters except VO₂ max. The anthropometric parameters (i.e., the passive system) have a low impact in a cool climate (Co; 20°C, 50%). Mass and A_d have the highest impact overall, and fat has a high impact in the warm humid (WH; 35°C, 80%) climate only. Where evaporative heat loss is not restricted [hot dry (HD); 45°C, 20%], A_d has the highest effect. Where heat loss is restricted, mass and fat content play the bigger role, representing the “size” of the heat sink. Increasing VO₂ max has a high impact in lowering body temperature when evaporation is not limited and work rates are equal for all (HD/Abs) but has no effect in HD when the work rate is relative to VO₂ max.

In WH, with a limited evaporation, a high VO₂ max is still beneficial when work rates are equal (WH/Abs) but has a strong detrimental effect when work rates are relative (WH/Rel). In that case, because of the limited cooling power in that climate, the higher absolute workload is not compensated by the better heat loss capacity. Because of its effect on sweat production, acclimation has the highest impact in HD and a lower impact in WH, again related to sweat evaporation capacity of the climate. All these principles, including the reversal of the VO₂ max effect depending on the condition, have been observed in the real data set as well (11), except for the effect of VO₂ max in the Co climate, which was not significant in the real data. This may explain the low predictive power of the model for that condition.

**Validation Methods**

With all the listed changes incorporated in the model, the question needs to be answered whether the
changes actually lead to an improvement of the prediction results on an individual basis. For this purpose, both the original and new model’s predictions for individual heat stress responses were evaluated with the use of data sets from our laboratory. These data sets had not been used in the design of the new model and are therefore independent. The experiments for these data sets were specifically designed for the study of individual characteristics and their interactions with climate and work type. Subject groups were selected to show a wide variation in individual characteristics (contrary to most experiments, in which subjects are matched for all but one characteristic), and typical paradigms for the study of thermal responses were used for both climate (Co, WH, HD; stressing different parts of the thermoregulatory system) and work type (Rel, Abs; Refs. 11–13, 15). An overview of the subjects’ characteristics in these data sets is presented in Table 2.

The validation was performed by using data for body core (rectal) temperature. The original model, without individualization, produced a single mean response for all subjects per condition. For the new model, for each subject and condition, a separate simulation run with the actual data for climate, external work rate, V\textsubscript{O2} max, body mass, height, body fat content, and acclimation status was performed. Acclimation was set to zero for all subjects and was thus not a part of this validation. The approach used for heat acclimation in the current model has been evaluated before by Neale et al. (33) with good results, and repetition was not deemed necessary.

The validation of the new model with the data sets mentioned resulted in 181 (3 \times 24 + 80 + 29; see Table 2) simulation runs. Simulations followed the same pattern as the actual experiments, starting with a 30-min rest period and then moving on to 60 min of exercise (Table 2). The model’s performance will be discussed for the new vs. original model, for the new model on its own (the individualization), and for the new model vs. a regression model that was based on the data sets used for the evaluation (11). It was chosen to evaluate how the individualization resulted in discrimination between subjects’ heat tolerance as defined by the response measured at the end of the exposures, rather than analyzing the dynamics of the response. The dynamics are considered to be more related to the general model used than to the individualization, and even when the subjects would not have achieved a steady state after the 90-min exposure, their ranking in terms of heat (in)tolerance is not expected to change thereafter. It is this ranking that is considered most relevant to test the model’s individualization.

Parameters used for the quantitative validation are (1) the mean of the difference (error) between computed and real output values at the end of the exposure and

### Table 2. Description of methods of the 5 experiments used for the validation

<table>
<thead>
<tr>
<th>Condition</th>
<th>Rel (HD, WH, and Co)</th>
<th>WH/Abs</th>
<th>HD/Abs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature/humidity/wind</td>
<td>WH: 35°C; 80%; &lt;0.2 m/s</td>
<td>35°C; 80%; &lt;0.2 m/s</td>
<td>45°C; 20%; &lt;0.2 m/s</td>
</tr>
<tr>
<td>Workload regime</td>
<td>30 min at rest, followed by 30-min work at 25% V\textsubscript{O2} max, and 30-min work at 45% V\textsubscript{O2} max</td>
<td>30 min at rest, followed by 60 min at 60 W</td>
<td>30 min at rest, followed by 60 min at 60 W</td>
</tr>
<tr>
<td>Subjects</td>
<td>n = 24 \times 3 conditions; 12 men and 12 women in each climate</td>
<td>n = 80; 57 men, 23 women</td>
<td>n = 29; 14 men, 15 women</td>
</tr>
<tr>
<td>Age</td>
<td>22.9 ± 2.4</td>
<td>25.7 ± 4.6</td>
<td>23.1 ± 3.0</td>
</tr>
<tr>
<td>Mass, kg</td>
<td>70.6 ± 8.1</td>
<td>71.2 ± 13.0</td>
<td>69.3 ± 12.6</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.78 ± 0.08</td>
<td>1.79 ± 0.10</td>
<td>1.77 ± 0.11</td>
</tr>
<tr>
<td>A\textsubscript{D}, m\textsuperscript{2}</td>
<td>1.88 ± 0.14</td>
<td>1.89 ± 0.20</td>
<td>1.85 ± 0.21</td>
</tr>
<tr>
<td>V\textsubscript{O2 max}, l/min</td>
<td>2.96 ± 0.56</td>
<td>3.66 ± 0.88</td>
<td>3.09 ± 0.66</td>
</tr>
<tr>
<td>V\textsubscript{O2 max}, l\textsuperscript{-1}kg\textsuperscript{-1}</td>
<td>42.0 ± 7.0</td>
<td>51.2 ± 7.9</td>
<td>44.6 ± 4.9</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>23.0 ± 7.5</td>
<td>16.8 ± 6.8</td>
<td>20.2 ± 8.6</td>
</tr>
</tbody>
</table>

Values are means ± SD. Rel, workload relative to individual V\textsubscript{O2} max; Abs, same absolute workload for all; HD, hot dry climate [45°C, 20% relative humidity (rh)]; WH, warm humid climate [35°C, 80% rh]; Co, cool climate [21°C, 50% rh]; A\textsubscript{D}, body surface area.

### Table 3. Sensitivity of the model’s T\textsubscript{co} prediction for changes in the main individual characteristics

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mass, kg</th>
<th>Fat, %</th>
<th>A\textsubscript{D}, m\textsuperscript{2}</th>
<th>V\textsubscript{O2 max}, l\textsuperscript{-1}kg\textsuperscript{-1}</th>
<th>Acclimation, days</th>
</tr>
</thead>
<tbody>
<tr>
<td>5th–95th percentile</td>
<td>53.6–89.2</td>
<td>8.8–32.9</td>
<td>1.6–2.2</td>
<td>30.9–56.1</td>
<td>0–15*</td>
</tr>
<tr>
<td>Co/Rel</td>
<td>-0.13</td>
<td>+0.18</td>
<td>-0.22</td>
<td>+0.95</td>
<td>-0.26</td>
</tr>
<tr>
<td>WH/Rel</td>
<td>-0.61</td>
<td>+0.61</td>
<td>-0.55</td>
<td>+1.47</td>
<td>-0.17</td>
</tr>
<tr>
<td>HD/Rel</td>
<td>-0.43</td>
<td>+0.19</td>
<td>-0.67</td>
<td>-0.14</td>
<td>-0.44</td>
</tr>
<tr>
<td>WH/Abs</td>
<td>-0.61</td>
<td>+0.61</td>
<td>-0.55</td>
<td>-0.39</td>
<td>-0.17</td>
</tr>
<tr>
<td>HD/Abs</td>
<td>-0.43</td>
<td>+0.19</td>
<td>-0.67</td>
<td>-0.94</td>
<td>-0.44</td>
</tr>
</tbody>
</table>

Numbers represent change in T\textsubscript{co} when a parameter is changed from the 5th percentile value of the population in the validation data set to the 95th percentile, keeping all other parameters constant. *For acclimation, the full range available in the model was used.
the mean squared error; both compared for old vs. new
model (paired \( t \)-test and Wilcoxon signed rank test for
related samples); 2) the correlation (both Pearson and
Spearman rank order) between the computed and the
real output values; and 3) the differences in explained
variance (\( r^2 \)) between simulation and regression model.

Validation Results

New vs. old model. In Table 4, the performance of the
original model (27) vs. that of the new model is illus-
trated on the basis of the mean values for the predic-
tion error in Tco of the models (computed minus mea-
sured value) for each condition. These numbers in
Table 4 clearly show a reduction in the mean error in
Tco. Thus the average systematic under- or overestima-
tion (mean error) by the new model, including all
changes, is smaller. These improvements are statisti-
cally highly significant \( (P < 0.001) \) for all data lumped,
as well as for three out of five of the different experi-
ments. For the other two conditions, WH/Rel and HD/
Abs, no significant change was observed. For the latter
condition, the systematic error was negligible for both
old and new model. From this it can be concluded that
the performance of the new model has improved com-
pared with the original model. Quite a substantial
error in individual predictions remains, however, as
can be seen in Table 4 and in the graphic presentation
of the old and new model’s results in Fig. 4.

Individualization (new model). Although the perfor-
mance of the new model represented by the mean error
has improved compared with the old one, this improve-
ment is not necessarily due to individualization. The
mean error may have improved because of a lower
systematic error alone, without actually improving the
prediction of an individual’s deviation from the group
mean. The latter can be studied in two ways: first by
looking at the correlation between computed and mea-
sured points (Fig. 4) and second by looking at the mean
squared error of the prediction, which represents the
quality of individual predictions. The latter (Table 4)
has been significantly improved overall \( (P < 0.001) \) and
in four out of five of the conditions used \( (P < 0.05) \).

The correlations between computed and real data
values are presented in Table 4 (for the old model,
when analyzed per condition, these are 0, because of
the lack of variance within each condition). Correla-
tions were calculated as Pearson correlation coeffi-
cients for continuous data and secondly by using the
presumption that the performance of the model can be
judged on whether it ranks the individuals correctly for
their heat tolerance using a Spearman rank-order cor-
relation test. Table 4 shows that for both criteria the
individual predictive value for the model varies
strongly between conditions. Both correlations are
highly significant overall \( (P < 0.001) \) and also in three
out of five of the conditions simulated. Overall correla-
tion has improved drastically compared with the old
model. Differences between Pearson and Spearman
correlation coefficients are small, indicating that the
rank orders closely follow the continuous data.
New model vs. empirical regression model.

In the papers in which the used data were described (11–13, 15), the data for $T_{co}$ were analyzed for the influence of individual characteristics on the heat stress response, separately for each condition, by multiple linear regression analysis (for the actual constants in the equations, please refer to Refs. 11–13, 15)

$$T_{co} = \beta_1 + \beta_2 \cdot V_{O_2,\text{max}} + \beta_3 \cdot \text{fat}\% + \beta_4 \cdot \text{mass}$$

$$+ \beta_5 \cdot A_D + \beta_6 \cdot A_I/\text{mass} \quad (16)$$

Because all other influences (climate, work) are constant within each of the tested conditions, this regression model analyzes purely the contribution of individual characteristics to the variation in $T_{co}$ response; i.e., all predictive power in the regression models is to be attributed to individual characteristics. It is therefore interesting to compare the analytical computer model’s predictive capacity for these data with the descriptive power of the multiple-regression models. This comparison is presented in Table 5. Column three gives the correlation between predicted values and real values when the regression models (Eq. 16) are used to predict core temperatures. Because this empirical regression model was derived from these specific data sets and from the characteristics of actual participating subjects, the explained variance in these regression models may be considered as the maximum achievable explained variance. In column 4 of Table 5, the $r$ values are given for the prediction of the analytical computer model, which was developed independently of the data sets. Comparison of the two model types ($r^2$ new model/$r^2$ regression) shows that, except for the cool condition, the computer model predicts quite well the variance in the data for $T_{co}$ that could be attributed to individual characteristics (last column in Table 5).

**Overall performance.** The pattern that is visible in both Table 4 and Table 5 is that the individualized model provides significant improvement in body core temperature prediction. For the individual person, the predictions are improved over the old model in all conditions except for the Co and HD/Rel conditions (based on the $r$ values). In general, one may expect this for all those Rel conditions in which the climate does not limit evaporative cooling. Here, differences in heat strain between individuals are drastically reduced when relative workloads (same $\% V_{O_2,\text{max}}$), compared with absolute workloads, are used (15). The smaller the expected differences in actual data, the lower the correlation one can expect to obtain, given the low signal-to-noise ratio in this case. For the WH/Rel condition, however, a good correlation between predicted and observed values is found. In this situation, in which evaporative heat loss is limited, the passive system of thermoregulation (mass, heat capacity, tissue heat resistances) is more important, and this seems to be well represented by the current model. An additional factor in the deficient prediction in the cool climate may be a too-small effect of body fat content on insulation in the model, given that in the multiple-regression model it was adiposity that had the strongest influence in this condition (11). The insulative effect of adipose tissue is in the new model strongly dependent on skin blood flow. In the model, for most subjects, this increases above 30 $l \cdot m^{-2} \cdot h^{-1}$ for the cool condition, which is about one-third of the maximum skin blood flow. In the actual experimental data, the forearm blood flow is for most subjects below 3 ml $\cdot 100 \, ml^{-1} \cdot min^{-1}$, which is about one-tenth of the maximum. Thus the insulative effect in the cool condition may well be underestimated because of a too-high skin blood flow, which may explain the poor predictive effect for that situation.

Apart from the possible causes mentioned above, it should be noticed that a large amount of “noise” is always present when comparing heat stress responses. In the present case, any test-retest difference for an individual would have added to the overall reduction in explained variance. Jette and coworkers (24) have given a detailed report on the day-to-day variation in a person’s response in terms of body core temperature. They found this to be so high that they questioned the use of body temperature responses as indicator of, e.g., clothing insulation differences. Hence, given this noise, the observed explained variances in the present study (except for the Co and HD/Rel conditions) can be considered to be substantial.

In conclusion, the changes and additions to the model have significantly improved the prediction of individual heat strain, be it that the size of the improvement varies with the climate and work type. However, a substantial part of the differences in individual responses remains unexplained, suggesting that the current knowledge of causes for individual differences is far from complete.

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