Why wrapping premature neonates to prevent hypothermia can predispose to overheating

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Agourram B, Bach V, Tourneux P, Krim G, Delanaud S, Libert JP. Why wrapping premature neonates to prevent hypothermia can predispose to overheating. J Appl Physiol 108:1674–1681, 2010. First published March 11, 2010; doi:10.1152/japplphysiol.00799.2009.—Wrapping low-birth-weight neonates in a plastic bag prevents body heat loss. A bonnet can also be used, since large amounts of heat can be lost from the head region, but may provide too much thermal insulation, thus increasing the risk of overheating. We assessed the time required to reach warning body temperature (t_{38°C}), heat stroke (t_{40°C}), or extreme value (t_{43°C}) in a mathematical model that involved calculating various local body heat losses. Simulated heat exchanges were based on body surface temperature distribution measured in preterm neonates exposed to 33°C air temperature (relative air humidity: 35%; air velocity: <0.1 m/s) and covered (torso and limbs) or not with a transparent plastic bag. We also compared metabolic heat production with body heat losses when a bonnet (2 or 3.5 mm thick) covered 10%, 40%, or 100% of the head. Wrapping neonates in a bag (combined or not with a bonnet) does not induce a critical situation as long as metabolic heat production does not increase. When endogenous heat production rises, t_{38°C} ranged between 75 and 287, t_{40°C} between 185 and 549, and t_{43°C} between 287 and 702 min. When this increase was accompanied by a fall in skin temperature, overheating risk was accentuated (37 ≤ t_{38°C} ≤ 45; 99 ≤ t_{40°C} ≤ 117; 169 ≤ t_{43°C} ≤ 194 min). Thus plastic bag and bonnet may result in hyperthermia but only when metabolic heat production rises while skin temperature falls (impeding body heat losses), as can sometimes happen with fever.

hyperpyrexia; overheating; safe body temperature; computer model

since the initial work by Besch et al. (7), it has been considered that an effective method for reducing body cooling consists of wrapping the neonate in a plastic bag. Several studies have shown that this strategy is particularly efficient and reduces skin water loss and oxygen consumption and dampens the decrease in body temperature (3, 5, 19, 25) by providing a microenvironment around the body. Recently, it has been demonstrated that wrapping preterm neonates (i.e., those with gestational ages below 29 wk) in a polyethylene bag prevents a fall in rectal temperature on admission to the neonatal intensive care unit (20, 36, 37). Additional measures include the use of a bonnet, which reduces the heat loss from the surface area of the head. Covering this region is also a simple complement to the application of a plastic bag for the prevention of body heat dissipation, since large amounts of heat are lost to the air through the head’s exposed skin surface area (8, 12, 24, 33, 35). However, the effect of these measures on thermal stress has not been well characterized, and elevated body temperatures observed in neonatal intensive care units are most often related to infections rather than occlusive plastic bags (10, 23, 26, 30). In 2007, a study involving the Neonatal Research Network (21) showed that there is a need for additional work on dissociating the respective affects of infection and occlusive wraps on elevated body temperature that is sometimes recorded on admission to the neonatal intensive care unit. In the present study, we aimed to clarify this point. For ethical reasons, the length of time required to reach a warning threshold (defined as a body temperature value of 38°C; t_{38°C}), heat stroke (a body temperature of 40°C; t_{40°C}), and 43°C (an extreme value; t_{43°C}) is impossible to investigate in human neonates; such extremely hot experimental conditions cannot be safety achieved. Hence, mathematical models of body heat balance have been developed to address this question and to define guidelines. This is particularly important, since the pathological effects of hyperthermia are devastating; in heat stroke, cellular degeneration can occur in all organs (especially the cerebral cortex and cerebellar regions) and may result in severe neurological deficits.

The operation of this type of model depends on assessment of the rates of heat loss from the various segments of the body, to distinguish between the heat transfers involving covered and uncovered skin surface areas. The model needs to be anatomically accurate and should take into account the large interregional differences in local skin temperatures and local heat transfer coefficients, differences that depend on the shapes of each body segment (4). At present, most models evaluate heat losses from the body as a whole (1, 22, 27). Heat transfer coefficients have generally been evaluated in studies performed on adults and cannot be simply extrapolated to low-birthweight neonates. The neonatal body shape and strong segment curvatures give rise to larger heat transfer coefficients than those found in adults.

To limit the number of empirical determinations, we used heat transfer coefficients that were appropriate for the scale of each neonate’s body segment (4). The values of local skin temperature introduced into the mathematical model are of major importance, since they condition all body heat exchanges. The local skin temperatures were measured by infrared thermometry on small birth-weight-neonates in the presence or absence of plastic bag and exposed to a slightly cold environment (such as those potentially encountered during a surgical intervention).

The mathematical model was used to analyze the effects of care practice (use of a plastic bag, with or without a bonnet) in the development of hyperthermia in preterm neonates. In
covered neonates, hyperthermia can occur through a variety of routes: 1) decreased body heat losses due to excessive insulation or heat gain, 2) increased endogenous heat production, which exceeds heat losses, and 3) increased heat production associated with a fall in skin temperature, which impedes heat losses (as is seen in fever). In the model, these parameters can be independently manipulated, so that it is possible to clarify their respective influences on the times required to reach harmful body temperatures.

**METHODS**

*Basic principles of heat transfer.* We developed a multimodal model based on body heat balance that includes metabolic heat production (M) and the various routes of heat loss [by conduction (K), radiation (R), convection (C), and skin evaporation (E)]. In the model, the heat losses are calculated for each of six body segments: the head, the trunk, the two arms, and the two legs. For the calculation of the overall body heat exchange, segmental heat losses were added to the convective (C_{conv}) and evaporative (E_{resp}) heat losses from the mucosa of the respiratory tract. All heat exchanges are expressed in kilojoules per hour per kilogram of the neonate’s body mass (W).

Conductive heat loss depends on 1) the local skin surface area (A_{sk-seg}, m²) of the segment in contact with the mattress, 2) the conductive heat transfer coefficient (h_{c} = 0.84 kJ·h⁻¹·m⁻²) (27), and 3) the temperature difference (in °C) between the skin surface of each body segment (measured by infrared thermometry) and the mattress (T_{m}) in direct contact (T_{sk-seg}). Hence:

$$K_{seg} = h_{c}(T_{sk-seg} - T_{m})A_{sk-seg}W^{-1}$$  \hspace{1cm} (1)

The radiative heat loss is calculated from the Stefan-Boltzmann law:

$$R_{seg} = \sigma \cdot e_{SK} \cdot A_{c-seg} \left(\left(T_{sk-seg} + 273\right)^4 - \left(T_{m} + 273\right)^4\right)W^{-1}F_{ecl}$$  \hspace{1cm} (2)

where \(T_{m}\) is the mean radiant temperature (°C) measured with a black-globe thermometer [as recommended by Standards ISO 7726 (16c)], \(T_{sk-seg}\) is the mean skin temperature (°C; measured by infrared thermometry), \(F_{ecl}\) is the dimensionless reduction factor due to clothing thermal insulation [0.86 for the plastic bag combined with a diaper (5)], \(\sigma\) is the Stephan-Boltzmann constant (10⁻⁸ kJ·h⁻¹·m⁻²·K⁻⁴), \(e_{SK}\) is the skin emissivity (0.97), and \(A_{c-seg}\) is the percentage of radiative skin surface area for the segment.

The convective heat loss from the skin (C_{seg}) depends on the difference between the air temperature and the segment’s skin temperature (T_{sk-seg}):

$$C_{seg} = h_{c-seg}(T_{a} - T_{sk-seg})A_{c-seg}F_{pel}W^{-1}$$  \hspace{1cm} (3)

where \(A_{sk-seg}\) is the segment’s skin surface area (in m²) available for convective heat exchange, \(T_{a}\) is the air temperature and the segment’s segment’s convective heat transfer coefficient (in kJ·h⁻¹·m⁻²·°C⁻¹).

The segment’s skin evaporative heat loss (E_{resp}) equates to:

$$E_{seg} = h_{c-seg} \cdot \left(P_{e,H_{2}O} - P_{a,H_{2}O}\right)A_{c-seg}F_{pel}W^{-1}$$  \hspace{1cm} (4)

where \(h_{c-seg}\) is the segment’s evaporative heat transfer coefficient (in kJ·h⁻¹·mb⁻¹·m⁻²) of 1.67h_{c-seg} (Lewis’s equation), \(w\) is the skin wettedness [assumed to be 0.06 in a cool thermal environment with no sweating activity (14)], \(P_{e,H_{2}O}\) - \(P_{a,H_{2}O}\) is the partial water vapor pressure difference between the segment’s skin surface area and the air (20.10 mb), and \(A_{sk-seg}\) is the segment’s skin surface area (A_{sk-seg} = A_{sk-seg}). \(F_{pel}\), reduction factor of water vapor transfer is 0 for impermeable fabric.

The heat loss from each body segment is the sum of the various modes of heat loss (R_{seg} + C_{seg} + K_{seg} + E_{seg}). Next, the heat loss from the body as a whole was obtained by summing the segmental heat losses and C_{resp} and E_{resp}:

$$C_{resp} = V_{E}C_{p}(T_{E} - T_{i})W^{-1}$$  \hspace{1cm} (5)

$$E_{resp} = V_{E}E_{T} \cdot \delta \cdot \left(M_{E} - M_{i}\right)W^{-1}$$  \hspace{1cm} (6)

where \(C_{p}\) is the heat capacity of air (1.044 kJ·kg⁻¹·°C⁻¹) and T_{E} - T_{i} is the temperature difference between expired (T_{E}) and inspired air (T_{i}, equivalent to the air temperature). \(T_{i}\) is calculated according to the equation recommended by Hanson (15):

$$T_{E} = \frac{(32.6 + 0.066T_{a} + 32P_{a,H_{2}O})}{462(T_{a} + 273)}$$  \hspace{1cm} (7)

where \(\delta\) is the latent heat of water vaporization (2.43 kJ/g of water), \(V_{E}\) is the pulmonary ventilation rate (in kg/h) (27), and \(M_{E} - M_{i}\) is the difference in water content (kg water/kg dry air) between expired (M_{E}) and inspired (M_{i}) air.

\(M_{E}\) (kg water/kg air) is calculated as recommended by the ISO 7726 standard (16c):

$$M_{E} = 0.622 \times \frac{P_{E}}{(100 - P_{E})}$$  \hspace{1cm} (8)

where \(P_{E}\) is the partial pressure of water vapor in expired air (kPa), expressed according to:

$$P_{E} = 0.611 \times e^{\left(17.27 \times T_{E}\right)\left(V_{E} \times 2373\right)}$$  \hspace{1cm} (9)

\(M\) is compared with body heat losses to assess the heat stored in the body (5):

$$M - \sum\left(R_{seg} + C_{seg} + K_{seg} + E_{seg} + C_{resp} + E_{resp}\right) = S$$  \hspace{1cm} (10)

\(M\) is defined according to the infant’s postnatal age (\(A\), in days) (9):

$$M = 0.00165A^{3} - 0.138A^{2} + 3.56A + 35.4\times 10^{-14}/A^{2}$$  \hspace{1cm} (11)

A factor of 4.185 is used to convert the value (into kJ·h⁻¹·kg⁻¹).

When the body is in thermal equilibrium with the environment, the overall body heat losses \(\sum R_{seg} + C_{seg} + K_{seg} + E_{seg} + C_{resp} + E_{resp}\) balance M and body temperatures are kept constant (S = 0). If S > 0, heat is stored in the organism and the neonate’s body temperature will rise.

*Parameters of the model.* In all computer models of heat exchange, the main problem is to use appropriate parameter values in the various above-defined equations. To solve this in the present study, we took into account the local thermal heterogeneity over the body surface observed previously in separate thermographic experiments on 30 low-birth-weight neonates undergoing a surgical operation (epicutaneous cava catheterization) and exposed to a decrease in air temperature from 33.0 to 31.8°C over 30 min (i.e., −0.04°C/min). The front (long) side of the incubator was opened, and the mattress support tray was pulled forward so that the neonate (lying in the prone position, with the face straight up) was situated outside the incubator. However, an enclosing canopy was then formed over the aperture by attaching a surgical sheet to the top of the incubator and the outer edge of the mattress. The incubator’s end doors were opened, allowing free exchange with the nursery room’s air (air temperature: 23.2 ± 0.2°C; mean radiant temperature: 19.9 ± 0.2°C; relative air humidity: 44.0 ± 1.9%). As the air surrounding the neonate mixed partly with the cooler room air, the incubator temperature was set to 36°C. Air velocity was 0.06 m/s, and the relative air humidity was 35 ± 4%. The mattress’s surface temperature was 31.4°C, as measured continuously using five thermistors (Yellow Springs Instruments, series 409A, accuracy of ±0.10°C). The air temperature was also continuously recorded with thermistors. Air humidity was measured with a hygrometer (RHU 207, General Eastern, Mulhouse, France; error range of <5% over the operating humidity range of 20–90%). These sensors were located 10 cm above the center of the mattress. T, was recorded using a
conventional black-globe thermometer, as recommended by the ISO 7726 standard (16c). Air velocity was recorded with a hot-wire anemometer (TESTO 490; TESTO Forbach, France, accuracy of ±0.05 m/s). Given the size of these two latter devices and to minimize the potential influence of radiant heat transferred from the neonate’s skin to the black-globe surface, $T_r$ and air velocity were measured in the absence of the neonate.

Fourteen neonates (body mass: 1,060 ± 26 g; gestational age: 29 ± 0.8 wk; postnatal age: 4.5 ± 0.4 days; body surface area: 0.100 ± 0.010 m²) were wrapped in a thin, impermeable, plastic polyethylene bag (GE Medical Systems; thickness: 50 μm; mass: 5 g), which was transparent to infrared radiation (98% transmittance through the polyethylene film). The torso and the limbs were entirely covered. The skin temperatures, exposed to air temperatures of 33.2 ± 0.5°C, were monitored. $T_r$ was 30.6°C.

Sixteen neonates (body mass: 1,065 ± 24 g; gestational age: 30.5 ± 0.7 wk; postnatal age: 4.4 ± 0.3 days; body surface area: 0.106 ± 0.010 m²) were uncovered. Local skin temperatures were used to simulate the restriction of body heat loss through peripheral vasoconstriction when the air temperature was 31.8 ± 1.2°C and $T_r$ was 29.8°C.

Local skin temperatures were recorded with an infrared camera (the Thermovision 550 from AGEMA, Danderyd, Sweden; sensitivity of ±0.10°C at 30°C; accuracy of ±2°C between 20 and 250°C). Infrared scans were digitized with a microcomputer. Image analysis software (Thera CAM TM Reporter, FLIR Systems, Boston, MA) was then used to calculate the various surface temperatures from the different colored areas (outlined as geometrical shapes). This method generates a temperature map over the different body skin surfaces and avoids any direct stress caused by direct attachment of temperature probes to the skin.

The inguinal temperature was monitored by thermistor probe on the central body line between the navel and the xiphoid region. This thermistor temperature served as a reference value for calibrating the camera before each set of measurements.

The mean skin temperature was calculated from the set of mean local skin surface temperatures weighted according to relative area of each body segment (0.28 for head, 0.23 for the trunk, and 0.19 and 0.30 for the arms and legs, respectively). The protocol was approved by the local investigational review board.

The estimation of segmental heat losses in neonates is complicated by difficulties in measuring the various heat transfer coefficients $h_{c-seg}$, $h_{r-seg}$, and the degree of clothing thermal insulation ($F_{cl}$, $F_{pel}$). However, these factors (which depend on the geometrical shapes of the body elements) can be successfully assessed with a thermal mannequin with the same geometrical shape as the population studied. Hence, we have previously assessed these factors (4, 5) by using a manikin that simulated a very premature newborn, with a body surface area of 0.086 m² and a birth weight of 900 g.

In separate experiments, each segment’s skin surface area available for convective ($A_{c-seg}$), evaporative ($A_{e-seg}$), and radiative ($A_{r-seg}$) heat losses was calculated by subtracting the area in contact with the mattress ($A_{k-seg}$) from the total skin surface area. For the trunk region, the surface of the upper part of the trunk covered by the diaper was also subtracted. For the radiative surface area, we accounted for the opposite skin surface areas of similar temperatures, so that the cumulative radiation was nil. For each segment, five measurements were made by separate experimenters, to assess repeatability.

The local skin temperatures, the different segmental heat transfer coefficients, and the skin surface areas exchanging heat over the different body segments are shown in Table 1. To simulate the effect of a reduction in head heat losses, the bonnet’s thermal insulation was assessed as recommended by the ISO 9920 standard (16b), taking into account the percentage of the head’s skin surface area covered by the bonnet ($A_{co}$, as a percentage) and the thickness of the fabric ($Th$, in meters), using:

$$I_{cl} = 0.067 \cdot 10^{-2} A_{co} + 0.217 \cdot Th \cdot A_{co} \quad (12)$$

where $I_{cl}$ is the thermal insulation (expressed in m²·°C·W⁻¹).

The thickness of the fabric of the bonnet was measured with a compressometer (pressure as 69.1 N/m²), as recommended by the ISO standards. Thermal insulation was calculated by considering that the fabric was composed of acrylic fibers (thickness of 2 mm) or a 50:50 wool-polyester mixture (thickness of 3.5 mm).

Simulations were performed with the bonnet covering 10%, 40%, 80%, and then 100% of the head’s skin surface area. An example is

<table>
<thead>
<tr>
<th>Covered</th>
<th>Uncovered</th>
<th>Area, 10⁻³ m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\bar{T}_{sk-seg}$</td>
<td>$h_{c-seg}$</td>
<td>$\bar{T}_{sk-seg}$</td>
</tr>
<tr>
<td>Head</td>
<td>35.53 ± 0.72</td>
<td>3.63 ± 0.11</td>
</tr>
<tr>
<td>Trunk</td>
<td>34.93 ± 0.79</td>
<td>2.84 ± 0.09</td>
</tr>
<tr>
<td>Arm</td>
<td>32.10 ± 0.65</td>
<td>4.02 ± 0.03</td>
</tr>
<tr>
<td>Leg</td>
<td>34.36 ± 0.79</td>
<td>3.84 ± 0.04</td>
</tr>
<tr>
<td>Whole body</td>
<td>34.37 ± 0.68</td>
<td>3.63 ± 0.07</td>
</tr>
</tbody>
</table>

Values are means ± SD. Values of $h_{c-seg}$ (local heat transfer coefficient, W·m⁻²·°C⁻¹) are those previously determined by Belghazi et al. (4). The percentages of skin surface areas exchanging radiative ($A_1$), convective ($A_2$) and conductive ($A_3$) heat are also indicated. Average values for the body as a whole are calculated from the set of local values weighted according to the relative surface area of each segment. $\bar{T}_{sk-seg}$, local skin temperature (°C).

Fig. 1. Examples of skin surface areas of the head covered by the bonnet. Left: 2 mm thickness, covering 40% of the head. Right: 3.5 mm thickness, covering 80% of the head.
given in Fig. 1. The bonnet’s reduction factor was calculated using the standard equations recommended by Nishi and Gagge (31) and the ISO 9920 standard (16b). For radiative and convective heat losses from the head, the factor is:

\[ F_{cl-head} = \left( \frac{h_{c-head} + h_{t-head}}{I_d} + (1 + 1.97I_d)^{-1} \right)^{-1} \]  \hspace{1cm} (13)

For evaporative skin cooling, it is:

\[ F_{pocl-head} = \left[ (1 + 2.22 h_{c-head}) \left\{ I_d - [1 - (1.97I_d)^{-1}(h_{c-head} + h_{t-head})^{-1}] \right\} \right]^{-1} \]  \hspace{1cm} (14)

The values of \( F_{cl}, F_{cl-head}, \) and \( F_{pocl-head} \) are shown in Table 2 for the various proportions of the head’s skin surface area covered by the bonnet.

**Calculations.** The simulations were performed in three sets, in which we manipulated selected variables to define how long it took to reach harmful body temperatures for a neonate wrapped in a plastic bag under the following circumstances: 1) the body temperature rises as a result of the thermal insulation provided by the bonnet (related to the proportion of the head exposed and to the thickness of the fabric; and 2) \( M \) rises with body temperature according to the \( Q_{10} \) effect, where skin temperatures are kept constant. Metabolism is the driving force in the development of hyperthermia. 3) \( M \) increases, whereas skin temperatures fall. Hyperthermia occurs through endogenous heat production (and the restriction of peripheral body cooling (as it can be encountered in fever).

The elapsed time (in min) required to progress from 37°C to 38°C was calculated using the postnatal age of the neonates enrolled taking into account the fact that the rate of body warming can be an accelerating function. The driving force is \( M \), which increases logarithmically with rising body temperature according to the \( Q_{10} \) effect (Van Hoff – Arrhenius’s law):

\[ t_{43°C} = (3.49W_i \times 6)S^{-1} \]  \hspace{1cm} (18)

In second and third sets of experiments, we replicated these simulations by taking into account the fact that the rate of body warming can be an accelerating function. The driving force is \( M \), which increases logarithmically with rising body temperature according to the \( Q_{10} \) effect (Van Hoff – Arrhenius’s law):

\[ M = M_{min} 2.29^{(T_b-37)/10} \]  \hspace{1cm} (19)

where \( M \) is in kilojoules per hour per kilogram and \( M_{min} \) is the minimal metabolic heat production (in kJ·h\(^{-1}\)·kg\(^{-1}\)). The \( Q_{10} \) using 2.29 represents a 9% rise per 1°C increment in body temperature.

**Statistics.** The effect of the thickness of the fabrics and the proportion of the head covered by the bonnet were tested using two-way ANOVA. When overall \( F \) values were significant, the differences between the experimental conditions were computed by using a Student’s \( t \)-test. \( F \) and \( t \)-test values are quoted with their corresponding degrees of freedom (subscripts beneath \( F \) and \( t \) values). Regression analyses were used to relate the times required to reach warning and lethal thresholds on one hand to body temperature on the other. The level of significance was set to 0.05 for all tests. All values are given as means ± SD.

**RESULTS**

**Step 1: influence of the thermal insulation provided by the bonnet.** Figure 2 shows the partition of the different modes of heat loss from the head and the torso + limbs regions calculated for 14 infants wrapped in a polyethylene bag. The dry heat losses (\( R + C \)) were 2.63 and 4.00 kJ·h\(^{-1}\)·kg\(^{-1}\) for the head and torso + limbs regions, respectively. The magnitude of the radiative heat loss is particularly relevant, since the bag was transparent to infrared radiation (\( R = 83\% \) vs. \( C = 17\% \)). The evaporative skin cooling (limited to the head’s uncovered skin surface area) was 1.65 kJ·h\(^{-1}\)·kg\(^{-1}\). The evaporative and convective heat losses from the mucosa of the respiratory tract were small in magnitude (0.08 and 0.04 kJ·h\(^{-1}\)·kg\(^{-1}\), respectively). Quantitatively, the respiratory exchanges and the conduction between the skin and the mattress (head: 0.05 kJ·h\(^{-1}\)·kg\(^{-1}\); torso + limb: 0.16 kJ·h\(^{-1}\)·kg\(^{-1}\)) were the least relevant factors in the body heat balance. When all the segmental and respiratory heat losses were summed, the magnitude of body heat loss as a whole was 8.61 ± 0.40 kJ·h\(^{-1}\)·kg\(^{-1}\), a value that is very close to the basal rate of metabolism heat production (8.70 kJ·h\(^{-1}\)·kg\(^{-1}\)) calculated from Eq. 11 and taking into account the postnatal age of the neonates enrolled.

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**Table 2.** \( I_d \) results according to the different proportions of the head’s \( A_{co} \) and thickness of the bonnet fabric (2.0 or 3.5 mm)

<table>
<thead>
<tr>
<th>( A_{co} )</th>
<th>Thickness, mm</th>
<th>( I_d, ) m(^2)·C·W(^{-1})</th>
<th>( F_{cl} )</th>
<th>( F_{pocl} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>10%</td>
<td>2</td>
<td>0.011</td>
<td>0.94</td>
<td>0.94</td>
</tr>
<tr>
<td></td>
<td>3.35</td>
<td>0.014</td>
<td>0.92</td>
<td>0.92</td>
</tr>
<tr>
<td>40%</td>
<td>2</td>
<td>0.044</td>
<td>0.79</td>
<td>0.78</td>
</tr>
<tr>
<td></td>
<td>3.35</td>
<td>0.058</td>
<td>0.74</td>
<td>0.73</td>
</tr>
<tr>
<td>80%</td>
<td>2</td>
<td>0.088</td>
<td>0.64</td>
<td>0.64</td>
</tr>
<tr>
<td></td>
<td>3.35</td>
<td>0.114</td>
<td>0.58</td>
<td>0.58</td>
</tr>
<tr>
<td>100%</td>
<td>2</td>
<td>0.099</td>
<td>0.59</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>3.35</td>
<td>0.143</td>
<td>0.52</td>
<td>0.52</td>
</tr>
</tbody>
</table>

\( A_{co} \), percentage of covered skin surface area; \( F_{cl} \) and \( F_{pocl} \), dimensionless reduction factors for dry and latent heat exchanges, respectively; \( I_d \), thermal insulation of the bonnet.
in the present study. Under this condition, the body’s heat storage was nil (Eq. 10), since the heat production balanced the heat losses. The body was in thermal equilibrium with the environment, which explains why the mean skin and the inguinal temperatures remained nearly constant (mean skin temperature: 34.37 ± 0.68°C; coefficient of variation: 1.98%; inguinal temperature: 36.44 ± 0.14°C; coefficient of variation = 0.3%) during the 75 min of exposure.

Table 3 shows the reduction in local heat losses from the head when 10, 40, 80, and 100% of the skin surface area of this part of the body was covered by a 2-mm or 3.5 mm-thick bonnet. As a result, body heat storage increased. Depending on the thickness of the fabric, the excess body heat increased from 0.39 kJ·h⁻¹·kg⁻¹ with 10% of the head covered by the bonnet to 2.16 kJ·h⁻¹·kg⁻¹ with 100% covered. Under these conditions, the data generated from the model show that the times required to reach 38°C, 40°C, or 43°C decreased as the bonnet thickness and the surface of the head covered by bonnet increased (F1,39 = 335.8 and F3,39 = 6,461.8, respectively; P < 0.0001). These times are very long, and sufficient heat was lost from the exposed skin surface area of the head or through the fabric of the bonnet to prevent hyperthermia (284 ± 5 ≤ t40°C ≤ 1,620 ± 29 min; 575 ± 12 ≤ t43°C ≤ 2,667 ± 77 min). Nevertheless, the time required to reach the safety threshold of 38°C was particularly shortened when more than 10% of the head was covered by the bonnet (t38°C = 200 ± 5 min).

Step 2: influence of a rise in M. In a second simulation, we took account of the fact that M can drive the development of body hyperthermia. According to Eq. 19, M increased from 8.61 kJ·h⁻¹·kg⁻¹ at 37°C to 14.15 kJ·h⁻¹·kg⁻¹ at 43°C. This excess M increased the body’s heat storage and reduced the time required to reach harmful body temperatures. The rate of body warming increased exponentially (Fig. 3).

The times required to reach the safety limit (t38°C) and hyperthermia thresholds (t40°C and t43°C) are shown in Table 4. Depending on the proportion of the head covered by the bonnet, t38°C was strongly reduced and ranged from 287 min (0%) to 75 min (100% covered by a 3.5-mm-thick bonnet).

The effect of the fabric thickness is smaller than that induced by reducing the proportion of the head exposed to the air. Our statistical analysis showed that increasing the bonnet thickness shortened the time required to reach a body temperature of 38°C (F1,52 = 82.12; P < 0.0001) or 40°C (F1,52 = 19.42; P < 0.0001) or 43°C (F1,52 = 9.35; P < 0.0001). The time reductions due to the thickness of the fabric ranged between 9 and 16 min (for t38°C), between 20 and 29 min (for t40°C) and between 22 and 27 min (for t43°C). The influence of the proportion of the skin surface area covered by the bonnet (t38°C: F4,52 = 473.04, P < 0.0001; t40°C: F4,52 = 382.64, P < 0.0001; t43°C: F4,52 = 366.15, P < 0.0001) is more pronounced than that of the fabric thickness. Thus, when the bonnet covers 10% of the head, t38°C decreased by 75 and 91 min (with a bonnet thickness of 2.0 and 3.5 mm, respectively), t40°C decreased by 113 and 142 min, and t43°C decreased by 126 and 153 min.

Figure 4 shows the time to go from 38°C to 43°C under the different experimental conditions. The equations describing the body temperature time response pattern are given in Table 5. These relationships provide guidelines for determining the times required to reach a given body temperature.

Step 3: influence of a rise in M combined with a decrease in peripheral heat losses. The times required to reach warning and hyperthermia thresholds are shown in Table 4. When the rise in body temperature resulting from increased M is com-

Table 3. Heat loss from the head and heat stored in the body as a whole

<table>
<thead>
<tr>
<th>Acm</th>
<th>Thickness, mm</th>
<th>Head Heat Loss, kJ·h⁻¹·kg⁻¹</th>
<th>Body Heat Gain, kJH⁻¹·kg⁻¹</th>
<th>t38°C, min</th>
<th>t40°C, min</th>
<th>t43°C, min</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td></td>
<td></td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10%</td>
<td>2</td>
<td>4.07 ± 0.06</td>
<td>0.39 ± 0.01</td>
<td>543 ± 11</td>
<td>1620 ± 29</td>
<td>2667 ± 77</td>
</tr>
<tr>
<td></td>
<td>3.5</td>
<td>3.98 ± 0.06</td>
<td>0.47 ± 0.02</td>
<td>445 ± 13</td>
<td>1332 ± 36</td>
<td>3699 ± 67</td>
</tr>
<tr>
<td>40%</td>
<td>2</td>
<td>3.41 ± 0.02</td>
<td>1.05 ± 0.02</td>
<td>200 ± 5</td>
<td>598 ± 13</td>
<td>1203 ± 23</td>
</tr>
<tr>
<td></td>
<td>3.5</td>
<td>3.20 ± 0.01</td>
<td>1.26 ± 0.03</td>
<td>166 ± 5</td>
<td>495 ± 15</td>
<td>998 ± 24</td>
</tr>
<tr>
<td>80%</td>
<td>2</td>
<td>2.7 ± 0.01</td>
<td>1.68 ± 0.01</td>
<td>125 ± 3</td>
<td>371 ± 7</td>
<td>752 ± 13</td>
</tr>
<tr>
<td></td>
<td>3.5</td>
<td>2.53 ± 0.01</td>
<td>1.94 ± 0.04</td>
<td>108 ± 3</td>
<td>321 ± 7</td>
<td>652 ± 15</td>
</tr>
<tr>
<td>100%</td>
<td>2</td>
<td>2.57 ± 0.01</td>
<td>1.90 ± 0.03</td>
<td>111 ± 2</td>
<td>330 ± 5</td>
<td>667 ± 11</td>
</tr>
<tr>
<td></td>
<td>3.5</td>
<td>2.27 ± 0.01</td>
<td>2.16 ± 0.05</td>
<td>95 ± 2</td>
<td>284 ± 5</td>
<td>575 ± 12</td>
</tr>
</tbody>
</table>

t38°C, t40°C, and t43°C, times required to reach warning and hyperthermia thresholds. The body heat storage was calculated from Eq. 10, in which metabolic heat production was 8.61 kJ·h⁻¹·kg⁻¹ and the overall heat losses from the covered torso + limb regions + respiration amounted to 4.27 kJ·h⁻¹·kg⁻¹.
bined with a decrease in peripheral body heat losses, increasing the proportion of the head covered by the bonnet or increasing the latter’s thickness strongly reduced $t_{38^\circ C}$ ($F_{4,60} = 7.64, P < 0.001; F_{1,15} = 8.97, P = 0.009$; respectively), $t_{40^\circ C}$ ($F_{4,60} = 7.89, P < 0.001; F_{1,15} = 9.07, P = 0.008$), and $t_{43^\circ C}$ ($F_{4,60} = 8.15, P < 0.001; F_{1,15} = 9.11, P = 0.008$). The elapsed times for progressing from 38°C to 43°C are shown in Fig. 5, and the equations describing the different relationships are given in Table 5.

**DISCUSSION**

The multi-segment model developed in the present study accounts for 1) the complexity of the varying heat losses over the different body segments, 2) the nonuniform distribution of thermal insulation due to a transparent plastic bag covering the extremities and the torso of infants, and 3) the presence or absence of a bonnet. The segment-by-segment approach limits the errors induced when using whole-body values of heat transfer coefficients to calculate body heat losses in a nonuniform thermal situation.

Our results relate to ambient temperatures near the lower critical boundary of the thermoneutral zone, since the neonates included in the present study were mostly nursed naked at air temperatures of around 34°C to 35°C (16). In the present study, the elapsed times required to reach warning or lethal body temperatures of around 34°C to 35°C are quantified when neonates are exposed at temperatures (36.2 to 36.5°C), which defines the thermal neutral zone (9). The value of inguinal skin temperature (36.4°C) was also in the range of temperature (36.2 to 36.5°C), which defines the thermal neutral environment in skin temperature-servo-controlled incubator (34).

As reported by Jardine (17) for newborns heavily covered by blankets, it takes a long time to reach lethal hyperthermia when the head is not covered by a bonnet. The neonate is able to lose enough heat from the uncovered head to avoid hyperthermia, confirming reports by many authors that this region is an important route for heat loss (2, 5, 24, 36, 37). The effect of bonnet thickness is smaller than that produced by reduction of the exposed proportion of the head’s skin surface area, indi-
cating that more attention must be paid to the exposed skin surface than to the nature of the fabric.

In the thermal environment encountered in the present study (and as long as $M$ does not increase through a positive feedback process), lethal hyperthermia cannot occur within 10 h of exposure unless the head’s ability to lose heat is restricted by a bonnet. In contrast, lethal hyperthermia may occur rapidly when energy expenditure becomes the driving force and induces excess $M$. The rate of body warming may increase according to Van’t Hoff’s law, as it is the case in pyrexia in adults (11) and infants (18). The body temperature increase can thus be described by an accelerating system (Fig. 3); in an extreme situation (a 3.5-mm-thick bonnet covering the entire head), the time required to reach a body temperature of 40°C is 3 h. In this situation, the body can still lose dry and evaporative heat from the head and radiative heat from the skin surface area of the torso + limbs region covered by the plastic bag. This could become a critical situation, since the neonate’s thermoregulatory capabilities are limited. The sweat glands are only mature and functional after 32 wk of gestational age (29), whereas the peak response of each sweat gland is about one-third of that observed in the adult (13).

Our simulation of a combination of increased $M$ and a fall in skin temperature demonstrated that warning and lethal thresholds may rapidly occur ($T_{38°C} \leq 45 \text{ min}; \Delta T_{4°C} < 117; T_{43°C} \leq 194 \text{ min}$) under these circumstances. In fact, this situation simulates fever, during which the set point of the thermoregulatory controller is reset upward by cytokines, so that the cold defense reactions (increased metabolism and peripheral vasoconstriction) are activated and bring the body temperature up to the new setting. These results refer to neonates in whom fever increases the body temperature, as is the case in septicemia and pneumonia since they may also suffer severe infection without increased body temperature. A recent study (6) has shown that ~7% of patients with early-onset group B Streptococcus disease occurring in the first week of life have a fever (mortality: 100%). This percentage increased to 58% with late-onset disease (mortality: 27%).

In addition to the $Q_{10}$ effect described by Van’t Hoff’s Law, other calorigenic factors resulting from activation of the sympathetic nervous activity contribute to an increase in heat production, i.e., heat storage in the body (cardiac and respiratory muscle activity and adrenalin release). Our model does not consider factors such as dehydration, malignant hyperpyrexia, central nervous system impairments, or severe congenital anomalies, which can shorten the time needed to reach lethal hyperthermia. Thus hyperthermia may rapidly occur under conditions that appear to be normal in a standard inspection, since the level of consciousness is usually depressed, so that the neonate is not aroused when faced with this dangerous situation. A rapid increase in body temperature may trigger vagally mediated central ischemia, which may be the cause of febrile convulsions.

In conclusion, the present study is (to the best of our knowledge) the first to provide information on assessing the risk of exceeding body temperature safety limits and reaching lethal hyperthermia (Table 5) when low-birth-weight neonates are wrapped in a plastic bag and when a variable proportion of the head’s skin surface area is covered by a bonnet. Further refinement of this segment-by-segment approach could help quantify the impact of a highly asymmetric or a nonisothermal environment (including nonuniform air flow over the head, in particular). It would be also useful to assess the effect of occlusive wraps on the increased body temperature in heat gain.

Table 5. Equations defining the time required (in min) for $T_{b}$ to reach the warning ($T_{38°C}$) or the lethal threshold ($T_{43°C}$)

<table>
<thead>
<tr>
<th>$A_{co}$</th>
<th>Bonnet Thickness of 2 mm</th>
<th>Bonnet Thickness of 3.5 mm</th>
<th>Bonnet Thickness of 2 mm</th>
<th>Bonnet Thickness of 3.5 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>$y = 4.328 \ln (T_{b}) - 15491$</td>
<td>$y = 1.202 \ln (T_{b}) - 4.322$</td>
<td>$y = 1.188 \ln (T_{b}) - 4.272$</td>
<td>$y = 1.166 \ln (T_{b}) - 4.195$</td>
</tr>
<tr>
<td>10%</td>
<td>$y = 3.617 \ln (T_{b}) - 12.965$</td>
<td>$y = 3.467 \ln (T_{b}) - 12.431$</td>
<td>$y = 3.467 \ln (T_{b}) - 12.431$</td>
<td>$y = 3.467 \ln (T_{b}) - 12.431$</td>
</tr>
<tr>
<td>40%</td>
<td>$y = 2.654 \ln (T_{b}) - 9.537$</td>
<td>$y = 2.472 \ln (T_{b}) - 8.884$</td>
<td>$y = 2.472 \ln (T_{b}) - 8.884$</td>
<td>$y = 2.472 \ln (T_{b}) - 8.884$</td>
</tr>
<tr>
<td>80%</td>
<td>$y = 2.158 \ln (T_{b}) - 7.762$</td>
<td>$y = 2.007 \ln (T_{b}) - 7.221$</td>
<td>$y = 2.007 \ln (T_{b}) - 7.221$</td>
<td>$y = 2.007 \ln (T_{b}) - 7.221$</td>
</tr>
<tr>
<td>100%</td>
<td>$y = 2.019 \ln (T_{b}) - 7.262$</td>
<td>$y = 1.882 \ln (T_{b}) - 6.773$</td>
<td>$y = 1.882 \ln (T_{b}) - 6.773$</td>
<td>$y = 1.882 \ln (T_{b}) - 6.773$</td>
</tr>
</tbody>
</table>

Data were calculated from individual values ($n = 84$). All the fitted relationships were highly significant ($0.80 \leq r^2 \leq 0.84$). The equations were calculated from simulation of increased metabolism and constant skin temperature (left) or increased metabolism combined with a fall in skin temperatures (right). $T_{b}$, body temperature (°C).

Fig. 5. Time required to progress from a $T_{b}$ of 37°C to 43°C when increased metabolism is associated with a fall in skin temperatures. Top and bottom: data calculated with a bonnet thickness of 2 and 3.5 mm, respectively. The different symbols represent the proportion of the skin surface area covered by the bonnet. The $y$-axis intercepts represent the times needed for $T_{b}$ to increase from 37°C to 38°C.
(for example, in an environment encountered under a radiant warmer).

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**DISCLOSURES**

No conflicts of interest, financial or otherwise, are declared by the authors.

**REFERENCES**


