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NEONATAL THERMOREGULATION*

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The human being is a homeotherm. Homeothermy is a result of thermoregulation which includes many physiological processes. Thermoregulation maintains an equilibrium between heat production (thermogenesis) and heat loss (thermolysis). There are three principal modes of heat production:

1. **Voluntary muscle activity.**
2. **Involuntary tonic or rhythmic muscle activity known as "shivering".**
3. **Non-shivering thermogenesis (NST) essential for newborns.**

Heat loss occurs in two stages:

1. **The flow of heat from the center of the body to its surface.**
2. **The flow of heat from the body surface to the environment by conduction, convection, radiation or water evaporation.**

Even in the very small premature baby, we find that metabolic and vasomotor control responses are developed.

To protect the newborn from stress resulting from hypo or hyperthermia, one should take into consideration the concept of the neutral temperature range which is also called the "Thermoneutral Zone" in (TNZ) or "Thermal Neutrality". Curves, proposed in 1971 by Hey[16] are essential for keeping newborns in the TNZ. *Key words: thermoregulation, neonate.*

The human being is a homeotherm. His internal temperature varies within the limits of 37 ± 1 °C. Homeothermy is a result of thermoregulation which includes many physiological processes. Thermoregulation maintains an equilibrium between heat production (thermogenesis) and heat loss (thermolysis). The maintaining of a constant body temperature is a result of the thermoregulatory function of the cells, particularly those of the nervous system.

The notion of homeothermy has been known in medicine since antiquity. It is interesting to note that in the past pediatricians ignored this fact when dealing

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with newborns and considered them to be poikilothermic organisms (body temperature showing wide fluctuations which depend on changes in environmental temperature). In fact, it was only in the beginning of the sixties that the importance of this concept was accepted in neonatal medicine.

In the last two decades of the 19th century, Pierre Budin[1] (Paris) demonstrated the importance of the thermal environment on newborn infants. He observed in premature infants weighing less than 2000 g, that if their temperatures fell to 32 °C, 98 percent of them died and if their temperatures were between 32.5 °C and 33.5 °C, 90 percent of them died. While on the contrary, if their temperatures were maintained between 36 °C and 37 °C , the survival rate rose to 77 percent.

Based on these observations, Budin produced an incubator that had the same operating principles as the modern incubators of today[2]: circulation of humidified and warmed air; control of ambient temperature; infant dressed with a cap on its head and placed over a support which is covered by a sheet. Subsequent studies by Blacfan et al[3], Hill[4], Buetow et al[5], and Day et al[6] demonstrated the following:

1. Importance of a thermal control of the environment especially for premature infants;
2. Fundamental role of thermoregulation during the first days of life.

Physiology of Thermoregulation

Thermoregulation is essentially controlled by the nervous system. It originates in the deep and superficial thermoreceptors that send nerve impulses to the spinal cord and brain. The physiologic adaptive reactions originating in the hypothalamus and behavioral (flexion position, clothing, etc.), and technological responses, functions of the cerebral cortex, are elaborated herein.

Thermoreceptors: They consist of the following two types which are sensitive to heat and cold:

1. Superficial receptors (cutaneous and mucosal)
2. Deep receptors which are present in the abdominal cavity, medulla, and also in the anterior hypothalamus.

Hypothalamus and spinal cord: The spinal cord plays an important role in vasomotor reactions and in the reflex. The hypothalamus is the most important part of the thermoregulatory system. It has been demonstrated that entire destruction of the hypothalamus does not eliminate thermoregulatory reactions, but makes them much less adaptive. It has also been shown that there are two groups of cells in the hypothalamus: a posterior and an arterior group. The posterior group coordinates reactions to cold while the anterior group coordinates reactions to heat.

Orders for thermoregulation are sent along two neural pathways: the somatomotor system and the sympathetic system. The somatomotor system, originating in the posterior hypothalamus, acts on the skeletal muscles and produces heat by the mechanism of shivering, while, the sympathetic system acts on the sweat glands, vessels, and brown adipose tissue.

The Role of the Endocrine System: Exposure to cold stimulates the secretion of adrenaline. This hormone increases energetic metabolism by hepatic glycogenolysis and lipolysis in adipose tissue (brown adipose tissue in neonates) and activates cutaneous vasoconstriction and directs blood from the skin to the deep parts of the body. The role of the thyroid hormones (T_3, T_4) are uncertain. It is thought that these hormones adapt the body to cold by increasing general metabolic activity. Their action is synergic with that of adrenaline.

It is accepted that there is a thermostat in the hypothalamus, which keeps the body temperature within the limits of 37 ± 1 °C. This set-point can be increased or decreased as a result of various causes. Whatever the level of this set-point temperature, the thermoregulatory system maintains this temperature as the body temperature.

Deviations from this temperature will actuate one or more appropriate effector systems to restore the temperature field by extra heat production or by heat loss.

Modes of Extra Heat Production

There are three principal modes of heat production:

1. Voluntary muscle activity.
2. Involuntary tonic or rhythmic muscle activity known as "shivering".
3. Non-shivering thermogenesis (NST)

* Though voluntary muscle activity can be a good source of energy for an adult, the newborn infant is not capable of using this mechanism.

* Normally, in the adult male, shivering is quantitatively the most important involuntary mechanism of thermoregulatory heat production. NST develops to a greater extent only after long-term exposure. On the contrary, in the newborn infant, NST is an important and effective mechanism of heat production. This system is controlled by two mechanisms: neural and hormonal. In the newborn infant, brown adipose tissue is the principal element of NST. It constitutes 2-6 percent of the body mass in full-term newborn infants[7]. Only in the early sixties, was it demonstrated that in vitro metabolic activity of brown adipose tissue was much higher than that of white fat. Two important features can be recognized by electron microscopy:

(1) The richness in mitochondria, and (2) The synaptic contact between sympathetic nerve terminals and cell membranes.

Brown adipose tissue is located around the neck and on the back between the scapulae, in the axillae, on the surface of the heart and kidneys and adjacent to the large vessels within the thoracic cavity. It is shown that the venous blood of the cervical and thoracic interscapular adipose tissue is partly drained into the inner vertebral sinus (plexus venousus vertebralis internus) which surrounds the spinal cord like a heat exchanger[8]. In this manner, the two effector systems, NST and shivering are interlocked. With external cooling, NST is initiated by the cooling of thermoreceptors in the skin, which leads to an increase in the temperatures of the interscapular brown adipose tissue and of the cervical vertebral canal (by heat flow from the adipose tissue to the spinal cord). As a result of the temperature of the spinal cord being maintained at a high level, shivering remains suppressed.

However, if we block NST, the temperature of the cervical spinal cord begins to fall and shivering occurs. Thus, under natural conditions, shivering occurs only after NST is evoked to its fullest extent. The neonate, therefore, shivers only when subjected to the stress of severe cold. On the contrary, in the adult, since brown adipose tissue does not exist, NST is not an important source of heat production, and occurs only when shivering is not sufficient to increase the body temperature. Fig. 1 shows the importance of NST and shivering during the first 12 months of life[9].

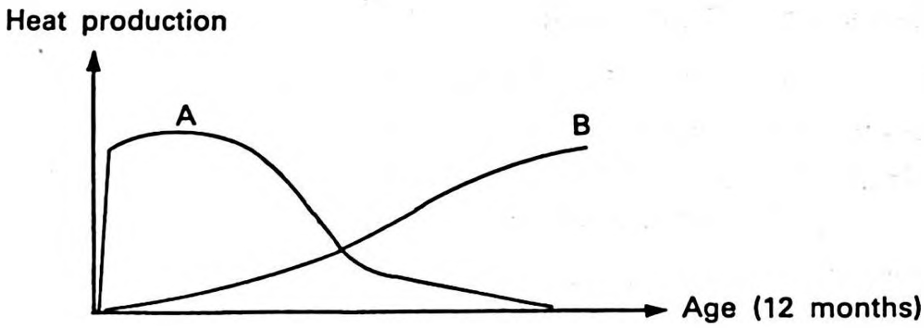


Fig. 1: Importance of NST (A) and shivering (B) during the first 12 months of life.

Modes of Heat Loss

Heat loss occurs in two stages:

1. The flow of heat from the center of the body to the surface.
2. The flow of heat from the body surface to the environment.

1* According to the equation:

$$H_{int} = A.C\ (T_{re} - T_s) \quad \text{in kcal / h or in W}$$

Where H_{int} represents internal heat flow; A the body surface area, W the number of watts, T_{re} the deep body (rectal) temperature, T_s the mean skin temperature, and C the thermal conductance. Heat transfer to the body surface is determined by the internal temperature gradient (Tre - Ts) and thermal conductance. This compound quantity "C" is determined mainly by three factors:

1. specific heat conductivity of these tissues;
2. absolute thickness of these tissues, particularly the thickness of subcutaneous fat, which has relatively low heat production,
3. the rate of blood flow to the surface of the trunk and extremities.

Thus, cutaneous vasoconstriction diminishes heat loss and vasodilatation increases it. But vasoconstriction, as a cold defence reaction, is much less effective in the neonate than in the adult, due merely to differences in body mass. Thin subcutaneous fat in the newborn increases the conductance of the skin and heat loss.

2* Heat transfer from the body to its surroundings is a complex process. For quantitative consideration, we distinguish four components: heat transfer by conduction, convection, radiation and water evaporation expressed as follows.

$$H_{ext} = H_k + H_c + H_r + H_e$$

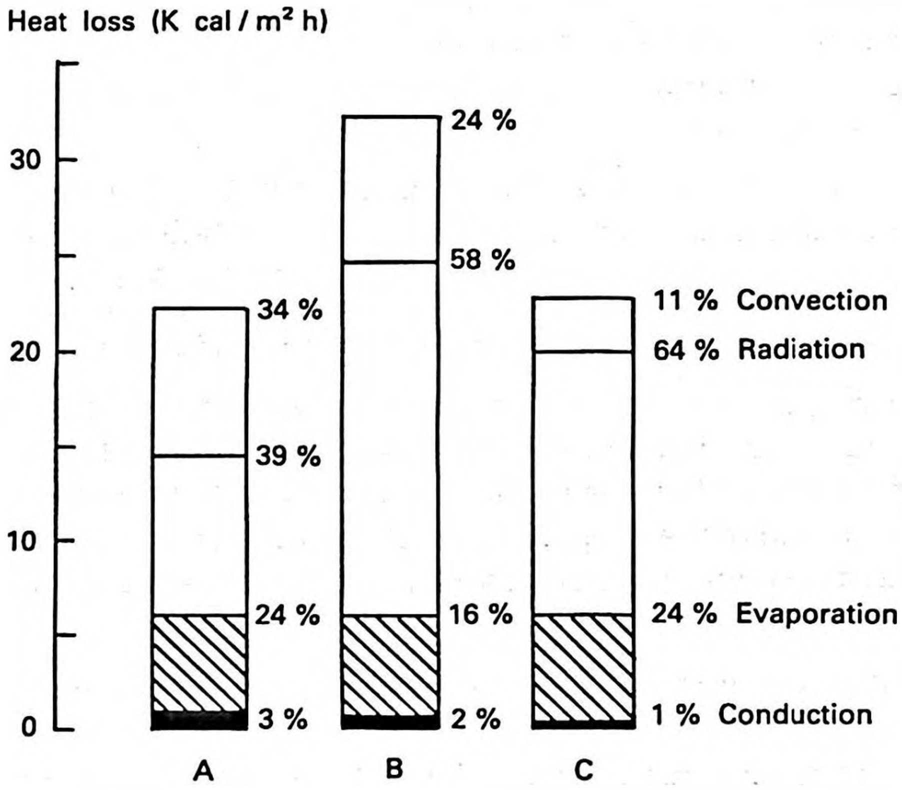
Conductive heat loss is a result of simple thermal conductibility between the body surface and the objects with which it is in contact. It occurs, for example in the small area of the back when the infant is in contact with the support. Depending on the heat insulation of the support, conductive heat loss may be very important, but it may also be so small as to be negligible if the baby is laid on a well-insulated mattress.

The parts of the body that are neither in contact with the support nor covered by clothes are enveloped in a layer of still air that is termed the "boundary layer". If there is no wind outside this layer, which may be as thick as 4-8 mm, the moving air carries heat by mass flow. This phenomenon is called heat transport by convection. Within the boundary layer, heat is transported by conduction.

Heat loss by radiation occurs by means of electromagnetic waves. There is an interchange of heat between the naked newborn infant and its environment (walls, windows, people). Therefore, it can easily lose its body heat even when it is placed in a warm incubator if the walls of the incubator are cold. This kind of heat loss can be reduced in the following manner:

- Insulating the walls of the incubator.
- Placing a plastic tunnel over the child.
- Placing a radiant heater over the incubator.
- Heating the room.

In the adult male, under conditions of thermal neutrality, about 20-25 percent of the total heat loss is due to evaporation from the skin and respiratory tract (insensible water loss). Similar values have been found in two to ten day-old newborn infants upon exposure to neutral temperatures and a Relative Humidity (RH) of 50 percent. The driving force for evaporation is the difference between the vapor pressure and the environment. In one study, when RH fell from 80 to 20 percent, heat loss doubled in full-term newborn infants. The metabolic rate was found to be at a minimum of 50 % RH under these conditions. Figure 2 shows the different types of heat loss of a premature infant weighing less than 1500 g. under different conditions[9].



Incubator	: 34°	34°	36°
Room	: 34°	21°	21°
Humidity	: 50 %	50 %	50 %

Fig. 2: Thermal environment and heat loss of a premature infant weighing less than 1500 g with a rectal temperature of 37 °C

Evaporative heat loss can be increased considerably by sweat secretion and by an increasing respiratory rate. In a hot environment, evaporative heat loss may represent the only, but a very effective avenue, of heat loss. Evaporation of one liter of sweat dissipates about 580 kcal (2430 J) from the body. The most effective to date heat-dissipation mechanism is sweat secretion in the newborn infant as well as in the adult. Maximum sweat secretion is slightly different in the full-term infant and in small-for-dates and slightly premature infants, but there is a considerable difference in the threshold esophageal temperature for the onset of sweating in smaller and larger infant groups. (Fig. 3)[10].

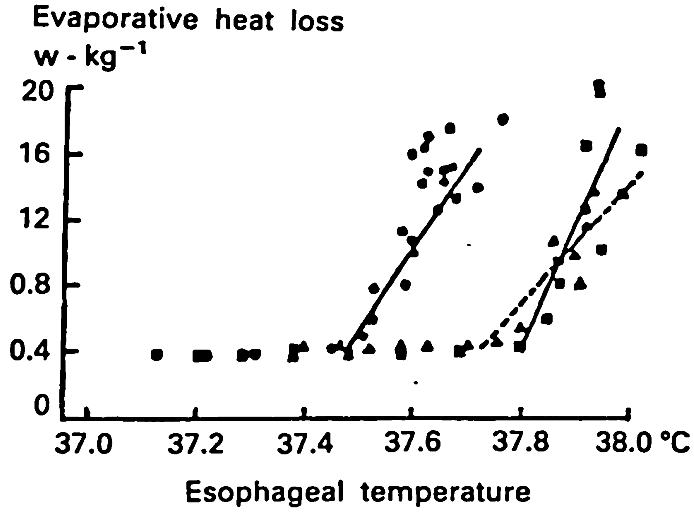


Fig. 3: Evaporative heat loss in relation to esophageal temperature in 22 full-term (●), 9 small-for-dates (■), and 8 premature (▲) infants. Note the equal maximum response but increased threshold in the small-size infants.

Sweating due to thermal stimuli could not be detected in infants less than 210 days postconception, even when the rectal temperature rose as high as 37.8 °C. In such infants, the sweat glands did not even respond to intradermal injection of acetylcholine[11]. It is thus assumed that the failure of the sweat response is due mainly to an immaturity of the sweat glands. In comparison to adults, the maximum sweat response is minimal in the neonate. Thus, it can be said that the newborn infant is markedly less heat-resistant than the adult.

Stage of Maturity of the Thermoregulatory System at Birth

Temperature regulation is frequently said to be "not fully developed" at the time of birth. Caution should be used in asserting that the control centers are immature, even though the neonate shows more fluctuations in body temperature than the adult. Even in the very small premature infant, metabolic and vasomotor control responses are developed. Thus, instability of the body temperature seems to be due, to a large extent, to the discrepancy between the efficiency of the effector system and body size; growth alone will slowly enlarge the control range.

Pathophysiology and Clinical Aspects

Hypothermia: The fetus lives in a constant thermal environment. Its body temperature is approximately 0.5 °C higher than that of its mother. At birth, the newborn infant finds himself in an environment which is 12 °C colder than that of intrauterine life (25 °C vs. 37 °C), wet with amniotic fluid, and loses heat by evaporation, radiation, convection and conduction.

In addition to these environmental factors, birth trauma (intracranial pathologies), cerebral malformations, and certain drugs play an important role in disturbing the regulation of normal neonatal temperature, thus resulting in hypothermia. Morever, respiratory deficiency leading to hypoxia and hypercapnia may contribute to a rapid development of hypothermia. As a result of many experiments, it has been shown that the extra heat produced in the brown adipose tissue is especially susceptible and suppressed by hypoxia and hypercapnia.

Signs and symptoms :

- Drop in rectal temperature.
- Apathy.
- Refusal of food.
- Edema of the extremities.
- Coloration of the extremities may change; they may be pale or cyanotic or deceivingly red (dissociation of oxyhemoglobin is restricted).
- Respiration may become slow, superficial or irregular and bradycardia may occur. However, the neonate is generally thought to be less susceptible to the dangerous corollaries of hypothermia such as cardiac arrest and respiratory distress.
- Risk of intraventricular hemorrhage.
- Digestive problems (distension, vomiting) are frequent.
- Oliguria is the rule.
- Metabolic disorders such as metabolic acidosis, hypoglycemia, hyperkalemia, hyperazotemia are common.

In the prolonged and severe forms, generalized bleeding (especially intrapulmonary) is seen as a result of Disseminated Intravascular Coagulation.

Prevention of Hypothermia

Delivery room : Immediately after birth, the skin temperature drops considerably, and is followed by a drop in deep-body temperature. Heat loss occurs especially as a result of water evaporation from the moist skin, but there is also significant heat loss which occurs as a result of convection and radiation. Under normal conditions in a delivery room, and if no precautions are taken, the deep-body temperature of the newborn may drop two to three degrees in half an hour. Figure 4 shows the change in rectal temperature during the first thirty minutes of life under varied conditions[12].

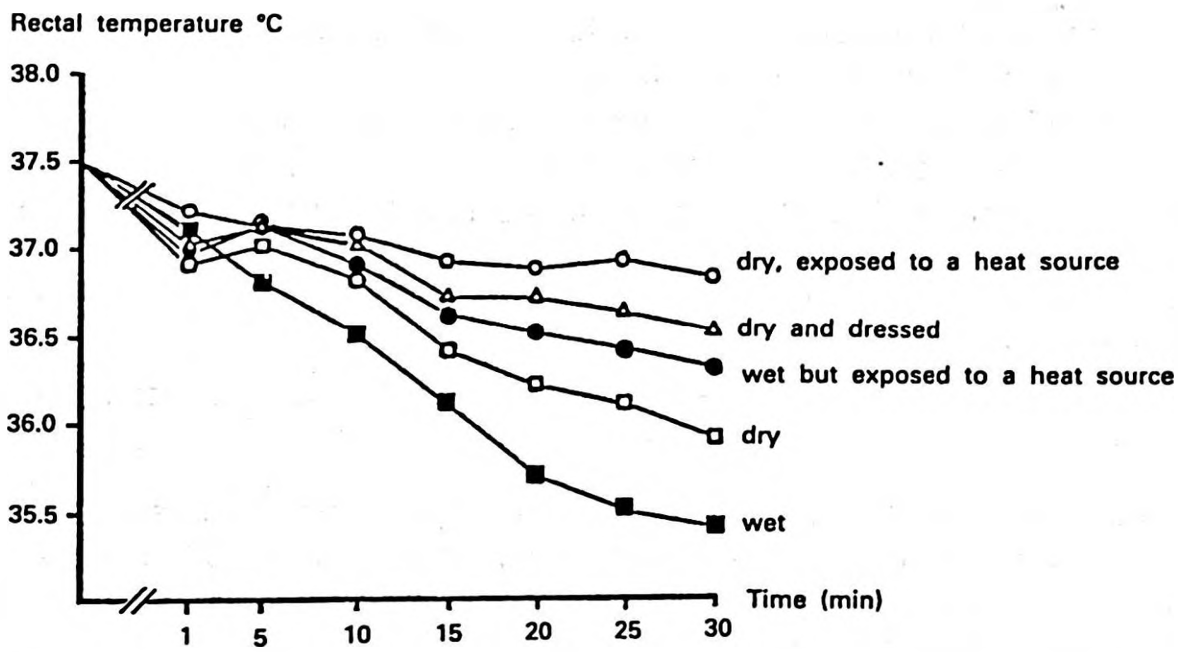


Fig. 4: Change in rectal temperature during the first 30 minutes of life.

In fact, the drop in temperature can play a beneficial role at birth by stimulating skin receptors thereby initiating respiration. At the same time, increased peripheral vasoconstriction will reduce the right-to-left shunt of ductus arteriosus. However, it is preferred that the newborn be kept in a warm atmosphere, adequate enough to prevent the dangerous effects of cold. The following measures should be taken to prevent hypothermia from occurring in the delivery room.

- Ambient temperature should be 22 °C (25 °C is more efficient) with a RH of 60 to 65 %, and devoid of air currents.
- Skin of the child (especially face, head and hair) should be dry. This precaution will diminish evaporative heat loss.
- Conductive heat loss should be diminished by placing the newborn on a dry, warmed sheet.
- The newborn should be systematically exposed to a radiating heat source, especially if reanimation is necessary.
- The baby's first bath should be delayed because washing a baby soon after birth contributes to a fall in body temperature[13].

During Transport:

- An incubator having a convection heating system is almost always used. An insulator is used to cover the incubator for decreasing the heat loss caused by radiation.
- If the child is on mechanical ventilation or oxygen, the gases should be heated and humidified.

- The ambient temperature of the vehicle should be between 25 ° and 28 °C (which is difficult to attain in winter).
- Head and hair of the child should be covered with a cap.
- The rectal temperature should be monitored at least two times during transport (at the beginning and at the end). If the infant is transported over a long distance, the rectal temperature should be taken regularly.
- Since the newborn infant is in need of energy, glucose should be given per os or intravenously.
- If severe hypothermia is present, the temperature should be increased slowly (2°/hour).

Hyperthermia : As mentioned previously, the hypothalamus, more precisely, the anterior hypothalamus (Pre-Optic Anterior Hypothalamus = POAH) is the neural center which receives different signals from the periphery and initiates mechanisms of heat loss or gain. According to Ranson[14] this region functions as a "thermostat". It is set around 37 °C. It should be emphasized that fever is not hyperthermia and hyperthermia is not fever.

Fever is the augmentation of the set-point of the human thermostat. The body activates all of its functions to be able to increase its temperature to the level of the thermostat. Fever is most frequently produced by such stimuli as bacteria, viruses and yeasts, but, it is also known to occur as a result of immune reactions, hormonal substances and drugs. It has been postulated that these stimuli liberate an intermediary substance termed endogenous pyrogen (E P). EP is known to be identical to interleukin-1 (IL-1), a product of monocytes and macrophages which initiates many of the reactions termed collectively the "acute phase response". Within the hypothalamus EP/IL-1 appears to act by inducing the synthesis of prostaglandins of the E series, particularly prostaglandin E2 (PGE2) (Fig. 5)[14]. Endogenous pyrogens shift the set-point of the thermoregulatory system to a higher level. In the neonate there is an unresponsiveness to pyrogen in the hypothalamus, which explains the absence of fever in infection.

Hyperthermia appears when metabolic heat production exceeds the capacity of thermolysis. In the neonate, it is observed in the case of thermoregulatory center perturbation, for example after peri-natal central trauma. It may also be seen when the incubator is exposed to the sunshine or in the case of phototherapy for the treatment of jaundice.

Signs and symptoms :
- The first sign is hyperpnea.
- tachycardia.
- red color of extremities (vasodilatation).
- increased sweating.

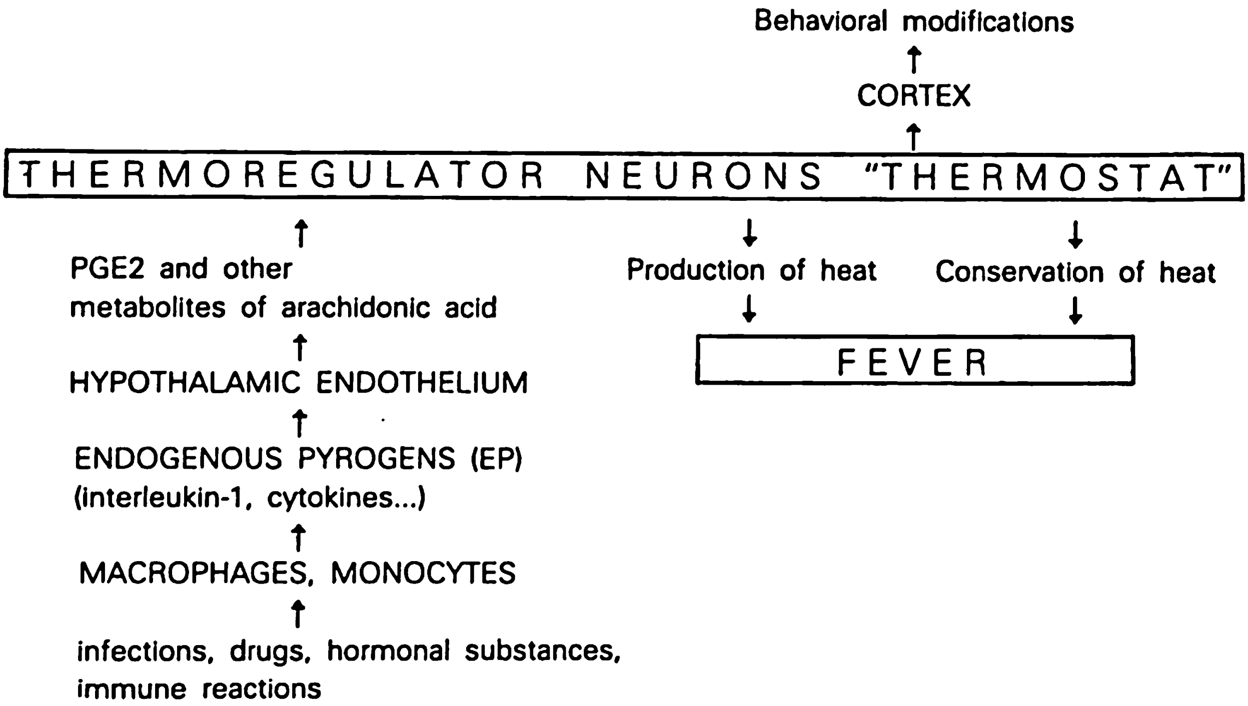


Fig. 5: Physiopathology of fever

Treatment: Cooling should be done slowly and simply by decreasing the temperature of the incubator. In order to protect the newborn infant from the stress of hypo or hyperthermia, one should take into consideration the concept of a neutral temperature range (also termed "Thermoneutral Zone" (TNZ) or "Thermal Neutrality". The Thermoneutral Zone (Fig. 6)[15] is defined as the range of ambient temperature within which:

- temperature regulation is achieved only by a nonevaporative physical process (sweat gland activity = 0).
- Oxygen consumption is the least
- The metabolic rate is at a minimum.

This range is delineated by the symbols T3, T4 (Fig. 6). In small premature infants, the lower limit of TNZ may be as high as 35 °C. The ambient temperatures which are necessary to create thermal neutrality in naked and dressed neonates are shown in Fig. 7[16].

These curves were proposed in 1971 by Hey[16]. These temperatures are valid under the following conditions:

- still air.
- RM = 50 %
- Child covered by another plastic tunnel or an incubator with double walls.

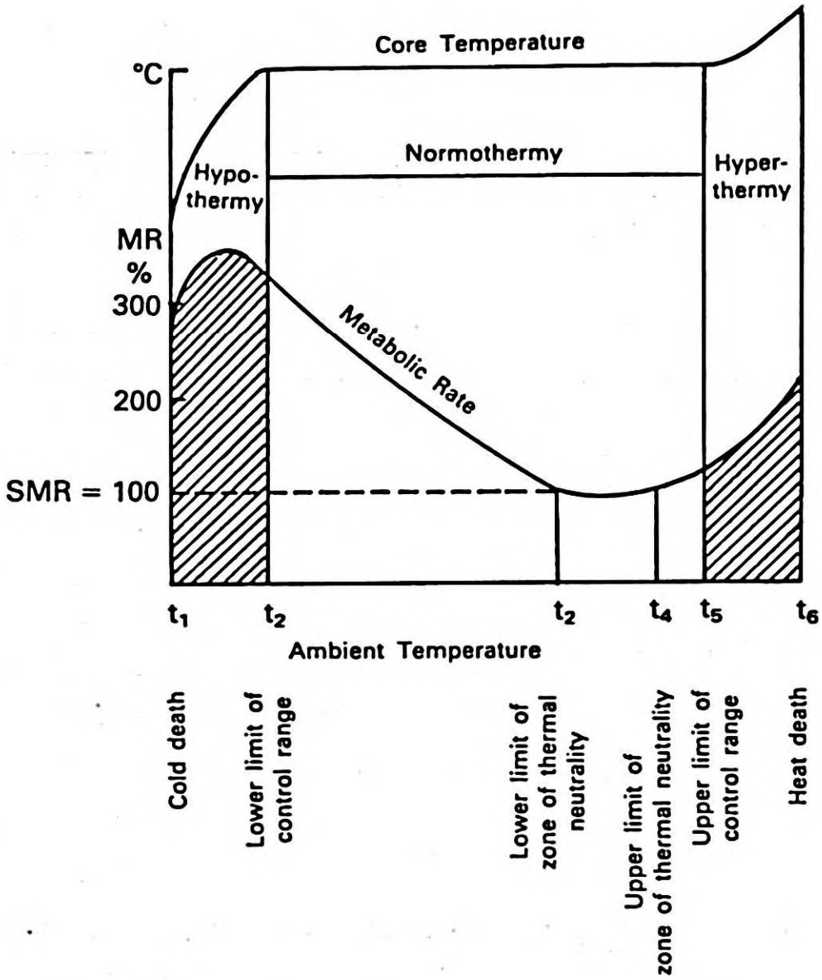


Fig. 6: A schematic representation of the relationship between metabolic rate and ambient temperature in homeotherms; zone of thermal neutralitiy (t3...t4).

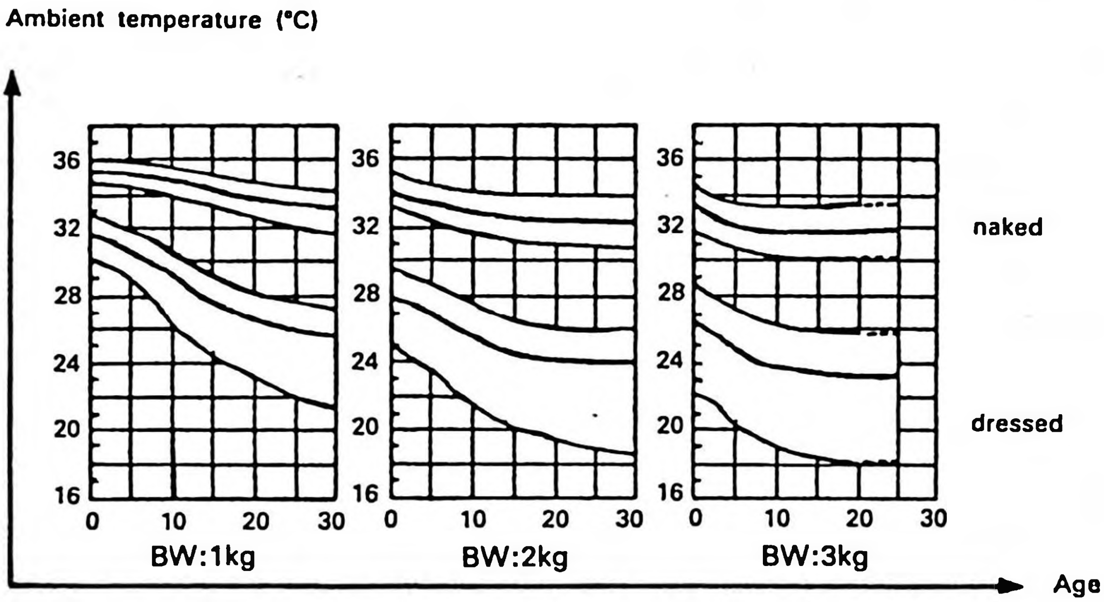


Fig. 7: Diagrams showing the optimal ambient temperature for a neonate as a function of weight, age and state of dress in the incubator.

These values can be changed :

- If RM is increased, the temperature should be decreased 0.5 °C for the naked child and 1 °C for the dressed child.
- If the incubator has one wall, the temperature should be increased 1 °C for each 7 °C of difference between the temperature of the incubator and the temperature of the room.
- In case of convulsion, agitation or left-to-right shunt, temperatures should be reduced.

In conclusion, the newborn is capable of thermoregulation within limits by ways different from that of the adult. It is usually exposed to hypothermia. Premature infants are at a greater risk of hypothermia. However, we can help in the maintenance of TNZ, essential for the optimal functions of body cells, by adhering to certain simple procedures.

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