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Thermochimica Acta 309 (1998) 39–47

thermochimica acta

# Thermometry and calorimetry in the neonate: Recent advances in monitoring and research[1]

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Received 15 July 1997; accepted 30 July 1997

**Abstract**

Due to its small body size, which in the case of prematurity is associated with increased skin permeability and incomplete brown fat development, the human neonate is highly prone to heat loss. Hence, thermal protection is mandatory to prevent neonatal hypothermia with its adverse metabolic and hemodynamic effects. This is usually attempted by the selection of "thermoneutral" ambient temperatures to maintain core temperature constant without regulatory metabolic increase. Since, however, core temperature decreases only after metabolic increase has failed to counteract heat loss, and metabolic increase in its turn is preceded by peripheral vasoconstriction, recording of thermal gradients between core and peripheral temperatures has now proven superior in early detection of thermal stress and maintenance of thermal comfort in the neonate. The long-lasting thermal lability of preterm babies partly results from the fact that an elevated basal metabolic rate, which in term neonates compensates for the small body size, is only achieved with delay. As this is correlated to the growth retardation typical of prematurity, the postnatal metabolic increase is usually considered to be a precondition for growth. However, a comparative calorimetric investigation has revealed that in a marsupial species normally born in a very immature state, a rapid weight increase occurs at a low metabolic rate. Obviously, these animals retain a growth efficiency which in humans is confined to intrauterine life and interrupted by preterm birth. Moreover, their low $O_2$ consumption rate is adaptive to restricted respiratory surface area and incomplete tissue vascularization and contributes to hypoxia tolerance. Therefore, although postnatal metabolic increase promotes thermal stability and weight increase in term and slightly preterm human neonates, metabolic reduction may be the more appropriate strategy in cases where $O_2$ and substrate supply are limited by extreme immaturity. As long as the factors mediating natural metabolic suppression are unknown, careful thermal protection seems to be one of the most promising ways to prevent uneconomic metabolic activation in highly preterm human neonates. © 1998 Elsevier Science B.V.

*Keywords:* Calorimetry; Growth; Hypoxia tolerance; Metabolic rate; Preterm neonate; Thermoregulation

## 1. Introduction

### 1.1. Neonatal heat balance – the impact of small body size

The main thermoregulatory problem of the neonate is its small body size. Due to the small size and the correspondingly high surface-to-volume ratio, it is

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[1]Presented at the Tenth Conference of the International Society for Biological Calorimetry, Ascona, Switzerland, 27–30 April, 1997.


*PII* S0040-6031(97)00427-9

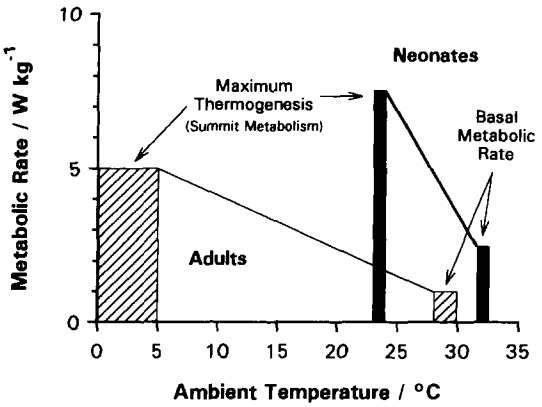


Fig. 1. Relationship between specific metabolic rate and ambient temperature in human adults and neonates. The bars represent the basal and maximal ("summit") metabolic rates, and the connecting lines the thermoregulatory metabolic increase. The full-term neonate is adapted to its small body size by a higher basal metabolic rate and and a steeper metabolic increase than in adults. Modified from [1,2].

especially prone to heat loss. However, it is also adapted to this risk by an elevated metabolic rate. This is illustrated in Fig. 1, where the specific (i.e. size-related) metabolic rate is plotted against ambient temperature: In unclothed adults, in an ambient temperature of 28°C, the basal metabolic rate of roughly 1 W $kg^{-1}$ suffices to maintain heat balance ("thermoneutral conditions"). As the ambient temperature falls, the metabolic rate increases up to a "summit" value of ca. 5 W $kg^{-1}$, reached at near-zero temperatures. In term neonates, the specific basal metabolic rate is more than twice that of adults so that their thermoneutral temperature of 32°C is not as much higher than in adults as would be expected from the smaller body size alone. Moreover, the thermoregulatory metabolic increase is steeper than in adults, thus compensating for the higher surface-to-volume ratio. Hence, thermoregulation is not insufficient in full-term neonates. However, their total thermoregulatory range is narrower than in adults. Additionally, in contrast to the obvious shivering reaction occurring in adults, their thermoregulatory metabolic increase is mostly due to non-shivering thermogenesis in the brown adipose tissue. Thus, the "invisibility" of the cold defense reaction may lead to an underestimation of the maximum thermal stress exerted on the neonates by ambient temperatures which would still be quite comfortable for adults [1–5].

In preterm neonates, the risk of cooling is even higher, partly due to the smaller body size and an inappropriately low basal metabolic rate (cf. below), partly to the immaturity of the effector systems of thermoregulation. Thus, on the one hand, the permeability of the skin increases with decreasing gestational age so that the evaporative heat loss is enhanced, unless a correspondingly higher ambient humidity is provided [6,7]. On the other hand, the brown adipose tissue is more or less underdeveloped so that the capacity for non-shivering thermogenesis is limited before term [8,9]. Hence, although the overall incidence of neonatal hypothermia (i.e. a body temperature of <36°C on admission to the neonatal ward) has been greatly reduced during the last forty years, it is still markedly increased in the subgroup of the VLBW (very low birth weight) infants, weighing <1500 g at birth [10].

Both from natural adptation strategies and from clinical organ preservation, hypothermia is known to have a protective effect against oxygen and substrate deficiency [11]. However, this is only true if thermoregulation is switched off and a direct cold-related decrease in metabolic rate occurs ("induced hypothermia"). Therefore, a potential beneficial effect of hypothermia on the neonate is limited to the rare cases, where thermoregulation is suppressed by hypoxia/hyperkapnia or by a rapid fall in body temperature itself, thus leading to a kind of "self-induced" cooling. However, even though the preterm neonate has a poor capacity to regulate its own body temperature, it is not poikilothermic in a strict sense. Thus, in most cases, exposure to cold elicits a thermoregulatory reaction which, due to the coincidence of peripheral vasoconstriction and metabolic increase, leads to severe metabolic disturbances ("accidental hypothermia") and might finally endanger the successful transition from intra- to extrauterine life [12].

### *1.2. Thermal monitoring and thermal protection – from thermoneutrality to thermal comfort*

In view of these risks, the benefits of thermal monitoring and thermal protection are now undisputed in neonatology. Nevertheless, the most appropriate site and technique of measurement are still a matter of debate. Thermal monitoring is traditionally performed by measurement of rectal temperature which, however, is not a very reliable parameter of core

temperature and, more importantly, decreases only *after* the peripheral vasoconstriction and the metabolic increase as the first and the second line of cold defense have failed to counteract heat loss. Therefore, a "two-point technique" has recently been introduced into clinical monitoring which is based on the gradient between core and peripheral temperature and has proven clearly superior in early detection of thermal stress [13].

In this context, it is worth mentioning that (in contrast to the more recent "interthreshold range", indicating the very narrow range of body temperatures at which there is no thermoregulatory reaction at all) the traditional "thermoneutral range" (cf. aforesaid) focuses on metabolic rate and, therefore, ignores preceding vasoconstriction [14,15]. This is of interest since the current temperature settings of neonatal intensive care incubators are commonly taken from nomograms in which the *thermoneutral* temperature is given as a function of gestational and postnatal age [16,17]. As is demonstrated by an example of thermal monitoring in a human preterm neonate (Fig. 2), it is possible, by choosing these values, to maintain a constant body temperature of ca. 37°C. If, however, a peripheral temperature is simultaneously recorded and the resulting thermal gradient calculated, it becomes evident that any minor manipulation leads to a vasoconstrictory reaction and, thus, to considerable thermal stress for the preterm neonate. This example thus clearly demonstrates that thermal neutrality is not necessarily the same as thermal comfort. Hence, it is conceivable that even higher ambient and body temperatures could be necessary to prevent not only metabolic stimulation, but also peripheral vasoconstriction and to guarantee optimal thermal comfort in the human preterm neonate [13]. This assumption is reinforced by the fact that the human fetus, while submerged in the amniotic fluid, exhibits a body temperature which is 0.5°C higher than the mother's "normal" 37°C [18,19].

### *1.3. Body weight and metabolic rate – the biological basis for perinatal metabolic adaptation*

As pointed out at the beginning, the term neonate is adapted to its small body size by an elevated metabolic rate. The increase in specific metabolic rate with decreasing body mass corresponds to the overall metabolic size relationship of mammals, known as the mouse-to-elefant curve or Kleiber's rule [20,21]. Most remarkably, however, the metabolic size relationship is "switched on" only after birth [22–26]. In other words, the mammalian neonate starts at the maternal metabolic level and then increases more or less rapidly up to the value to be expected from body mass (Fig. 3). The postnatal metabolic

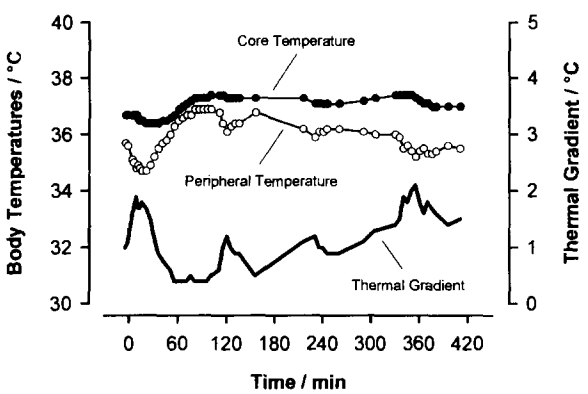


Fig. 2. Example of thermal gradient monitoring in a human preterm neonate (gestational age 28 weeks, birth weight 1100 g, postnatal age 11 days). Note that any medical or nursing manipulation leads to a decrease in peripheral temperature and, thereby, to an increase in the thermal gradient although the core temperature itself remains largely unaffected.

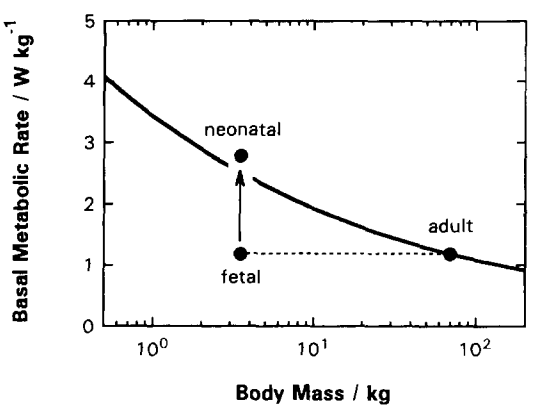


Fig. 3. Body mass relationship of basal metabolic rate and postnatal metabolic increase in mammals. Following an overall size relationship, the specific basal metabolic rate of neonates is higher than that of adults (cf. Fig. 1). However, immediately after birth, it is still at the feto-maternal level and, thereafter, increases up to the value to be expected from body mass (numerical values are for humans).

increase is accomplished, in human term neonates, within a few days and seems to be retarded in preterm neonates [1–3,13,27–29]. However, relatively little is known about the extent of metabolic reduction and the dynamics of metabolic increase in the perinatal period, nor about the adaptive value of postnatal metabolic behaviour in various degrees of neonatal immaturity. Therefore, we decided to conduct a calorimetric investigation on this phenomenon, comparing the postnatal metabolic increase in human preterm neonates to the metabolic behaviour of a mammalian species that is normally born in a very immature state.

## 2. Materials and methods

### 2.1. Indirect calorimetry in human preterm neonates

Human data derived from clinical routine measurements of resting metabolic rates in preterm neonates of various gestational and postnatal ages [30]. Babies were otherwise healthy (apart from prematurity itself) and all spontaneously breathing at the time of measurement. Metabolic measurements were performed with a Deltatrac II Metabolic Monitor (Datex, Finland) operating in the "canopy mode" whereby the oxygen consumption rates were calculated from the difference in $O_2$ contents between inflowing and outflowing air, multiplied by the highly constant flow rate [31,32]. Details of the measuring procedure are described elsewhere [33]. Results were divided by the actual body weights to gain "specific" metabolic rates and plotted as percentages of the values to be expected from the above-mentioned metabolic size relationship.

### 2.2. Direct and indirect calorimetry in Monodelphis neonates

As an example of natural adaptation to extreme neonatal immaturity, the short-tailed opossum (*Monodelphis domestica*) was studied. Being marsupials, *Monodelphis* neonates are born after a short gestational period and move by themselves into an abdominal "pouch" of the mother (which in this species is merely a wrinkle in the abdominal fur) to continue their development while attached to a nipple. Due to their "embryonic" state and their extremely low birth weight of some 100 mg, they are one of the most impressive examples of neonatal immaturity among mammals [34].

Animals were obtained from a breeding colony at the Department of Anatomy and studied with permission of the local authorities. Metabolic measurements were performed with a 2277 Thermal Activity Monitor (ThermoMetric, Sweden) [35], the measuring ampoules having been previously flushed with pure oxygen. Details of the experimental procedure are described elsewhere [36]. To ensure comparability with the human data, results were divided by the actual body weights to gain "specific" metabolic rates and plotted as percentages of the values to be expected from body mass whereby a modified metabolic size relationship applying to marsupials was used [37].

In addition to these experiments which were performed at an incubation temperature of 37°C (corresponding to the temperature in the mother's abdominal "pouch"), heat output rates at 27°C were also measured and the resulting temperature coefficients ($Q_{10}$-values) calculated. Moreover, complementary to heat output, oxygen consumption rates were determined using the traditional Warburg apparatus [38] so that the calorimetric/respirometric (*C/R*) ratio, known earlier as the "oxycaloric equivalent", could be calculated [39,40].

## 3. Results

### 3.1. Metabolic behaviour in human preterm neonates

Clinical measurements indicate that, in contrast to birth weights which – of course – are much higher after forty than after thirty weeks of gestation, the specific oxygen consumption rates of human neonates immediately after birth (i.e. within the first 48 h of life) are fairly independent of gestational age and amount to roughly 5.5 ml $kg^{-1}min^{-1}$ (Fig. 4(a)). Although this is not exactly at the maternal level, it corresponds, in preterm neonates of 27 to 33 weeks of gestation, to only 60% of the metabolic rate to be expected from body mass. Starting from there, the turnover rate increases within three weeks to ca. 110% of the predicted level (Fig. 4(b)). Interestingly, the

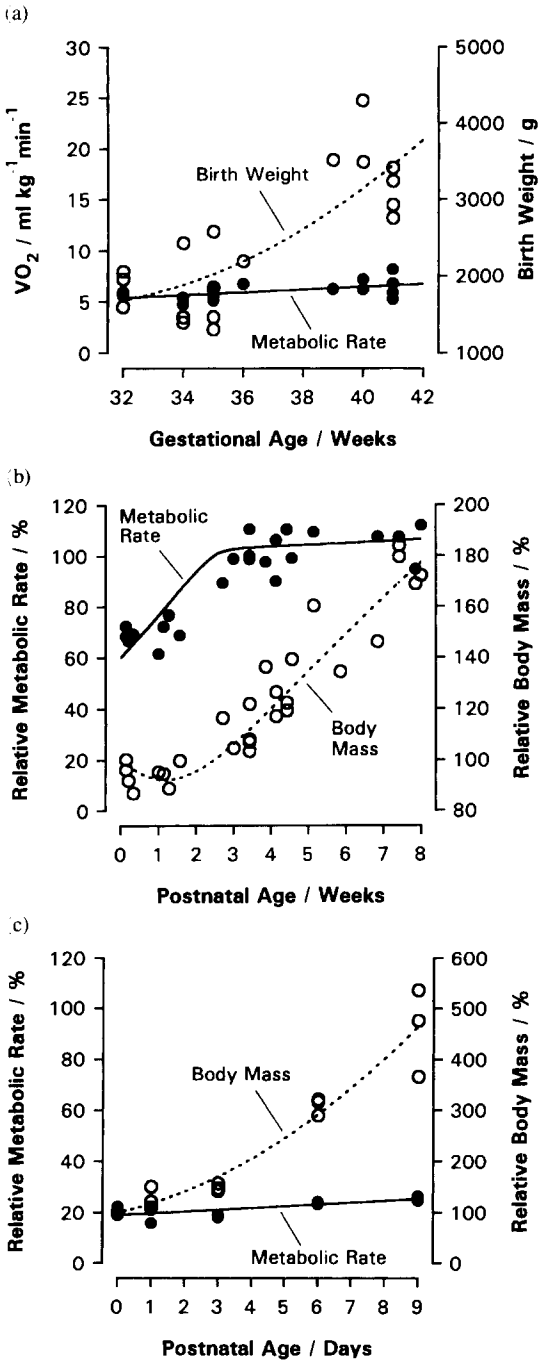


Fig. 4. (a) Early postnatal oxygen consumption rates and birth weights in human term and preterm neonates as related to gestational age. The specific $O_2$ consumption rate immediately (i.e. less than 48 h) after birth amounts to a relatively invariable 5.5 ml kg$^{-1}$ min$^{-1}$ whereas mean birth weights are nearly twice as high after 40 as after 30 weeks of gestation. (b) Body weight and metabolic rate in human preterm neonates (ranging from 27 to 33 weeks of gestation). The specific $O_2$ consumption rate rate increases within about three weeks from 60% to 110% of the value to be expected from body mass. However, the body mass, given as a percentage of birth weight, starts increasing only after the metabolic rate has reached its new higher level. (c) Body weight and metabolic rate in *Monodelphis* neonates. The specific heat output rate amounts to only 20% of the value to be expected from body mass and remains fairly constant whereas the body mass increases in a nearly exponential manner to 500% of birth weight during the first ten days of life. The data points represent three different individuals on each particular day.

body weight resumes increasing only after the metabolic rate has reached its new, higher level, suggesting that the temporary growth retardation typical of preterm neonates is closely related to their metabolic behaviour.

### 3.2. Metabolic behaviour in Monodelphis neonates

In *Monodelphis* neonates, the specific heat output rate at birth amounts to roughly 5.5 mW g$^{-1}$ which is exactly at the maternal level and, thus, amounts to only 20% of the metabolic rate to be expected from body mass. From here on, there is virtually no metabolic increase although the body mass increases in a nearly exponential manner to 500% of birth weight during the first ten days of life (Fig. 4(c)).

When the heat-output rates of *Monodelphis* neonates, whether on postnatal day 0 or 9, are measured at an incubation temperature of 27°C, a temperature coefficient of 1.7 or 2.2, respectively, is obtained, i.e. the metabolic rate is about half the value found at 37°C. Micro*respirometric* measurements confirm the results obtained by micro*calorimetry*, both with respect to the extent of perinatal metabolic reduction and to the missing postnatal increase in metabolic rate. The average oxygen consumption rate amounts to 15 µl g$^{-1}$ min$^{-1}$ so that, based on the mean heat-output rate of 5.5 mW g$^{-1}$, a *C/R* ratio of ca. 480 kJ mol$^{-1}$ results.

## 4. Discussion

### 4.1. Perinatal metabolic reduction and growth efficiency

Just as in the case of body temperature, there is still no unanimous view on the adaptive significance and

the "physiological" behaviour of metabolic rate in the case of neonatal immaturity. As has been shown by the foregoing measurements, the postnatal metabolic increase in human preterm neonates is much slower than in term neonates, and in view of the fact that an elevated metabolic rate compensates for the higher surface-to-volume ratio (cf. above), it is evident that the slow metabolic increase contributes to their long-lasting thermal instability. Since, moreover, the body weight increases only after the metabolic rate has reached the new higher level (Fig. 4(b)), it seems obvious that the metabolic increase in human preterm neonates is "too slow". Had they, however, not yet been born, they would not experience a metabolic increase at this early stage of development so that, from this point of view, the metabolic increase appears rather "too fast".

When the *Monodelphis* neonate is regarded as an "experiment of nature" and the relationship between metabolic rate and body weight is studied in this species, exactly the inverse situation compared with human preterm neonates is found, that is, a high growth efficiency at a low metabolic rate (Fig. 4(c)). This means that the metabolic increase is neither an unavoidable consequence of birth nor a necessary precondition of postnatal growth and that in the case of extreme immaturity, a continuing metabolic reduction could be the "natural" adaptation strategy [41,42].

Of course, it might be argued that the different types of metabolic behaviour may simply reflect different species-specific peculiarities. However, when the specific metabolic rates of human neonates immediately after birth are related to birth weights, it becomes evident that, during the *intrauterine* development of human beings, there is a similar combination of high growth efficiency and low metabolic rate to that continued even *after birth* in *Monodelphis* (Fig. 4(a)). Obviously, in humans, preterm birth interrupts a condition of metabolic economy and elicits a (predetermined?) program which leads to a metabolic increase at the expense of temporary growth retardation [43].

The persisting energetic economy of *Monodelphis* neonates is at least partly due to the fact that they do not attempt to thermoregulate: As is shown by the temperature coefficient of ca. 2, *Monodelphis* neonates exhibit a passive "biochemical" temperature dependence of metabolic rate without any thermoregulatory reaction. In other words, they are "truely poikilothermic" (again similar to the intrauterine situation in higher mammals) whereas human preterm neonates, though with little chance of success, try to thermoregulate and, thereby, consume part of the energy which otherwise would have been used for growing.

### 4.2. *Perinatal metabolic reduction and oxygen supply to tissues*

As can be concluded from the *C/R* ratio, the heat output of *Monodelphis* neonates corresponds to their oxygen consumption so that there is no evidence of partial anaerobiosis in these animals [39,40]. This is of special interest since they bear some aspects of immaturity which might impair $O_2$ supply to tissues. Firstly, their lungs are still in the "pseudo-glandular" stage of development which means that there are no alveoli and that (despite some anatomical peculiarities enabling respiration at all) the total surface area for respiratory gas exchange is markedly restricted [44]. Hence, a low $O_2$ consumption rate appears to be a prerequisite for aerobic survival at this stage of development. Secondly, their brains are still not capillarized and exclusively supplied with $O_2$ by diffusion from the surroundings. Therefore, it is advantageous that the "critical depth" of penetration of $O_2$ into tissues by diffusion is improved by reduction of $O_2$ consumption [20,26,38,45,46]. Thus, in summary, the low metabolic rate is not only correlated with a high growth efficiency, but seems to be an important adaptation to lung immaturity and incomplete tissue vascularization, as well.

### 4.3. *Perinatal metabolic reduction and hypoxia tolerance*

When these results are compared to data from the literature [47–51], it turns out that the perinatal "switching-off" of usual metabolic size relationship not only occurs in some selected species, but is a more general adaptation strategy of mammalian neonates with the distance between the "expected" and the actual metabolic rate being the larger, the smaller the neonate is, and the postnatal metabolic increase being the slower, the more immature it is at birth (Fig. 5).

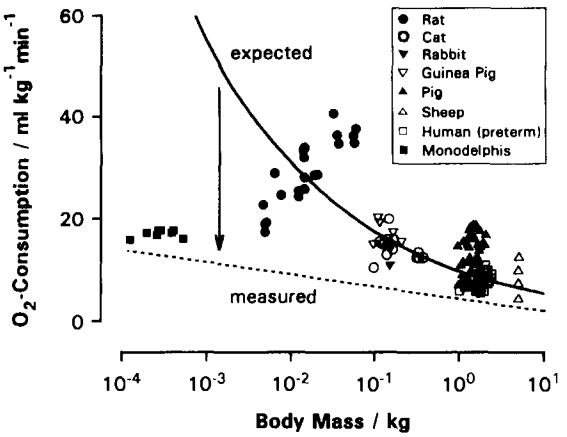


Fig. 5. Perinatal suppression of metabolic size relationship in various mammalian species. The difference between "expected" (according to Kleiber's rule) and measured metabolic rates is the larger, the smaller the neonate is (as compared to the maternal body mass), and the postnatal metabolic increase is the slower, the more immature it is at birth. Data are from [47–51] and from this study.

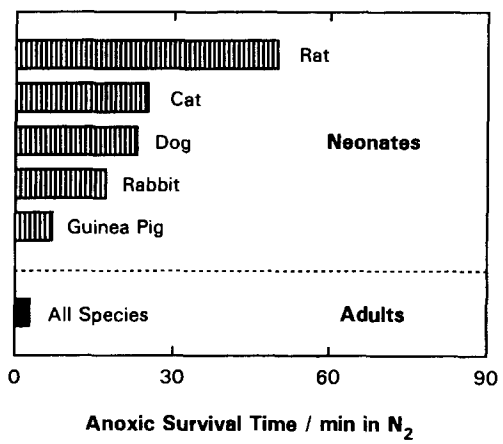


Fig. 6. Enhanced tolerance to hypoxia in mammalian neonates. The survival time in a nitrogen atmosphere is markedly prolonged in neonatal as compared to adult individuals of various species, the highest tolerance being exhibited by the species with the smallest and most immature neonates. The analogy to the size relationship of perinatal metabolic reduction (cf. Fig. 5) is evident. Redrawn from [52,53].

Most interestingly, this corresponds to a very old observation which, however, has not yet been fully understood, namely, the increased hypoxia tolerance of mammalian neonates [52–55]. In fact, the survival time under hypoxic conditions is markedly prolonged in neonatal as compared to adult individuals, and this is most evident in the species with the smallest and most immature neonates (Fig. 6). Keeping in mind the above considerations on $O_2$ supply to tissues, it can be assumed that the combination of small body size and an "inappropriately" low metabolic rate facilitates $O_2$ diffusion to tissues in a way that improves survival at very low $pO_2$ values.

## 5. Conclusion

As was pointed out at the beginning, the term neonate is adapted to its small body size by an elevated metabolic rate. As is shown by the above considerations, temporary metabolic reduction may be of equally important adaptive value in the perinatal period, not only for growth efficiency, but also for $O_2$ supply and for hypoxia tolerance. The human term and slightly preterm neonate probably profit from a rapid postnatal increase in metabolic rate with respect to both thermal stability and growth. However, in cases where $O_2$ and substrate supply are limited by extreme immaturity, continuing metabolic reduction is likely to be the more appropriate strategy. Unfortunately, the factors mediating perinatal metabolic suppression in "specialized immatures" such as marsupials are still unknown. Therefore, very careful thermal protection with the aim of attaining true thermal comfort seems to be one of the most promising ways to avoid premature and uneconomic metabolic increase in highly preterm human neonates.

## Acknowledgements

The author is greatly indebted to Ms. Barbara Hallmann for excellent technical assistance, to his undergraduate medical students Eckhard Hehenkamp, Markus Röbl, Meike Schröder, and Anne Waldow for industrious clinical, laboratory, and library work, to Professor Ulrich Zeller (Institute of Systematic Zoology, Berlin) for generous and fruitful cooperation in the field of marsupial biology, to Professor Hans-Jürg Kuhn (Department of Anatomy, Göttingen) for continuous support in the comparative-physiological approach to clinical problems, and to Ms. Cyrilla Maelicke, B.Sc., for valuable help with the English manuscript. Experimental work referred to in this

paper is supported by the Deutsche Forschungsgemeinschaft (SI 480/2-1).

## References

[1] K. Brück, Heat production and temperature regulation, in: U. Stave (Ed.), Perinatal Physiology, Plenum, New York, 1978, Chap. 21, pp. 455–498.
[2] K. Brück, Neonatal thermal regulation, in: R.A. Polin, W.W. Fox (Eds.), Fetal and Neonatal Physiology, Vol. 1, Saunders, Philadelphia, 1992, Chap. 48, pp. 488–515.
[3] J.C. Sinclair (Ed.), Temperature Regulation and Energy Metabolism in the Newborn, Grune and Stratton, New York, 1978.
[4] P.J.J. Sauer, Neonatal thermoregulation, in: R.M. Cowett (Ed.), Principles of Perinatal–Neonatal Metabolism, Springer, New York, 1991, Chap. 31, pp. 609–622.
[5] D. Singer, H. Schiffmann, Thermoregulatorische Besonderheiten des pädiatrischen Patienten, in: W. Weyland, U. Braun, D. Kettler (Eds.), Perioperative Hypothermie: Probleme, Prävention und Therapie, Aktiv, Ebelsbach, 1997, Chap. 11, pp. 110–122.
[6] N.J. Evans, N. Rutter, Development of the epidermis in the newborn, Biol. Neonate 49 (1986) 74–80.
[7] K. Hammarlund, G. Sedin, B. Strömberg, Transepidermal water loss in newborn infants, VIII. Relation to gestational age and post-natal age in appropriate and small for gestational age infants, Acta Paediatr. Scand. 72 (1983) 721–728.
[8] J. Nedergaard, B. Cannon, Brown adipose tissue: Development and function, in: R.A. Polin, W.W. Fox (Eds.), Fetal and Neonatal Physiology, Vol. 1, Saunders, Philadelphia, 1992, Chap. 27, pp. 314–325.
[9] J. McIntyre, D. Hull, J. Nedergaard, B. Cannon, Thermoregulation, in: P.D. Gluckman, M.A. Heymann (Eds.), Perinatal and Pediatric Pathophysiology: A Clinical Perspective, Edward Arnold, London, 1993, Chap. 8A, pp. 357–368.
[10] D. Singer, M. Röbl, H. Schiffmann, K. Harms, Aufnahmetemperaturen von Neu- und Frühgeborenen: Retrospektive Analyse der Entwicklung von 1955 bis 1995, submitted.
[11] D. Singer, H.J. Bretschneider, Metabolic reduction in hypothermia: Pathophysiological problems and natural examples, Parts 1 & 2, Thorac. Cardiovasc. Surgeon 38 (1990) 205–219.
[12] S. Ritzerfeld, D. Singer, Ch.P. Speer, H. Schiffmann, K. Harms, Notfalltransporte von Neu- und Frühgeborenen: Vorausschauende Versorgung schützt vor Komplikationen, Notarzt 13 (1997) 1–7.
[13] A. Okken, J. Koch (Eds.), Thermoregulation of Sick and Low Birth Weight Neonates: Temperature Control, Temperature Monitoring, Thermal Environment, Springer, Berlin, 1995.
[14] D. Sessler, Thermoregulation and heat balance: General anesthesia, in: E. Zeisberger, E. Schönbaum, P. Lomax (Eds.), Thermal Balance in Health and Disease: Recent Basic Research and Clinical Progress, Birkhäuser, Basel, 1994, pp. 251–265.
[15] D. Singer, Bedeutung und Kontrolle der Körpertemperatur bei Homöothermen, in: W. Weyland, U. Braun, D. Kettler (Eds.), Perioperative Hypothermie: Probleme, Prävention und Therapie, Aktiv, Ebelsbach, 1997, Chap. 1, pp. 1–14.
[16] E.N. Hey, G. Katz, The optimum thermal environment for naked babies, Arch. Dis. Child. 45 (1970) 328–334.
[17] P.J.J. Sauer, H.J. Dane, H.K.A. Visser, New standards for neutral thermal environment of healthy very low birth-weight infants in week one of life, Arch. Dis. Child. 59 (1984) 18–22.
[18] G.G. Power, Fetal thermoregulation: Animal and human, in: R.A. Polin, W.W. Fox (Eds.), Fetal and Neonatal Physiology, Vol. 1, Saunders, Philadelphia, 1992, Chap. 46, pp. 477–483.
[19] H.J. Schröder, G.G. Power, Basic aspects of fetal thermal homeostasis, in: E. Zeisberger, E. Schönbaum, P. Lomax (Eds.), Thermal Balance in Health and Disease: Recent Basic Research and Clinical Progress, Birkhäuser, Basel, 1994, pp. 235–249.
[20] M. Kleiber, The Fire of Life: An Introduction to Animal Energetics, Wiley, New York, 1961.
[21] K. Schmidt-Nielsen, Scaling: Why is Animal Size so Important?, Cambridge University Press, Cambridge, UK, 1984.
[22] D.R. Wilkie, Metabolism and body size, in: T.J. Pedley (Ed.), Scale Effects in Animal Locomotion, Academic Press, London, 1977, Chap. 2, pp. 23–36.
[23] H. Rahn, Comparison of embryonic development in birds and mammals: birth weight, time, and cost, in: C.R. Taylor, K. Johansen, L. Bolis (Eds.), A Companion to Animal Physiology, Cambridge University Press, Cambridge, UK, 1982, Chap. 9, pp. 124–137.
[24] W. Wieser, A distinction must be made between the ontogeny and the phylogeny of metabolism in order to understand the mass exponent of energy metabolism, Respir. Physiol. 55 (1984) 1–9.
[25] W. Wieser, Bioenergetik: Energietransformationen bei Organismen, Thieme, Stuttgart, 1986.
[26] D. Singer, O. Schunck, F. Bach, H.-J. Kuhn, Size effects on metabolic rate in cell, tissue, and body calorimetry, Thermochim. Acta 251 (1995) 227–240.
[27] J.R. Hill, K.A. Rahimtulla, Heat balance and the metabolic rate of new-born babies in relation to environmental temperature; and the effect of age and of weight on basal metabolic rate, J. Physiol. (London) 180 (1965) 239–265.
[28] J.W. Scopes, I. Ahmed, Minimal rates of oxygen consumption in sick and premature newborn infants, Arch. Dis. Child. 41 (1966) 407–416.
[29] P.J.J. Sauer, Neonatal energy metabolism, in: R.M. Cowett (Ed.), Principles of Perinatal–Neonatal Metabolism, Springer, New York, 1991, Chap. 30, pp. 583–608.
[30] P.J.J. Sauer, H.K.A. Visser, Calorimetry of newborn infants: Techniques and applications, Thermochim. Acta 193 (1991) 49–56.
[31] P.T. Meriläinen, Metabolic monitor, Int. J. Clin. Monitor. Comput. 4 (1987) 167–177.
[32] J. Takala, O. Keinänen, P. Väisänen, A. Kari, Measurement of gas exchange in intensive care: Laboratory and clinical validation of a new device, Crit. Care Med. 17 (1988) 1041–1047.

[33] D. Singer, E. Hehenkamp, K. Harms, W. Schröter, Indirektkalorimetrische Untersuchungen zur Dynamik des postnatalen Energieumsatzanstieges bei Frühgeborenen, submitted.
[34] M.E. Nicoll, S.D. Thompson, Basal metabolic rates and energetics of reproduction in therian mammals: Marsupials and placentals compared, Symp. Zool. Soc. (London) 57 (1987) 7–27.
[35] J. Suurkuusk, I. Wadsö, A multichannel microcalorimetry system, Chem. Scripta 20 (1982) 155–163.
[36] D. Singer, U. Zeller, H.-J. Kuhn, Postnatal energetics of a marsupial species, *Monodelphis domestica*: A comparative calorimetric investigation, submitted.
[37] T.J. Dawson, A.J. Hulbert, Standard metabolism, body temperature, and surface areas of Australian marsupials, Amer. J. Physiol. 218 (1970) 1233–1238.
[38] W.W. Umbreit, R.H. Burris, J.F. Stauffer, Manometric Techniques and Tissue Metabolism, Burgess, Minneapolis, MN, 1949.
[39] E. Gnaiger, Heat dissipation and energetic efficiency in animal anoxibiosis: Economy contra power, J. Exp. Zool. 228 (1983) 471–490.
[40] R.B. Kemp, E. Gnaiger, Aerobic and anaerobic energy flux in cultured animal cells, in: W. Wieser, E. Gnaiger (Eds.), Energy Transformations in Cells and Organisms, Thieme, Stuttgart, 1989, pp. 91–97.
[41] D. Singer, E. Hehenkamp, U. Zeller, H. Schmidt, H.-J. Kuhn, W. Schröter, Postnatal development of metabolic rate in preterm human and small marsupial neonates: Different patterns in pathological and physiological prematurity, Europ. J. Ped. 154 (1995) 251.
[42] D. Singer, U. Zeller, E. Hehenkamp, H. Schmidt, H.-J. Kuhn, Suppression and activation of metabolic size allometry in marsupial and preterm human neonates: A comparative calorimetric investigation, Physiol. Zool. 68 (1995) 126.
[43] D. Singer, E. Hehenkamp, U. Zeller, H. Schmidt, H.-J. Kuhn, W. Schröter, Der vorzeitige Anstieg des Energieumsatzes unterscheidet menschliche Frühgeborene von einer an neonatale Unreife angepaßten Tierart, Z. Geburtsh. Neonatol. 199 (1995) 217.
[44] H. Schmidt, U. Zeller, D. Singer, J. Richter, Lungenentwicklung bei Beuteltieren (*Monodelphis*) als Modell einer physiologischen Frühgeburt, Z. Geburtsh. Neonatol. 199 (1995) 221.
[45] A. Krogh, The number and distribution of capillaries in muscles with calculations of the oxygen pressure head necessary for supplying the tissue, J. Physiol. (London) 52 (1918/19) 409–415.
[46] O. Warburg, Versuche an überlebendem Karzinomgewebe, Biochem. Z. 142 (1923) 317–333.
[47] G.S. Dawes, J.C. Mott, The increase in oxygen consumption of the lamb after birth, J. Physiol. (London) 146 (1959) 295–315.
[48] R.E. Moore, M.C. Underwood, Hexamethonium, hypoxia and heat production in new-born and infant kittens and puppies, J. Physiol. (London) 161 (1962) 30–53.
[49] R.E. Moore, M.C. Underwood, The thermogenic effects of noradrenaline in new-born and infant kittens and other small mammals: A possible hormonal mechanism in the control of heat production, J. Physiol. (London) 168 (1963) 290–317.
[50] K. Brück, B. Wünnenberg, Über die Modi der Thermogenese beim neugeborenen Warmblüter, Pflügers Arch. 282 (1965) 362–375.
[51] L.E. Mount, D.B. Stephens, The relation between body size and maximum and minimum metabolic rates in the new-born pig, J. Physiol. (London) 207 (1970) 417–427.
[52] J.F. Fazekas, F.A.D. Alexander, H.E. Himwich, Tolerance of the newborn to anoxia, Amer. J. Physiol. 134 (1941) 281–287.
[53] E. Opitz, M. Schneider, Über die Sauerstoffversorgung des Gehirns und den Mechanismus von Mangelwirkungen, Erg. Physiol. Biol. Chem. Exp. Pharmakol. 46 (1950) 126–260.
[54] P.L. Lutz, G. Nilsson, The Brain Without Oxygen: Causes of Failure and Mechanisms for Survival, Landes, Austin, TX, 1994.
[55] J.J. Volpe: Neurology of the Newborn, 3rd edn., Saunders, Philadelphia, PA, 1995, pp. 225–227.