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# Calorimetry of newborn infants: techniques and applications

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**Abstract**

Calorimetry was extensively used in a study of newborn infants, to estimate the optimal energy intake, the effects of changes in the composition of the feeding formula and to estimate the composition of weight gain. Calorimetry was also used to define the optimal environmental temperature of newborn infants. Most studies used indirect calorimetry; only a few studies used direct calorimetry. Whether both methods give identical answers is still a matter of debate.

## INTRODUCTION

All energy taken up with food by living individuals is either used for energy consuming processes or stored within the body. Energy consuming processes can be divided into energy used for maintenance of the body, energy for activity and energy for thermoregulation. Adults may also use energy for external work, while in growing infants energy is needed for growth. All energy used for maintenance, activity and thermoregulation is finally given off as heat. Most of the energy used for growth is stored within the body, while a small amount of energy used in the process of tissue synthesis is given off as heat. The amount of energy used by an infant for maintenance, activity and thermoregulation, together with a small amount of heat produced during tissue synthesis, is equal to the heat loss of the infant. This heat loss can be measured using a direct calorimeter. A direct calorimeter measures the heat lost by convection, conduction, evaporation and radiation. Direct calorimeters, however, are difficult to build for use with human infants, because of the small amount of heat lost by the newborn infant. Most studies estimating the heat production of newborn infants have therefore used indirect calorimeters, measuring the oxygen consumption, carbon dioxide production and nitrogen loss in urine. Using these figures, the total metabolic rate as well as the relative contribution of glucose, fat and protein to the metabolic rate, can be estimated.

## DIRECT VERSUS INDIRECT CALORIMETRY

Very few studies have compared the results of direct and indirect calorimetry in growing infants. Day and Hardy [1] were the first to compare the results of both methods. The results of direct and indirect calorimetry, however, are difficult to compare in their studies, as their studies lasted only a maximum of one hour and the body temperature of the infants fluctuated considerably during the study. The total heat loss can be over- or under-estimated by 30% when the body temperature either decreases or increases by $1°C\ h^{-1}$. A small difference between direct and indirect calorimetry is hard to detect in studies of short duration with considerable changes in body temperature.

Therefore, we decided to build a direct and indirect calorimeter to evaluate whether both methods give identical results in growing pre-term infants. This system was designed and built in the central research workshop of the Erasmus University, Rotterdam [2]. It consists of an airtight cylinder in which the infant is placed (Figs. 1 and 2). Air is pumped continuously in and out the incubator. The dry heat loss is measured by double gradient layers, measuring the heat leaving as well as the heat entering through the

Fig. 1. General overview of the direct and indirect calorimeter at the department of Pediatrics, Erasmus University, Rotterdam/Sophia Children's Hospital.

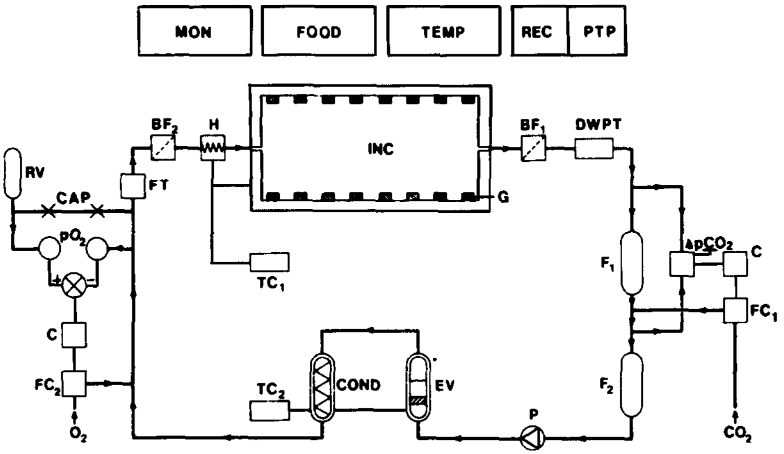


Fig. 2. Schematic diagram of the calorimeter.

walls of the calorimeter, and by the temperature difference of the air coming into and leaving the incubator. The evaporative heat loss is measured from the difference in humidity between the air entering and leaving the incubator. The oxygen consumption is measured as the oxygen introduced to the incubator to keep the oxygen pressure constant. The carbon dioxide production is measured using a differential pressure infrared $CO_2$ monitor. The difference between the results of direct and indirect calorimetry was measured by burning methanol. The difference was found to be less than 10 kJ day$^{-1}$.

Using this system, 57 measurements were performed with 14 pre-term infants [3]. We found a systematic, significant difference between the results of indirect and direct calorimetry: the results of indirect calorimetry were higher in all growing infants. The difference observed was 22 kJ kg$^{-1}$ per day or 7.2% of the indirect calorimetry results. We speculated that this difference is part of the energy cost of growth. Energy, needed for instance to form high energy bonds and osmotic gradients, is not given off as heat but requires the oxidation of food products. Therefore the results of indirect calorimetry will be higher than those of direct calorimetry in growing infants.

Very recently, Bell et al. repeated these studies [4]. They did not observe a systematic difference between the methods; however these studies lasted only 2–3 h, whereas our studies lasted at least 6 h. Moreover, in these studies, feeding was given intermittently, which makes it even more difficult to reach a stable situation. Therefore, the question whether direct and indirect calorimetry in growing pre-term infants give identical results still needs further study.

## ENERGY BALANCE

Calorimetry has been used extensively in pre-term and full-term infants in order to calculate their optimal energy intake and to evaluate the effect of changes in energy intake and in the composition of the feeding on metabolic rate.

The energy balance can be calculated to estimate the energy needs of the infant. The energy balance can be written as

$$\text{Energy}_{\text{intake}} = \text{Energy}_{\text{maintenance}} + \text{Energy}_{\text{activity}} + \text{Energy}_{\text{urine+faeces}} + \text{Energy}_{\text{growth}}$$

The energy used for maintenance and activity can be measured by indirect calorimetry; the energy losses from the excretion in urine and stools. The energy needed for growth can be calculated from the difference in energy intake and energy expended or lost. When the rate of weight gain is also known, is it possible to calculate the energy needed per gram of growth. Different studies have used this approach to calculate the energy cost of growth [3,5–8]. We estimated the optimal energy intake of the pre-term infant to be 460–545 kJ $kg^{-1}$ per day. Approximately 10% of this intake is lost in urine and faeces; this is dependent on the composition of the feeding given [9,10]. Around 40% of the intake is used for maintenance of the body and 6% for activity. The remainder, 44% of the energy intake, is used for growth.

The metabolic rate of the new-born infant is related to the energy intake: the higher the energy intake, the higher the metabolic rate [11]. There are different explanations for this increased energy expenditure. One explanation is that it represents the energy needed to absorb and utilise the energy intake, the so-called specific dynamic action. This process is not very well understood; it may consist of two parts: a facultative and an obligatory heat production [12]. Another explanation is that the increase in energy expenditure represents the energy needed for tissue synthesis during growth. The energy cost of synthesis calculated using this approach is 1.2–7 kJ per g weight gain [3,5–8].

The composition of the feeding solution also seems to influence the metabolic rate of newborn infants. In a group of full-term, intravenously fed new-born infants, we compared the metabolic rate when all calories were given as glucose with that when part of the energy was given as fat. We observed a lower metabolic rate in the infants receiving the mixed feeding [13], in accordance with studies in adults [14]. It was hypothesised that this decrease in metabolic rate was due to a lower lipogenesis, an energy-consuming process, in the fat-supplemented group. Recently, however, the possible effects of the composition of the intravenous nutrition on the metabolic rate have been challenged [15].

## MEASUREMENT OF SUBSTRATE UTILISATION

Indirect calorimetry has been used to estimate the relative contributions of carbohydrates and fat to the energy expenditure. When carbohydrates are oxidised, the RQ, the ratio of carbon dioxide production over oxygen consumption is equal to 1, compared with 0.7 when fat is oxidised. The RQ increases to above 1 when net fat synthesis takes place. From these data, together with the fat and carbohydrate intake and their losses in the excreta, is it possible to calculate the composition of new tissue during growth.

Using this approach, it was shown that the body composition of the growing pre-term infant is dependent on energy intake as well as on the composition of the feeding given [16–18]. An energy intake above approximately 500 kJ $kg^{-1}$ $day^{-1}$ does not result in a higher weight gain or gain in length and head circumference, but only in a higher fat content of new tissue. Reduction of the energy intake to approximately 420 kJ $kg^{-1}$ $day^{-1}$ on the other hand, results in a reduction in weight gain without affecting the gain in length or head circumference, with a fat accretion below that for infants growing in utero.

It is questionable, however, if the substrate utilisation of growing infants can be estimated from the RQ. The idea of using the RQ to calculate the relative contributions of carbohydrate and fat was first proposed by Lusk in 1924 [19]. This was done in fasting adults. Growing infants are quite different to fasting adults: part of the energy intake will be stored in the body. Most of the storage is in the form of fat, and carbohydrates will also be converted into fat. The conversion of glucose into fat significantly influences the RQ, the RQ of this process being between 2 and 8. Thus the RQ that is measured in growing infants can be the result of substrate oxidation and storage. To have a separate measure of substrate oxidation, we infused $^{13}C$-labelled glucose and octanoin in new-born infants [13,20,21]. These studies showed a difference between the results of indirect calorimetry and using stable isotopes: calorimetry overestimated glucose oxidation and underestimated fat oxidation. This can be explained from the conversion of glucose into fat that takes place at an energy intake above the maintenance level.

## CALORIMETRY AND THERMOREGULATION

It is well known from clinical experience that new-born infants are very susceptible to hypothermia. Nursing in environmental conditions that both prevent a drop in body temperature and an increase in heat production are very important for the new-born infant. Mortality increases when the body temperature drops. An increase in metabolic rate because of nursing in an environmental temperature that is too low, will result in a reduction, or even an absence of the growth that is vital for newborn infants.

The optimal environmental conditions (temperature, humidity, airvelocity), therefore, can be defined as the environment at which the metabolic rate of the infant is at a minimum while body temperature is within the normal range.

Over the past 25–30 years, calorimetry has been used to define the optimal temperature, which is also called the neutral temperature. Most of these studies have measured the metabolic rate of infants of different gestational ages, post-natal ages and weights at one or more environmental conditions. The neutral temperature, or actually a neutral range, was then constructed from all these studies [22,23]. The results have to be regarded with some caution. First of all, it was impossible to study each infant at a range of environmental temperatures; most infants were studied at two or three environmental temperatures only. Data from different infants, therefore, were grouped together. Not all infants of equal gestational age, post-natal age and weight will have an equal neutral temperature. In our studies we observed that the neutral temperature for an individual patient varied with a standard deviation of 0.7 °C around the mean value [24,25].

Different studies have used the above-mentioned approach to estimate the neutral thermal environment of pre-term and full-term new-born infants [22–24]. It was shown that the optimal thermal environment increased with a shorter gestational age and decreased with increasing post-natal age. The neutral thermal environment of an infant born after 26 weeks on the first day of life is around 37.5 °C. Applying these figures to the standard care of these infants has greatly improved the survival and further outcome of pre-term infants.

## CONCLUSIONS

The mortality of new-born infants has decreased quite dramatically over the past 50 years in developed countries. The mortality of very sick and pre-term infants has decreased in an equally dramatic way in the last 20–30 years. This can be partially explained by the introduction of neonatal intensive care. Neonatal intensive care is usually linked with techniques such as ventilation and the treatment of serious infections. The use of calorimetry, however, has certainly also been of utmost importance in the care of sick new-born infants and, thereby, in decreasing the mortality of these infants. As a result of calorimetry, important improvements have been made with respect to the optimal nutrition of the new-born infant, both regarding the required energy intake and the composition of the feeding solution. Moreover, the optimal thermal environment of pre-term and full-term infants is defined on the basis of measurements made with calorimeters. Most studies have been done using indirect calorimeters; the question whether direct and indirect calorimetry in new-born infants give indentical results still needs further study.

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