Metabolic response to cold in the newborn

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SUMMARY Blood concentrations of glycerol and free fatty acids were measured in healthy and sick 5-day-old infants during and after cold exposure. In apparently similar infants in similar circumstances, the blood concentrations varied widely. Although the concentrations of both glycerol and free fatty acids tended to be higher during cold exposure, it is not possible to use either as an index of cold exposure in individual infants.

One of the objectives of intensive care of the newborn is to maintain an ambience which reduces the environmental stresses, and hence the challenge to the infant's homeostatic responses, to a minimum. Cold presents a considerable challenge to the newborn infant and a number of clinical studies have shown the particular vulnerability of the sick preterm infant to cold environments (Hey, 1971). Unfortunately, it is just such infants who give very little indication that they are experiencing hot or cold and, if they are, whether or not they are responding to it.

In experimental studies on newborn animals, cold exposure has been shown to produce a predictable rise in metabolic rate and in the circulating concentrations of glucose and the products of lipolysis, glycerol, and free fatty acids (FFA) (Hardman and Hull, 1969; Alexander *et al.*, 1972). Experimental studies on healthy preterm and mature newborn infants have shown that they too have predictable thermoregulatory responses to cold. From these studies recommendations have been made on the environment required to provide comfortable temperatures (ones which do not stimulate thermoregulatory adjustments) for infants of varying size, gestation, and postnatal age (Hey, 1969). The use of a simple open-circuit system to study $\dot{V}O_2$ in infants in the nursery confirms that those measurements made under precise environmental conditions are a valuable guide, but they could be quite misleading for individual infants, particularly sick infants (Smales, 1978).

Also in newborn infants, many studies have been made on the circulating concentrations of glucose, glycerol, and FFA, and the changes which occur in response to cold exposure (Persson and Gentz, 1966; Melichar and Wolf, 1967; Dawkins and Scopes, 1965;

Příbylová and Novak, 1970; Gentz *et al.*, 1976). Again they are consistent with the animal studies in showing that cold provokes an increase in all three concentrations in newborn man as in animals. As blood samples are frequently taken from sick newborn infants, and as FFA and glycerol concentrations have been shown to increase with cold exposure, and as their concentration can now be measured on very small volumes of blood, the possibility that their concentrations might be used as an index of an individual infant's response to cold exposure was explored.

Methods

This study was performed on the fifth day when blood was being routinely taken for Guthrie test. 10 babies were in the department of neonatal medicine for various problems (Table) (called 'abnormal group'). Their mean ($\pm$ SD) birthweight was 2.28 ± 0.30 kg, and gestation was 35.7 ± 1.1 weeks. 10 were in the lying-in nurseries and had a mean birthweight of 3.02 ± 0.27 kg, and gestation

Table Clinical details of 10 infants in the 'abnormal group'

Case no.	Gestation (w)	Birth-weight (kg)	Clinical features
1	33	1.30	Twin; jaundiced; light-for-dates
2	36	1.76	Twin; light-for-dates
3	35	1.95	Twin; birth asphyxia
4	40	3.34	Transient tachypnoea; jaundice
5	35	2.34	Rh haemolytic disease; 3 exchange transfusions
6	35	2.02	Mild RDS; jaundice
7	39	4.30	Birth asphyxia; jaundice
8	40	2.71	Fetal distress; forceps delivery
9	36	1.99	Light-for-dates; birth asphyxia; convulsions
10	28	1.10	Apnoea of prematurity; jaundice

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of 38.4 ± 0.08 weeks ('normal group'). Permission for the study was obtained from the parents after they had been given a full explanation of what the investigation involved.

All the studies were performed one hour after each feed. The rate of O_2 consumption was measured via a face mask using a simple open-circuit technique (Smales, 1978). The infant's rate of O_2 consumption was first measured after 20 minutes exposure at an ambient temperature which was 6°C below the lower critical temperature as predicted from age and weight from the values reported by Hey (1971). The infants were then placed at the predicted thermoneutral temperature for one hour and their O_2 consumption and deep body temperature measured again. Blood samples were collected after each period and analysed for glucose by the method of Huggett and Nixon (1957), for FFA by the automatic method of Elphick (1975), and for glycerol using the Boehringer Kit.

Results

After 20 minutes at 6°C below the thermoneutral temperature there was no significant difference in the mean rate of O_2 consumption between the normal and abnormal babies and when transferred to a thermoneutral environment the fall in O_2 consumption was similar (Fig. 1). In normal babies rectal temperature was not significantly influenced by the

alterations in environmental temperature. However, the mean rectal temperature of the abnormal group was lower after cooling than after an hour at a thermoneutral temperature ($P < 0.02$) (Fig. 2).

Plasma glucose levels were not found to alter significantly when the environmental temperature was altered and there was no significant difference between the two groups (Fig. 3). Plasma glycerol levels were higher in normal babies exposed to cold than after an hour at a thermoneutral temperature

Fig. 1 Rates of O_2 consumption of two groups of infants. Measurements were first made in a cool environment calculated to be 6°C below the neutral range on the basis of the information provided by Hey (1971) and then again after the babies had been for an hour in a warm environment. In this and subsequent figures, $\bullet$ represents the mean, and the vertical line ± 1 SE of the mean.

Fig. 2 Rectal temperatures of the two groups of infants whose O_2 consumptions are shown in Fig. 1. The healthy but small infants in the 'abnormal' group had on average a significantly larger fall in rectal temperatures.

Fig. 3 Plasma glucose concentrations in the two groups of infants studied at the two environmental temperatures. Conversion: Traditional units to SI—Glucose: $1 \text{ mg}/100 \text{ ml} \approx 0.0555 \text{ mmol/l}$.

($P < 0.02$, paired 't' test). This did not occur in the abnormal group (Fig. 4). FFA levels did not alter in a consistent manner with the alteration in environmental temperature, but the wide range of values found in the abnormal group was a striking feature (Fig. 5).

Discussion

In previous studies of this nature it has been customary to discuss the trends as shown by changes in the average between groups. In the healthy 5-day-old infants a decrease in the metabolic rate occurred when the infants were transferred from the cool to the warm environment and this was accompanied by a decrease in plasma glycerol concentrations. These findings support the original observation of Dawkins and Scopes in 1965. A similar change in the mean values for the sick infants was also seen with respect to the rate of O_2 consumption, but did not occur in the glycerol concentrations. Although there was a trend in the healthy infants for the FFA and glucose concentrations also to fall, neither reached statistical significance.

These trends in mean values are in line with the observations on experimental animals when cold exposure led to a rise in all three metabolites. However, even in the healthy infants there was striking variation from one infant to another, for example the resting metabolic rate varied from

Fig. 4 Plasma glycerol concentrations in the two groups of infants studied at the two environmental temperatures. Conversion: SI to traditional units—Glycerol: $1 \text{ mmol/l} \approx 9.2 \text{ mg/100 ml}$.

Fig. 5 Plasma free fatty acid concentrations in the two groups of infants studied at the two environmental temperatures.

4.5 to 8.2 ml O_2 /kg per min. The FFA concentrations varied from 0.18 to 0.88 mEq/l. Animal studies suggest that both the plane of nutrition and previous experience of cold exposure will vary the infant's response, but it is perhaps surprising that there is such wide variation in apparently thriving, healthy, term infants. It is certainly of a magnitude to obscure the comparatively small influences of the ambient temperature.

What is true of the healthy infants is even more apparent in the infants nursed in the special care areas, where a similar variation in metabolic rate was noted and there was a much greater variation in the concentration of glycerol and FFA. From these data it could be argued that it is as important to investigate the factors which influence the infant's minimal metabolic rate and circulating concentrations of FFA as it is to determine whether or not the infant is experiencing a cool environment. It is not, of course, self-evident that it is desirable for the infant never to experience cold exposure, or to have a low metabolic rate.

The results are consistent with previous observations that cold exposure stimulated an increase in

the infant's rate of O_2 consumption and mobilisation of energy reserves. However, circulating concentrations of FFA and glycerol cannot be used as a guide to the infant's level of responsiveness.

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