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HEAT PRODUCTION IN NEW-BORN INFANTS UNDER NORMAL AND HYPOXIC CONDITIONS

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In 1955, Cross, Tizard & Trythall observed that the new-born baby, when breathing 15% oxygen, showed a drop in oxygen consumption which averaged 17% in full-term infants. Although this was accompanied by a 15% rise in respiratory quotient, calculation showed that if this rise were a measure of anaerobic glycolysis the energy so produced would by no means replace that lost by the fall in oxygen consumption. It was therefore concluded that a fall in energy production might be a primary response of the new-born human to hypoxia, whereas the adult shows this phenomenon only when hypoxia is very severe.

This paper describes an attempt to verify this conclusion by a comparison of the heat production of babies under normal and hypoxic conditions. It was originally planned to use the body plethysmograph (Cross, 1949) to measure the minute volume of respiration and simultaneously to measure the skin temperature at selected points, the rectal temperature, and the air temperatures inside and outside the plethysmograph. As will be explained later, the measurements of the skin and rectal temperatures caused restlessness of the babies and so were made only in a limited number of cases. Hypoxic conditions were realized by administering 15% oxygen, but as slight cyanosis was observed in some babies the administration of this gas was restricted to periods of 50 min, although it was realized that by imposing this limitation there would be little time for marked changes in body temperature to occur. (Since this work was planned Engelson, Booth & Sjöstedt (1956) working in Lund have kept full term babies on 15% oxygen for a week or more without apparent ill effects.) Some results of this investigation have already been communicated to the Physiological Society (Brodie, Cross & Lomer, 1956).

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METHODS

All experiments were carried out in a side room of the obstetric department at Paddington General Hospital. The infants used in this study were full-term and in their first week of life, and the experiment was only performed with the mother's permission. The room was in no way temperature controlled, and both in summer and winter there was a hot pipe running round three of the walls. In summer weather the room could be shielded from the direct rays of the sun by curtains, but the room temperature during different experiments varied between 16 and 25·0° C. Attempts were made during an individual experiment to keep the temperature more or less constant, without creating a draught which played directly on the plethysmograph or the room thermometer, but these were only partially successful. On sunny days in summer experiments had to be abandoned because the temperature was uncomfortably high. Cases were incorporated into this study only if the room temperature was constant to $\pm 0{\cdot}25°$ C for the period under consideration.

Skin temperature was measured with a 34-gauge copper-constantan thermocouple which was stretched tighly across a piece of grooved transparent plastic which was applied either to the skin of the left upper quadrant of the abdomen or to the skin of the anterior surface of the left thigh.

The rectal temperature was taken before and after each experiment with a clinical thermometer, and during the experiment with another copper-constantan thermocouple sheathed in 2 mm polyvinyl tubing which was sealed and smoothed off at the upper end by heat. This was inserted 2·5 cm into the rectum and held securely in place by tapes. The reference junction for both thermocouples was immersed in a Townson & Mercer Constant Temperature Bath, Type X-148, accurate to 0·01° C. This bath was kept at 27° C. The thermocouples were connected through a low resistance copper switch to a Kipp Mirror Galvanometer. The minute volume of respiration was measured in the body plethysmograph, which had been modified (for another purpose) by the application of four turns of half-inch copper tubing heavily soldered to the brass walls. This had certainly modified the thermal characteristics of the instrument by increasing its heat capacity. The air temperatures were taken with mercury thermometers, one fixed to the inner side of the lid of the plethysmograph and the other suspended at a fixed point shielded from draughts in the room in which the experiments were performed. Air was drawn over the face of the infant from a pipe, one end of which was open outside the building. A special chamber over the infant's face ensured that this was the only source of air, and when 15% oxygen was given it was supplied from cylinders through a humidifier into a gas balloon, and thence sucked over the face as for the atmospheric air. The oxygen content of the gas cylinders was measured regularly.

The babies were treated in one of two ways: they were studied in the plethysmograph while at rest either during a period of 1 hr while breathing atmospheric air, or during a period of 50 min while breathing 15% oxygen after a preliminary period of 10 min breathing air. An experiment was accepted for this study only if the infant had remained asleep for the greater part of the hour, and crying or restlessness was only admissible for a period of 10 min or less during the entire period of observation. It should be noted that these requirements are less stringent than those adopted in previous studies reported from this laboratory, but the length of time of observation was consistently longer and the manipulation of the infant in preparation for thermometry was more disturbing than the techniques we had previously adopted. Well over one hundred experiments were performed as described above, but only twelve of these fulfilled our criteria for an acceptable experiment. The average rise in rectal temperature of the six controls during the 1 hr in the plethysmograph was 0·2° C (S.D. $\pm 0{\cdot}6°$ C) and that for the babies breathing reduced oxygen was 0·14° C (S.D. $\pm 0{\cdot}5°$ C). The skin temperatures of the thigh also rose slightly during the experiment in both groups of babies, the average rise for the control group being 1·05° C (S.D. $\pm 0{\cdot}88°$ C) and for the babies breathing 15% oxygen being 0·9° C (S.D. $\pm 0{\cdot}55°$ C). When it thus became clear that no significant difference between the two groups was forthcoming from these temperature measurements, they were abandoned and an attempt was made to use Hatfield's (1950) disks to measure the heat flow from selected areas of the body. These disks were difficult to apply to the baby, and the use of an adhesive ('Nobecutane Spray', Evans Medical Supplies, Ltd.) had to be abandoned as it tended to give rise to skin reaction. We thought it desirable to apply the disks to an area of the body which is probably associated with temperature regulation and we chose the soles of the feet because these crease less than the palms of the hands and also provide a rather larger flat surface. We connected four disks in series in accurately drilled holes in Perspex shoes which could be tied with tape to the baby's feet. This arrangement allowed most of the free surface of the disk to be exposed to the air of the plethysmograph, but there was necessarily a small rim at the edge which was not so exposed. For this reason the disks could not be accurately calibrated but we

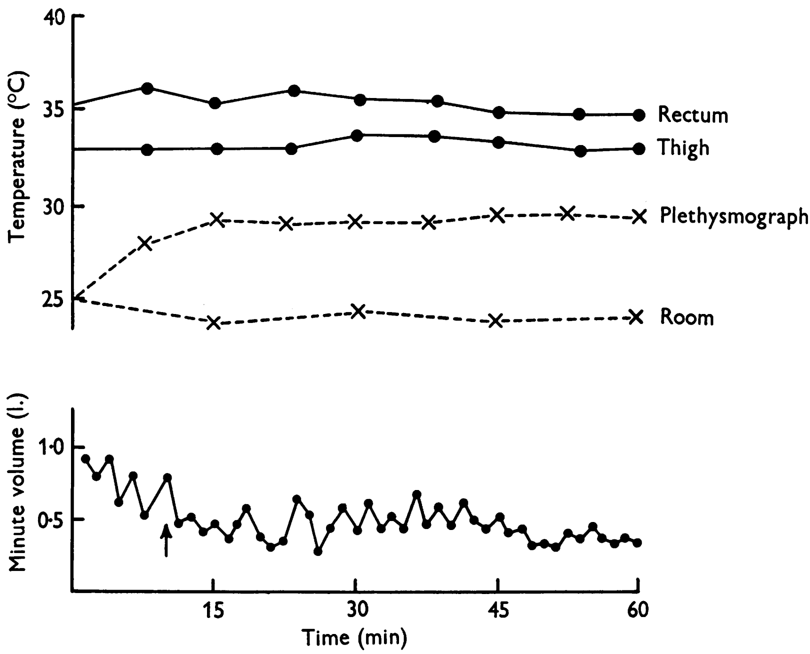

Fig. 1. Baby no. 15. Record of various temperatures and pulmonary ventilation plotted against time. The baby received 15% oxygen from the 10th min.

were able to observe changes in heat flow by the direction of change of the galvanometer deflexion. The disks were mounted so that they protruded just above the general level of the sole of the shoe, being thus closely applied to the skin, but even with the greatest care we were unable to maintain consistent contact and we found that changes which seemed to be associated with our experimental manoeuvres were far less than those which occurred with the least perceptible movement on the part of the baby. The largest changes occurred when the baby placed the plantar surface of one foot on the dorsal surface of the other.

As this method also failed we confined ourselves to observing the volume of respiration, together with the air temperatures. With this minimal interference we obtained results which satisfied our criteria of the resting state very much more easily.

RESULTS

The minute volume of respiration (after initial hyperventilation) was not significantly different in the two groups of babies, thus confirming the previous observations of Cross & Warner (1951) and Cross & Oppé (1952). Fig. 1

illustrates the results obtained in one of the earlier infants studied where the skin and rectal temperatures were still being measured. It will be noted that after conditions had reached a steady state there was a difference between the temperature within and without the plethysmograph which became almost constant. This difference was greater with the babies who were breathing air than with the babies breathing 15% oxygen. In this steady state the plethysmograph can be regarded as a calorimeter, and the level to which the plethysmograph temperature is raised above the room tempera-

TABLE 1. Data from the two groups of babies; one breathing air and the other breathing 15% oxygen. (Box = plethysmograph)

Baby no. and sex	Wt. (Kg)	Age (days)	Room temp. (° C)	Box temp. (° C)	Difference (° C)
			Breathing air		
1 M.	3·35	6	20·2	25·8	5·6
2 F.	3·60	5	20·0	26·5	6·5
3 M.	3·26	6	19·8	25·0	5·2
4 F.	3·74	4	16·0	23·0	7·0
5 M.	3·49	7	21·9	27·8	5·9
6 F.	3·37	4	18·8	25·3	6·5
7 M.	3·99	6	21·0	26·8	5·8
8 F.	3·62	5	22·3	26·5	4·2
9 M.	2·94	3	23·0	28·0	5·0
10 F.	2·83	5	22·0	26·8	4·8
Mean ± S.D.			20·5 ± 2·05	26·2 ± 1·47	5·65 ± 0·87
			Breathing 15% O_2		
11 M.	3·15	6	20·0	24·3	4·3
12 F.	3·46	3	23·3	27·3	4·0
13 F.	2·56	5	22·4	25·8	3·4
14 M.	3·40	7	21·0	23·8	2·8
15 M.	3·71	5	23·8	28·5	4·7
16 F.	3·54	4	23·8	26·5	2·7
7 M.	3·99	6	21·3	25·8	4·5
8 F.	3·62	5	23·6	26·8	3·2
17 M.	2·92	7	25·0	28·0	3·0
10 F.	2·89	3	22·0	25·3	3·3
Mean ± S.D.			22·6 ± 1·55	26·2 ± 1·52	3·59 ± 0·73

ture is a measure of the rate at which heat is lost from the infant. A direct calorimeter specifically designed to measure heat loss in the baby has been described previously by Day & Hardy (1942). In using the body plethysmograph for this purpose we claim to get only an index of the rate of heat loss.

In order to measure the temperature difference between the inside and the outside of the plethysmograph, a period of 12–30 min was selected towards the end of an experiment when the temperatures were reasonably stable. The average temperatures inside and outside the plethysmograph were estimated by eye from the graphed results of an experiment by an observer who did not know which gas mixture the baby had been breathing.

Table 1 shows the relevant data from the two groups of infants. It will be noted that the mean plethysmograph temperature is the same in both groups of infants, and although this occurred purely by chance it means that, on the average, the immediate environment of the babies was the same in the two groups. The differing amounts of heat lost cannot therefore be due to any environmental factor. It will be seen that the mean temperature difference on air was 5·65° C., while on 15% oxygen it was 3·59° C. Student's t test, comparing these means, gave $t = 5{\cdot}73$ ($P < 0{\cdot}001$). It will be further noted that the three babies who were examined both breathing air and 15% oxygen (nos. 7, 8 and 10), each showed a markedly lower temperature difference when

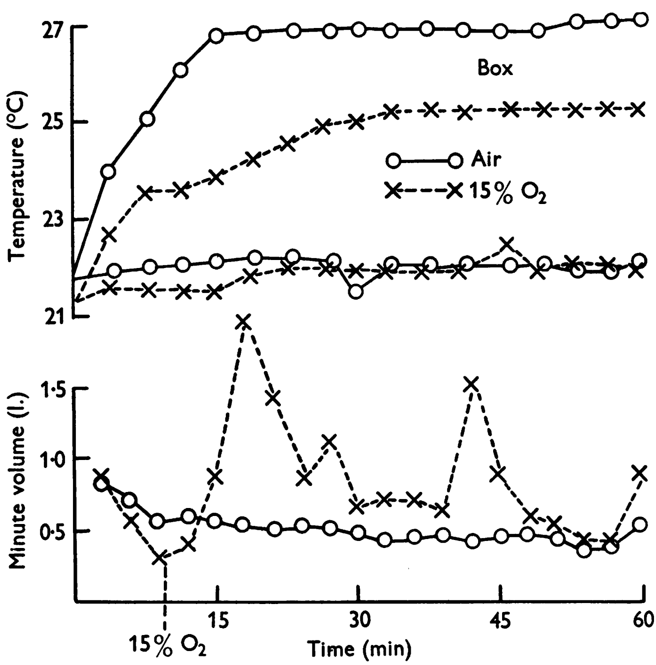

Fig. 2. Baby No. 10, F., 2·8 kg. Record of temperatures inside and outside the plethysmograph and minute volume plotted against time. ○—○, baby aged 5 days breathing air throughout; ×---×, same baby aged 3 days breathing 15% oxygen from the 10th min.

they breathed the low oxygen mixture. It would, of course, have been ideal to have examined each baby under the two conditions, but it is rarely that one finds an infant who will 'co-operate' for two such long sessions. To one particularly quiet infant, who had fulfilled the criteria listed above while receiving 15% oxygen for 50 min, air was then given and the temperature of the plethysmograph began clearly to rise, while the room temperature remained constant, but unfortunately the steady state was not achieved.

Fig. 2 shows the example of Baby 10 who was given the two different gases on different days, when by good fortune the room temperature was very similar on the two occasions. Although the trace of the minute volume shows that the baby was more restless when receiving 15% oxygen, which might have been expected to increase its heat production, it is seen that, in fact, the temperature difference between the inside and the outside of the plethysmograph is much less than when the baby breathed air throughout.

The fact that the room was not temperature-controlled made it possible to compare the performance of babies under different thermal conditions, and in Fig. 3 the temperature of the room is plotted against the temperature within the plethysmograph for the two groups of infants. The correlation coefficients were calculated for each group by the method of least squares and were

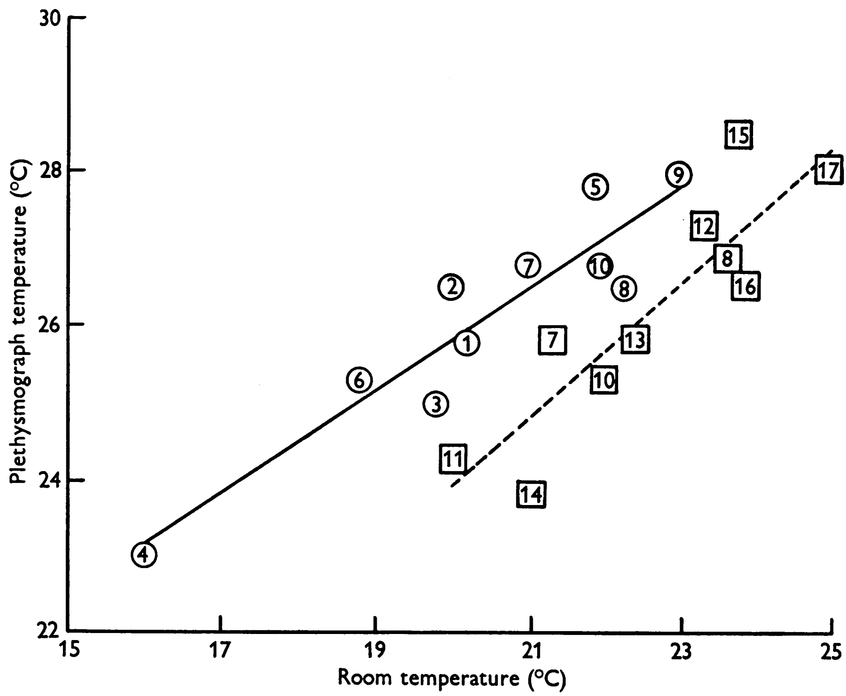

Fig. 3. Temperature inside the plethysmograph plotted against room temperature for both groups of infants. ○, babies breathing air; □, babies breathing 15% oxygen. Inset numbers refer to babies' numbers as in Table 1. — ---, calculated regression lines (plethysmograph temperature on room temperature) for babies breathing air and 15% oxygen respectively.

both highly significant ($P<0{\cdot}001$ for both). The regression lines for plethysmograph temperature on fixed room temperature are shown. They indicate once more, that for a given room temperature the plethysmograph temperature was raised more by the baby receiving air than by the baby receiving 15% oxygen.

DISCUSSION

It is important to assess to what extent the temperature difference between the inside and the outside of the plethysmograph provides an index of the total heat production of a baby. In the steady state all heat lost from that part of the body within the plethysmograph escapes to the outside by conduction through the walls and thence to the room. This quantity of heat is thus directly proportional to the measured temperature difference between the inside and outside of the plethysmograph.

In addition to the heat conducted away through the walls of the plethysmograph the infant might lose some heat by evaporation of water from its skin if the relative humidity inside the plethysmograph rose during the course of the experiment. However, calculation shows that even if the humidity increased from 0 to 100% during the experiment the loss of body heat by evaporation would not exceed 10% of the total body heat production.

The remaining heat loss, i.e. from the face and through the breath, can be shown by rough calculation to be only a small percentage of the total heat loss of the baby. In our experiments the exposed area of the face is of the order of 2·5–3% of the body surface. The minimal respiratory water loss as measured by Hooper, Evans & Stapleton (1954) is 8·6 g/kg/day. A 3 kg infant would thus lose about $25{\cdot}8 \times 0{\cdot}58$ kcal/day by evaporation of water in its breath, which is roughly 10% of the total basal heat production of 150 kcal/day as found by many authors quoted by Karlberg (1952). In our experiments the combined heat loss from the face and through the breath is thus only about 13% of the total heat loss, so that variations in this figure, such as might be caused by breathing different gas mixtures, could produce only small changes in the total heat loss of the body, and so it is clear that such possible variations in no way vitiate our conclusion that the total heat loss falls on breathing 15% oxygen. Furthermore, the 15% oxygen supplied to our subjects was probably warmer and more humid than the air, which was drawn from outside the building. It is likely therefore that less heat was lost by evaporation in the breath when the baby breathed 15% oxygen. A more important factor would arise if the 15% oxygen caused a significant increase in ventilation of humidification of the air. Hooper *et al.* (1954) estimated that the normal infant expired air that was about 80% saturated, and it has been shown by Cross & Oppé (1952) that after a very transient hyperventilation there is no significant stimulation of respiration by 15% oxygen. It would thus seem reasonable to suppose that with both air and 15% oxygen the infant would lose an approximately constant proportion of its body heat from the face and by respiration, and hence the temperature of the plethysmograph above that of the room would afford a reliable index of heat loss.

It is now essential to assess whether the heat loss from the baby can be equated with its heat production. Heat production will not equal heat loss if there is a significant change of mean body temperature. In our experiments, where body temperature was measured, there was neither a significant change nor a significant difference between the mean changes noted in the two groups (average rise of rectal temperature $= 0{\cdot}2 \pm 0{\cdot}6°$ C on air and $0{\cdot}14 \pm 0{\cdot}5°$ C on

15% oxygen). It would therefore seem that the index of heat loss which has been measured (difference between the temperatures within and without the plethysmograph) may fairly be regarded as indicating that there is significantly less heat production by a baby breathing 15% oxygen than by the same baby breathing air.

The previous work of Cross *et al.* (1955) and this present work have demonstrated, first by indirect and now by a type of direct calorimetry, that the new-born infant, when given 15% oxygen, shows a fall in energy production. As this is associated with a marked ability in the new-born infant to survive prolonged anoxia, it seems reasonable to suppose that at least part of the ability to survive is explained by this phenomenon. We have as yet no evidence whether this fall of energy production by the baby is a generalized lowering of cellular metabolism, or whether it is of different degrees in different regions.

SUMMARY

1. Two groups of new-born infants were studied, one breathing air, and the other breathing 15% oxygen. Body and environmental temperatures were recorded in an attempt to discover any thermal effects in the infant due to an artificially induced state of hypoxia.

2. It was shown that when the oxygen intake was reduced, the body heat production dropped significantly.

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