Oxygen consumption and evaporative water loss in infants with congenital heart disease

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Kennaird, D. L. (1976). Archives of Disease in Childhood, 51, 34. Oxygen consumption and evaporative water loss in infants with congenital heart disease. The relation between environmental temperature, heat production, oxygen consumption, and evaporative water loss was studied in 67 infants with congenital heart disease. The majority of the cyanosed infants had a low minimum oxygen consumption, a low evaporative water loss, and a diminished metabolic response to cold stress. Minimum oxygen consumption and evaporative water loss rose in 6 of these infants after the construction of a surgical shunt. Many of the ill acyanotic infants had an abnormally high minimum oxygen consumption, and those in cardiac failure often continued to sweat in an environment below the thermoneutral temperature zone.

Infants with congenital heart disease may have paradoxical problems with thermal homoeostasis, especially in the first 6 months of life; some sweat profusely while others have difficulty in maintaining a normal deep body temperature. Many babies with a large left-to-right shunt sweat excessively but the reason for this remains uncertain. Small cyanosed infants often become hypothermic during cardiac catheterization, but Baum and Mullins (1965) were able to show that body temperature could be maintained by a special hot water pad controlled by a thermistor in the colin. Such infants may even have difficulty in maintaining a normal deep body temperature when lying fully clothed in a cot.

The reported values for oxygen consumption in infants with congenital heart disease vary widely (Brück, Adams, and Brück, 1962; Lees et al., 1965; Levison, Delivoria-Papadopoulos, and Swyer, 1965; Kiéger, 1970; Stocker et al., 1972). Lees et al., (1965) found high values in infants with cardiomegaly and large left-to-right shunts, but Brasil (1968) was unable to detect any abnormality in older children with congenital heart disease.

Elliott and Cooke (1968) and McConnell, Rostan, and Puyau (1968), using a balance technique, both reported an increase in the basal evaporative water loss values in infants and children with heart disease, whereas Casey et al. (1964), using the same technique, concluded that infants with congestive heart failure do not have an increase in basal evaporative water loss values and that sensible sweat is rare. Morgan and Nadas (1963) studied sweat production in infants with congenital heart disease using the iontophoresis technique of Gibson and Cooke (1959). They found an increase in sweat production, and similar results were obtained by Goldware and Reynolds (1964) and by Alter, Czapek, and Rowe (1968). Simultaneous measurement of heat production, heat storage, and evaporative water loss were made during the present study in an attempt to establish whether the increased evaporative water loss was merely the result of thermal stress.

Materials and methods

Sixty-seven infants were studied at the London Hospital and the Hospital for Sick Children, London. Investigations were performed with full parental consent and co-operation and not infrequently a parent was present for part of the time. No infant showed any untoward effect that could be attributed to the investigative procedure, either at the time or subsequently. Ages ranged from 2 days to 10 months and weight from 2.25 to 6.25 kg. The infants were usually fed before the investigation as they tended to become restless when hungry. The majority settled quickly, and many slept. No sedation was used. The clinical
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Results

Minimum oxygen consumption. The various estimates of MOC are summarized in Fig. 1; most of the severely cyanosed babies had a low MOC whereas many of the acyanotic infants had an abnormally high MOC particularly in the presence of heart failure. 5 infants with cyanotic congenital heart disease who were in heart failure also had a high MOC. These babies had a systemic arterial oxygen saturation of more than 75% with either an atrioventricular defect or an anastomotic shunt between a pulmonary artery and the
diagnosis was confirmed by cardiac catheterization and cineangiography in all but 4 of the infants; the diagnostic details have been reported elsewhere (Kennaird, 1971). Measurements of arterial oxygen tension and oxygen saturation were made in most of the infants under comparable conditions during cardiac catheterization either immediately before or after most of the studies reported here. Babies were classified as being in heart failure on the basis of conventional clinical criteria.

Oxygen consumption and evaporative water loss were measured using the apparatus described by Hill and Rahimtulla (1965) and Hey and Katz (1969). Measurements were made at various environmental temperatures in a draught-free chamber with an absolute humidity of 9–13 mg H2O/l of air in order to determine the zone of minimum heat production. Rectal temperature and abdominal skin temperature were measured at one-minute intervals and operative environmental temperature was calculated according to the method of Hey (1969). The infant was naked apart from a napkin and lay on a foam mattress covered with polyethylene and a cotton sheet. Estimates of minimum oxygen consumption (MOC) in this paper relate to measurements made over a period of 10–40 minutes while the infant remained motionless. These data have been compared with the data for normal babies and older infants published by Hey (1969) and Karlberg (1952) which conform to a linear relation when the log of the MOC is plotted against body weight (Fig. 1). Karlberg never established that his clothed babies were in a neutral thermal environment, but this can be inferred with reasonable certainty from the work of Hey and O’Connell (1970).

The babies were studied naked, except for a urine collecting bag, lying on a foam mattress covered with polyethylene. They were also examined during and after each measurement period in order to ensure that estimations of evaporative water loss (EWL) were not invalidated by fluid loss from the mouth or the perineum. Water loss increased during periods of activity even when the baby did not cry, and estimates of basal EWL have therefore been confined to periods of inactivity or sleep. The presence of sweating was often clearly visible, but where there was any uncertainty specially prepared starch iodine papers were used to check for sweat gland activity.

Response to a cool environment. Most babies responded to cold stress by becoming more active, but overt shivering was never seen. Infants with an arterial oxygen tension of less than 60 mmHg usually had a diminished metabolic response to a short period of cold stress (Fig. 2), while 2 infants with an arterial oxygen tension of 40–50 mmHg failed to show any metabolic response to cold stress.

Zone of minimum heat production. Cyanosed babies with a low MOC had a relatively raised lower critical temperature and the temperature zone associated with minimum heat production in some severely cyanosed babies was as high as the age of 3 months as in a healthy infant at birth. In contrast, babies with a high MOC all had an abnormally low lower critical temperature while heat production remained at a minimum over an unusually wide range of environmental temperature.

Evaporative water loss. Minimum EWL while lying asleep or motionless in a cool environ-
ment is shown in Fig. 3. Cyanotic and acyanotic babies had comparable minimum values, and there is no clear correlation between EWL and MOC.

Almost all the babies sweated in a warm environment once the rectal temperature exceeded 37.2–37.5°C; the only exceptions were those severely cyanosed infants with low MOC values. However, in the majority of the acyanotic babies who were studied in sufficient detail for the lower critical temperature at the lower end of the zone of minimum heat production to be defined with precision, an abnormally high EWL was detected in an environment 0.5–1.5°C below the lower critical temperature. Thermally inappropriate sweating of this type was only seen in babies who were judged on clinical grounds to be in heart failure. An even larger number of babies appeared to sweat excessively in an environment within ±0.5°C of the lower critical temperature even though the rectal temperature was still less than 37.2°C (Fig. 4). All the babies judged to be in heart failure were receiving digoxin and diuretics at the time they were studied; most of the babies who showed a high EWL at or below the lower critical temperature were 2–6 months old and had a large left-to-right shunt (Qp/Qs > 2) with some degree of pulmonary hypertension. One infant appeared to sweat in an environment that was more than 3°C

Fig. 2.—Environmental temperature related to oxygen consumption in 10 infants with cyanotic congenital heart disease less than 21 days old. The area (hatching) within which 10% of all data are found in healthy babies of comparable age and weight (unpublished data, E. N. Hey, 1969) is shown.

Fig. 3.—Body weight related to basal evaporative water loss (EWL) at low environmental temperature.

Fig. 4.—Evaporative water loss (EWL) in infants with congenital heart disease while inactive in an environment in which heat production was at a minimum and the rectal temperature 36–37.1°C. All the infants who sweated were under treatment for heart failure. The broken line marks the upper limit of basal EWL in a cold environment. Some cyanotic infants in heart failure are represented more than once having been investigated on more than one occasion.
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TABLE I
Minimum oxygen consumption (mean ± SD) in 5 acyanotic infants before and within one week of operation for heart failure

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Weight (kg)</th>
<th>Age (w)</th>
<th>Preoperative oxygen consumption (ml/(kg per min) STPD)</th>
<th>Operation</th>
<th>Postoperative oxygen consumption (ml/(kg per min) STPD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preductal coarctation; persistent ductus arteriosus</td>
<td>3.7</td>
<td>2</td>
<td>10.0 ± 0.62</td>
<td>Resection of coarctation; ligation of duct</td>
<td>8.6 ± 0.69</td>
</tr>
<tr>
<td>Persistent ductus arteriosus; ventricular septal defect</td>
<td>4.0</td>
<td>15</td>
<td>9.7 ± 0.58</td>
<td>Ligation of duct</td>
<td>10.4 ± 0.72</td>
</tr>
<tr>
<td>Persistent ductus arteriosus; ventricular septal defect</td>
<td>2.4</td>
<td>4</td>
<td>8.9 ± 0.93</td>
<td>Ligation of duct</td>
<td>8.8 ± 1.6</td>
</tr>
<tr>
<td>Persistent ductus arteriosus; pulmonary hypertension</td>
<td>5.9</td>
<td>34</td>
<td>13.0 ± 0.42</td>
<td>Ligation of duct</td>
<td>9.6 ± 1.01</td>
</tr>
<tr>
<td>Persistent ductus arteriosus; ventricular septal defect; pulmonary hypertension</td>
<td>4.4</td>
<td>14</td>
<td>12.6 ± 0.60</td>
<td>Ligation of duct; pulmonary artery banding</td>
<td>9.8 ± 1.25</td>
</tr>
</tbody>
</table>

below the lower critical temperature even when the rectal temperature was less than 37 °C.

Effect of cardiac surgery. 5 ill dyspnoeic acyanotic infants in heart failure received surgical treatment. A fall in MOC occurred in each infant after operation (Table I) and the mean fall was significant at the 5% level. There was only a small fall in EWL after operation, and all 5 of these babies continued to sweat markedly in an environment below the lower critical temperature. Surgical shunts were constructed in 6 of the cyanosed infants. In each case there was a significant rise in MOC (Table II) and some increase in minimum EWL.

Discussion

Acyanotic babies. The high MOC in infants with acyanotic heart disease agrees with that of Lees et al. (1965), who investigated a group of babies with heart disease and concluded that high MOC rates showed a significant correlation with the presence of heart failure. The present series agrees with their findings as all the infants with raised MOC values were considered to be in heart failure and to be receiving medical treatment with

TABLE II
Minimum oxygen consumption (mean ± SD) in 6 infants before and after shunt operations to relieve hypoxaemia

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Age (w)</th>
<th>Oxygen consumption (ml/(kg per min) STPD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Before operation</td>
</tr>
<tr>
<td>Transposition of great arteries; ventricular septal defect; pulmonary stenosis</td>
<td>33</td>
<td>4.1 ± 0.35</td>
</tr>
<tr>
<td>Fallot's tetralogy</td>
<td>12</td>
<td>6.4 ± 0.55</td>
</tr>
<tr>
<td>Fallot's tetralogy</td>
<td>13</td>
<td>8.4 ± 0.45</td>
</tr>
<tr>
<td>Fallot's tetralogy</td>
<td>20</td>
<td>5.0 ± 0.56</td>
</tr>
<tr>
<td>Transposition of great arteries</td>
<td>12</td>
<td>5.7 ± 0.43</td>
</tr>
<tr>
<td>Tricuspid and pulmonary atresia</td>
<td>24</td>
<td>5.3 ± 0.27</td>
</tr>
</tbody>
</table>
digoxin and diuretics at the time of investigation. Brasil (1968) reported no increase in MOC values in children over one year of age with various heart defects, while Stocker et al. (1972) measured oxygen consumption using a diaferometer in infants with congenital heart disease and showed a significant positive correlation with heart failure.

Underweight babies often have a high MOC per unit body weight (Varga, 1959; Montgomery, 1962; Sinclair and Silverman, 1964; Wessel et al., 1969; Krieger and Whitten, 1969). This apparent hypermetabolism sometimes disappears if oxygen consumption is related to expected weight for their age, rather than actual weight, but such a manoeuvre failed to completely "normalize" the results in many of the babies in the present study.

The importance of factors other than dietary intake in the wasting process of heart failure have been discussed by Pittman and Cohen (1964, 1965) and compared to the pathophysiology of uncomplicated semistarvation in otherwise normal adults. In starvation there is a decrease in the cardiac index, a lowering of the systemic systolic blood pressure, a decrease in the peripheral circulation, a tendency for deep body temperature to fall, and a decrease in basal pulmonary ventilation (Keys et al., 1950); the patient with heart failure, in contrast, has evidence of increased sympathetic activity as shown by tachycardia, hyperpnoea, a rise in body temperature, and excessive sweating (Cohn and Steele, 1934; McMichael, 1939; Altschule, 1950; Chidsey et al., 1963, 1964, 1966).

Babies in heart failure almost certainly generate extra heat in their respiratory muscles and in their myocardium. All the infants with a raised MOC in the present study had radiological and electrocardiographic evidence of cardiomegaly. Impaired pulmonary function has been considered to be one of the factors responsible for a rise in metabolic rate in heart failure and the infants in the present study with large left-to-right shunts certainly had a raised respiratory rate. Cook (1960) showed that in infants with large left-to-right shunts there is a reduction in lung compliance and this has been confirmed by Howlett (1972). Lees, Way, and Ross (1967) reported that in infants with left-to-right shunts hyperventilation was associated with a decrease in tidal volume. An increase in the work of breathing has been well documented in adults with heart failure (Cosby et al., 1957; Knowles, 1959; McIlroy, 1959). Pittman and Cohen (1964) also suggested that though oxygen consumption per g of heart muscle may be normal in heart failure, the total myocardial extraction of oxygen is increased in the presence of hypertrophy and that the heart may account for a substantial proportion of the total oxygen consumption in patients with cardiomegaly and heart failure.

There is increasing evidence that overactivity of the sympathetic nervous system occurs in heart failure, and its role as an extrinsic mechanism providing support for the ailing myocardium in the presence of heart failure has been extensively studied by Chidsey and his co-workers (Chidsey, Harrison, and Braunwald, 1962; Chidsey et al., 1963, 1964, 1966). Intravenous noradrenaline in pharmacological concentrations has been shown to increase oxygen consumption in healthy newborn infants (Karlborg, Moore, and Oliver, 1965); and Lees (1966) reported that there was an increased catecholamine metabolite excretion in infants with heart failure of twice that of normal control infants. The evidence suggests that in infants with heart failure there is augmented catecholamine production and that it may be responsible for part of the increase in oxygen consumption in such patients.

All these factors may contribute to the raised MOC seen in many of the present infants. A sustained increase in heat production must stimulate an increase in heat loss by the production of sweat and this study has confirmed that those infants with congenital heart disease who had a high evaporative water loss also had a high MOC. However, the relation was not a direct one because almost all these infants were in incipient or frank congestive heart failure. Infants with severe congestive heart failure had an abnormally high evaporative water loss but most of the infants who sweated profusely at normal body temperature under conditions of minimum heat production had large left-to-right shunts and pulmonary hypertension.

In early heart failure the cardiac output is normal at rest, but on increased activity the patient fails to increase his cardiac output adequately to meet the increased requirements of the peripheral tissues (Hamilton et al., 1932). Changes in the regional blood flow take place secondary to a fall in cardiac output. Blood flow to the skin may be reduced to one-third of normal in moderately severe cardiac decompensation (Burch, 1946; Wood, Litter, and Wilkins, 1956; Donald, 1959; Mason and Braunwald, 1961). A diminution in peripheral blood flow to the limbs in adult patients with heart failure has been measured (Muth et al., 1958); and Talner (1968) has measured a decrease in limb blood flow in infants with heart failure.

Low skin blood flow and a high MOC combine to lower the thermoneutral temperature zone in these babies and this suffices to explain why babies
in heart failure sweat when nursed in an environment that is appropriate for a healthy baby of comparable age and weight. It does not, however, explain why sweating should persist in an environment below the lower end of the thermoneutral range.

**Cyanosed babies.** In the present study all the infants who had a low MOC (Fig. 1) had an arterial oxygen tension of less than 65 mmHg. Severe hypoxaemia has been shown to depress the oxygen consumption of animals in a thermoneutral environment (Hill, 1959) but there is little comparable evidence in man. Scopes (1966) found a low oxygen consumption in one infant with severe cyanotic congenital heart disease, and Levison, Delovoria-Papadopoulos, and Swyer (1964) reported a low MOC in newborn infants with the respiratory distress syndrome in its acute phase but found no such changes in infants with congenital heart disease accompanied by hypoxaemia (Levison et al., 1965). Brück et al. (1962) studied a group of infants with chronic hypoxaemia due to cardiac and respiratory disease and found no decrease in MOC; but it is doubtful whether they defined the lower critical temperature in their patients. However, on cold exposure, Brück et al. (1962) found that its magnitude was reduced in those infants with heart failure or whose arterial oxygen content was below 10 vols. %.

Six infants with chronic hypoxaemia in the present study had a low MOC and the increase seen in these infants after surgery (Table II) suggests that arterial desaturation, if severe, can depress resting metabolism. Many cyanosed infants suffer severe acidosis (Gootman, Scarpeis, and Rudolph, 1963) but the present results suggest that an arterial Po$_2$ of less than 55 mmHg is the most important factor depressing MOC in these babies. These observations agree with those of Bing et al. (1948) who also observed a significant increase in oxygen consumption in children with Fallot's tetralogy after operation. Cyanosed infants with a low MOC seldom sweated even when subjected to considerable heat stress.

**Response to cold stress.** Cyanotic and acyanotic infants behave differently in response to cold stress. Infants who were not hypoxaemic and who had an arterial oxygen tension of above 60–65 mmHg had a normal increase in oxygen consumption on cold exposure while those below this level had a diminished response, and infants with an arterial Po$_2$ of less than about 50 mmHg had a negligible metabolic response to cold stress. Non-shivering thermogenesis is important in the temperature regulation of many newborn animals and is almost certainly of importance in the human infant. Overt shivering was not observed in any infant during the present study. Hypoxia reduces thermogenesis within brown adipose tissue in newborn rabbits and this mechanism may also be operating in the human infant. Though the mechanism is speculative, it is important to stress the vulnerability of these hypoxaemic infants to hypothermia under conditions of only minor cold stress.

**Practical implications.** Oxygen consumption is very variable even under conditions of thermoneutrality; oxygen consumption must therefore be measured rather than estimated whenever cardiac output is being determined by the Fick principle. Cyanosed infants with a low MOC and a diminished metabolic response to cold stress are particularly vulnerable to hypothermia, especially during cardiac catheterization. Environmental temperatures which are warm to the clothed medical attendant often place a considerable thermal stress on the almost naked infant. Frequent observations of skin and rectal temperatures are important if hypothermia is to be avoided. Thermoneutrality is only achieved by an environment warmer than that appropriate for a healthy baby of comparable age and weight. Many babies with severe acyanotic congenital heart disease have a high MOC; they need to be nursed, therefore, in a cooler environment than most healthy babies of comparable age and weight.

There is some evidence that babies in heart failure, or incipient heart failure, continue to sweat until environmental temperature is lowered several degrees below the lower limit of the thermoneutral zone. These babies may suffer from an insensible water loss of as much as 60 ml/kg per day in an environment in which heat production is at a minimum, even when there is no detectable rise in deep body temperature.

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**REFERENCES**

D. L. Kennard


McIlroy, M. D. (1959). Dyspnoea and work of breathing in diseases of heart and lungs. *Progress in Cardiovascular Diseases*, 1, 284.


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(1) p. 791 under 'Uterine growth' line 3 should read, '... with a mean weight of 2.08 kg, ...

(2) p. 792 under 'Deaths' line 2 should read, '1 out of 16 was born between 1959 and 1967 and 7 out of 14 were born between 1967 and 1973.'