

Why does congenital heart disease cause failure to thrive?

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SUMMARY Metabolisable energy intake, determined by bomb calorimetry of food, vomit, stool and urine, and resting metabolism, assessed by respiratory gas exchange, were studied in 21 infants with congenital heart disease and nine control infants. Weight for age, growth rates, and daily metabolisable energy intake per kg tended to be lower in infants with heart disease than in control infants. Resting oxygen consumption was high in those infants with pulmonary hypertension and persistent cardiac failure. Energy intake, as a percentage of that recommended for age, correlated with weight gain, and resting oxygen consumption correlated inversely with both percentage body mass index and relative fatness. Failure to thrive in infants with congenital heart disease may be due to a combination of low energy intakes and, in some cases, high energy requirements allowing insufficient energy for normal growth. Increasing the energy intakes of infants with congenital heart disease may be a way of improving their growth.

Many children with congenital heart disease are small.¹ Their failure to thrive usually dates from early infancy, and postmortem studies suggest infants dying with congenital heart disease and failure to thrive are malnourished.² There are several possible explanations for this: hypoxia and breathlessness may lead to feeding problems; anoxia or venous congestion of the bowel may result in malabsorption; peripheral anoxia and acidosis may lead to inefficient utilisation of nutrients; and increased metabolic rate may mean that recommended energy intakes are insufficient for normal growth and nutrition.

Many of the studies investigating failure to thrive and congenital heart disease review children over wide age ranges.^{1,3} The findings in children of school age or adolescents will not necessarily indicate causes of poor growth that date from infancy. We have compared total energy intake, metabolisable energy intake (total energy ingested minus energy losses in stool, urine, and vomit), resting oxygen consumption, and growth rates of infants with congenital heart disease and normal infants to try to determine the causes of failure to thrive in infants with congenital heart disease.

Method

Children with congenital heart disease. These were

infants with congenital heart disease but without other associated abnormalities admitted to the Royal Liverpool Children's Hospital for investigation and management of their cardiac condition. Infants with congenital heart disease were studied during periods when their cardiac condition was fairly stable and no change in treatment or surgical intervention was taking place.

Controls infants. Control infants were inpatients at the Royal Liverpool Children's Hospital admitted for mild infection with delay in discharge, social reasons, failure to thrive without obvious cause and resolving spontaneously on admission, or, for respiratory gas studies only, normal neonates who were still inpatients at the Liverpool Maternity Hospital in the second week of life. The purposes and procedures of the investigation were explained to all parents and their consent obtained before study of either infants with congenital heart disease or control infants. The study was approved by the Liverpool Paediatric Sector Ethical Committee.

Metabolisable energy intake. The procedure was similar to that described by Brooke, Alvear, and Arnold for premature infants.⁴ Infants were studied for periods of five days. Prepacked infant formula was fed from weighed bottles. Intake was estimated by weighing bottles again after feeds. Spillage,

posset, and vomit were collected on absorbent pads placed under the infants' heads. Stools were collected on nappy liners of known weight placed inside tightly fitting disposable nappies. Urine soaked through the liners and into the nappies. The beginning and end of each stool collection was marked by feeding sterile carmine marker with the first feed of each balance and the first feed after the end of the balance period. Nappy liners were reweighed and pads, nappies, and nappy liners were stored in plastic bags at -20°C .

Estimation of energy content of feeds

Samples of prepacked feeds of known weight were frozen at -20°C and freeze dried and energy content was determined by bomb calorimetry.⁵

Estimation of energy content of vomit and urine

Vomit containing pads and urine soaked nappies were macerated in a known volume of water in a bucket and filtered. Aliquots of the filtrate were frozen at -20°C and freeze dried and energy content was determined by bomb calorimetry.

Estimation of energy content of stools

Stool was scraped from the liners and weighed; a weighed sample was frozen at -20°C and freeze dried and energy content was determined by bomb calorimetry.

Respiratory gas exchange. Infants were studied asleep or awake but at rest in a perspex chamber. Resting gas exchanges were recorded at minimum oxygen concentration obtainable for that child, thus assuming a thermoneutral environment.

Studies were performed at least an hour after the previous feed. Room air was drawn through the chamber past a baffle at a regular rate (between 5–10 l/min) measured by Hastings Mass flowmeter (Chell Instruments Ltd, Amersham). Concentrations of oxygen and carbon dioxide in entry and exit gases were determined by Taylor Servomex oxygen analyser (Servomex, Crowborough, Sussex) and PK Morgan carbon dioxide analyser (PK Morgan Ltd, Chatham, Kent), respectively, after the air had been dried over calcium chloride. Skin, rectal, and air temperatures within the chamber were monitored continuously. Body temperatures of the infants did not vary by more than 0.5°C from 36.5°C skin and 37°C rectally during study in the respiratory chamber.

Resting gas exchange studies were carried out for periods of 30–60 minutes. Oxygen and carbon dioxide concentrations in the exit gases were recorded continuously on a multichannel recorder,

and gas exchange was calculated by estimating the area under the curves with a planimeter.

Anthropometry. Weight was recorded daily. Length, biceps, triceps, and subscapular and suprailiac skinfolds were measured at the beginning and end of each study period.⁶ Percentage body mass index was calculated as the ratio of weight/height² to weight at 50th centile for age/height at 50th centile for age²×100%.⁷ Skinfolds were represented as the logarithmic value of the summed skinfolds measured.

Results

Infants. Twenty one infants with congenital heart disease and nine control infants were studied. Table 1 indicates diagnoses for both groups. Mean (SD) age was 0.18 (0.14) (range 0.01–0.62) years for infants with congenital heart disease and 0.14 (0.08) (range 0.01–0.24) years for control infants. Seven infants with congenital heart disease had energy balance studies only and three infants with congenital heart disease and four control infants had respiratory gas exchange studies only.

Growth. Figure 1 shows weight change during the balance period for the 18 infants with congenital heart disease and five control infants in whom metabolisable energy intake was studied. Almost all infants were below the 50th centile weight for age. Growth rates for all except one control were above the average rates expected for age, whereas those for infants with congenital heart disease were mostly

Table 1 Diagnoses of infants with congenital heart disease and control infants

Diagnosis	No of infants with congenital heart disease	No of control infants
Ventricular septal defect	9**	
Transposition great vessels	3*	
Tricuspid atresia	3†	
Ventricular and atrial septal defects	2**	
Mitral stenosis and coarctation repair	1	
Patent ductus arteriosus	1†	
Coarctation and double outlet left ventricle	1†	
Fallot's tetralogy	1*	
Failure to thrive		3†
Social problems		2
Suspected congenital heart disease		1
Normal neonate		3††

*Signifies one infant who had net energy intake studies only.

†Signifies one infant who had respiratory gas exchange studies only.

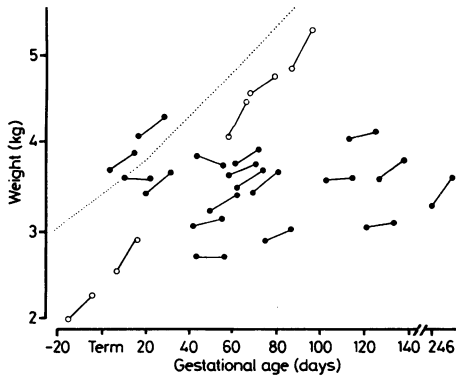


Fig. 1 Weight change during energy balance period for infants with congenital heart disease (●) and control infants (○) (50th centile weight for girls shown as).

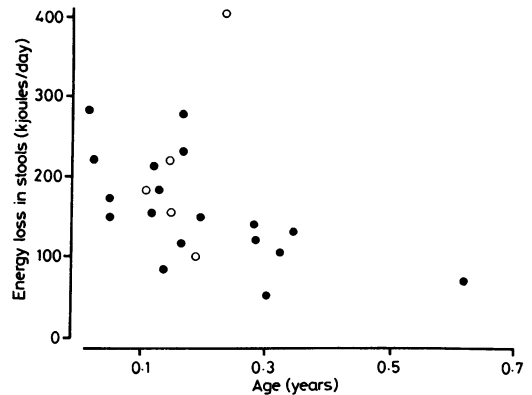


Fig. 2 Stool energy loss related to age for infants with congenital heart disease (●) and control infants (○).

below expected rates for age, and some lost weight during the study period.

Energy intakes and metabolisable energy intake. Table 2 indicates mean values for total energy ingested, energy lost in vomit and stool, and metabolisable energy intake for both groups. Mean total energy ingested per day and metabolisable energy intake were higher for control infants, even though the mean age of the infants with congenital heart disease was slightly greater. These differences were not significant.

Energy losses in posset and vomit were variable in both groups, but mean values were not significantly different. One infant with congenital heart disease vomited 11% of her feed and nine other infants with congenital heart disease and two control infants vomited 5–10% of ingested energy. Stool energy losses varied widely but tended to decrease in both groups with age (Fig. 2).

Figure 3 shows weight change per day related to metabolisable energy intake expressed as a percentage of the recommended daily allowance⁸ for the infants' weights and ages. There is a significant correlation between weight change per day and intake as a percentage of the recommended daily allowance for infants with congenital heart disease.

Resting respiratory gas exchange. Resting oxygen

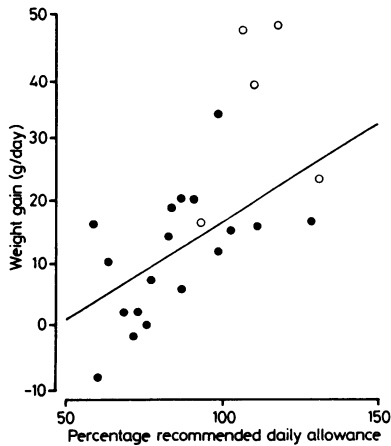


Fig. 3 Weight change (g/day) related to metabolisable energy intake expressed as a percentage of the recommended daily allowance for infants with congenital heart disease (●) and control infants (○) (for infants with congenital heart disease $r=0.53$; $p<0.01$).

consumption/kg body weight tended to increase with age in the first weeks of life and was particularly high in three infants with persistent cardiac failure and pulmonary hypertension (Fig. 4). There were no significant differences between mean resting oxygen consumption for the two groups when

Table 2 Mean (SD) for kilojoules of energy ingested daily by infants with congenital heart disease and control infants

	Total energy ingested	Energy loss in vomit	Energy loss in stools	Metabolisable energy intake
Infants with congenital heart disease (n=18)	1693 (319)	102 (40)	159 (70)	1423 (313)
Control infants (n=5)	1953 (584)	82 (23)	215 (123)	1655 (557)

oxygen consumption was related to either total body weight (mean (SD) ml/kg/min for infants with congenital heart disease was 10.2 (1.9); and for control infants was 9.3 (1.3)) or metabolic body size (weight^{0.75}) (mean (SD) ml/kg^{0.75}/min for infants with congenital heart disease 13.8 (2.6) and for control infants 13.0 (1.7)). The correlation between resting oxygen consumption (ml/min) and metabolic body size was much closer for control infants than for infants with congenital heart disease ($r=0.37$ for

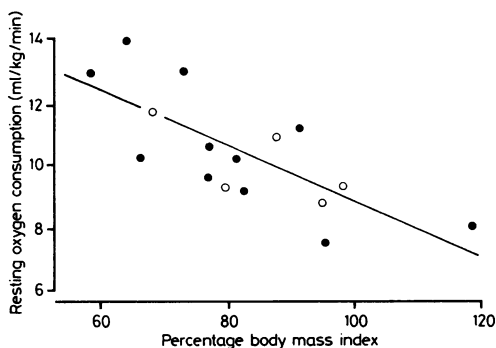


Fig. 5 Resting oxygen consumption (ml/kg/min) correlated with % BMI for infants with congenital heart disease (●) and control infants (○) (for infants with congenital heart disease $r=-0.73$, $p<0.01$).

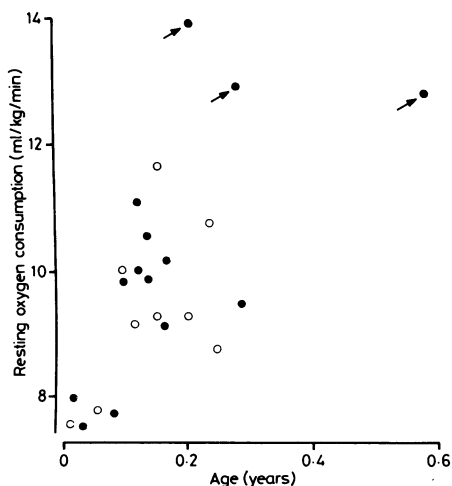


Fig. 4 Resting oxygen consumption (ml/kg/min) related to age for infants with congenital heart disease (●) and control infants (○) (spots arrowed represent infants with persistent cardiac failure and pulmonary hypertension).

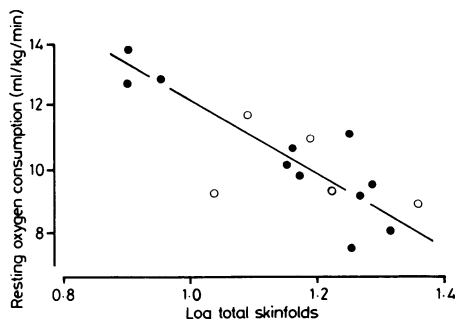


Fig. 6 Resting oxygen consumption (kg/min) correlated against log total skinfolds for infants with congenital heart disease (●) and control infants (○) (for infants with congenital heart disease $r=-0.90$, $p<0.01$).

Table 3 Twenty four hour metabolisable energy intake, estimated resting energy expenditure,* spare energy available for non-resting metabolism and growth, and weight gain of infants studied

Infant	Metabolisable energy intake (kjoules)	Resting energy expenditure (kjoules)	Spare energy (kjoules)	Growth rate (g)
<i>With congenital heart disease</i>				
1	1760	900	860	20
2	1225	1330	-5	2
3	1141	978	163	10
4	1417	1181	236	12
5	1651	979	672	15
6	1170	1227	-57	-8
7	1463	1266	198	34
8	1074	866	108	16
9	1555	1116	439	14
10	1450	953	497	20
11	1020	761	259	0
<i>Control</i>				
1	2328	1091	1237	48
2	1137	682	455	39
3	1843	1134	709	16
4	1910	1479	431	47
5	1016	679	337	24

*Daily energy expenditure=oxygen consumption ml/min . 1440 . caloric equivalent . 4.18 kjoules/24 hours.¹⁴

infants with congenital heart disease; $r=0.86$ ($p<0.01$) for control infants).

Resting oxygen consumption/kg was inversely related to both percentage body mass index (Fig. 5) and log total skinfolds (Fig. 6) in both groups. Respiratory quotients (carbon dioxide output/oxygen uptake) were not significantly different between the two groups (mean (SD) of 0.81 (0.04) for infants with congenital heart disease and 0.83 (0.03) for control infants).

Energy available for growth and activity. Table 3 lists metabolisable energy intake, calculated resting energy expenditure per 24 hours, 'spare' energy remaining for growth, activity and other non-resting metabolism, and daily weight gain for infants with congenital heart disease and control infants. There was wide variation in spare energy for both groups. Mean spare energy for infants with congenital heart disease was 306 (± 283) kJ/day and for control infants was 634 (± 364) kJ/day. This difference was not significant.

Discussion

This study has not included all aspects of energy balance as we have not attempted to assess time spent and energy expended in activity, thermogenesis, or other non-resting metabolism. Undoubtedly, energy expended in activity varied widely as the infants' ages ranged over the first six months of life. Energy spent in activity in early infancy is largely expended in crying and feeding. By six months of age considerable amounts of energy may be expended in purposeful activity. Healthy infants may be more active than infants with congenital heart disease sufficiently severe to require hospital admission. Despite the obvious deficiencies to this study, we feel some suggestions can be made to explain why infants with congenital heart disease fail to thrive.

Energy intake. Most infants with congenital heart disease in this study were below average weight for age and gaining weight at less than the expected rate for age. Control infants, although small, were showing catch up growth. Mean total energy intake and metabolisable energy intake expressed as kJ/kg/day were not significantly different for the two groups, but values for infants with congenital heart disease tended to be lower. Total energy intakes of infants with congenital heart disease were low compared with those recommended for normal infants of the same age who should be considerably heavier. Other studies have also found intakes of infants with congenital heart disease appropriate for

actual weight but inadequate when viewed in relation to the expected weight for age of many of these infants and their need for catch up growth.^{3,9}

Malabsorption did not seem to explain the low metabolisable energy intake in our infants with congenital heart disease. This is in contrast with the findings of Sondheimer and Hamilton where eight out of 21 infants with congenital heart disease had increased stool nitrogen loss and five had increased stool total energy loss.¹⁰ Jejunal biopsy of infants with malabsorption in that study showed no histological abnormality. The authors recommended that diets for infants with congenital heart disease should be designed with the possibility of malabsorption due to inadequate gut function in mind. Our findings suggest this is unnecessary. If attempts were made, however, to feed infants with congenital heart disease high energy diets to overcome failure to thrive, minor problems with food absorption might possibly then exert noticeable effects on metabolisable energy intake.

Growth. Weight gain in the infants we studied correlated with energy intake when expressed as a percentage of that recommended for weight and age. This would suggest that the energy intake of the infants with congenital heart disease was a critical factor in determining growth rate. The correlation between energy intake and weight gain in normal infants receiving normal energy intakes is usually weak. Weight gain correlates more closely with energy intake in underfed individuals. The high correlation between weight gain and energy intake of the infants with congenital heart disease in our study suggests these infants were underfed for their requirements even if intakes were within the recommended range for weight and age. Estimates of spare energy available for non-resting metabolism would suggest that infants with congenital heart disease had on average only about half as much energy available for growth and non-resting metabolism as control infants.

Gas exchange in relation to anthropometry. We found no significant difference in mean oxygen consumption/kg/min between the two groups. Three infants with congenital heart disease with pulmonary hypertension and persistent cardiac failure had particularly high values. Other studies have also shown wide ranges in oxygen consumption/kg/min in infants with congenital heart disease, with some infants having very high values. Persistent cardiac failure seems the main problem leading to high values of oxygen consumption/kg/min.¹¹ Kraus and Auld found higher mean values in neonates with congenital heart disease and cardiac failure than

with congenital heart disease alone.¹² This would fit our data. Extra respiratory work and cardiac inefficiency may account for the raised oxygen consumption. A high resting metabolic rate is a recognised feature of cardiac cachexia in adults.¹³

Basal metabolic rate has been shown to correlate closely with metabolic body size irrespective of overall size. When resting oxygen consumption was related to metabolic body size in the infants in this study correlations were high for control infants but low for infants with congenital heart disease. This suggests that the resting metabolic rate of the infants with congenital heart disease was strongly influenced by factors other than size. Again, differences in cardiac efficiency and/or extra respiratory work might account for this.

The significant inverse correlations between percentage body mass index and oxygen consumption/kg/min and between log skinfolds and oxygen consumption/kg/min in our infants require explanation. Low skinfolds and poor weight may have correlated with oxygen uptake because the infants with higher oxygen uptakes used more energy in basal metabolism and therefore had less energy to spare for deposition as fat. Or these infants may have had higher oxygen consumption because they were thin and even in thermoneutrality required higher metabolic rates to maintain their normal body temperature. Inverse correlations between low skinfolds, poor weight, and resting oxygen consumption may also indicate the problems inherent in relating metabolism to total weight in individuals who do not have normal body compositions,¹² a situation which is not totally corrected by relating oxygen consumption to metabolic body size. Lean body tissue has higher oxygen consumption/kg than fat. We were unable to estimate lean body mass in the infants we studied. As the leanest and most underweight infants had a higher proportion of body weight as lean body mass this would tend to give a bias towards a high oxygen consumption in these infants.

Does this study offer practical suggestions on how growth of infants with congenital heart disease can be improved? Food losses in vomit and stool seem minor causes of inadequate energy intake. Feeding regimens based on infants' actual weights are probably inappropriate when these infants are already failing to thrive. Such infants have need of extra energy for catch up growth, and they may have increased energy requirements on account of high resting metabolism. Theoretically these infants

should grow better if their energy intakes are increased substantially. Unfortunately, as those experienced in feeding these sick infants will recognise, this is a policy easier to formulate than to practise. Many of these infants are unable to tolerate the large volumes of breast milk or formula necessary to improve energy intakes appreciably. They need feeds of high energy density so intakes can be improved without overfeeding or fluid overload. Giving high energy feeds to these malnourished children may stimulate greater dietary induced thermogenesis and increased metabolic inefficiency.

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