

Applied nutritional investigation

# Energy metabolism in infants with congenital heart disease

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## Abstract

Failure to thrive is common in children with congenital heart disease and influences the metabolic response to injury and outcome after corrective cardiac surgery. Energy imbalance is a major contributing factor. However, the published literature is difficult to interpret as studies generally involve small patient numbers with a diverse range of types and severity of cardiac lesions and genetic and/or prenatal factors. The age and time of corrective surgery affects the potential for nutritional recovery. Although the immediate postoperative period is characterized by a hypermetabolic state, low total and resting energy expenditure are reported within 24 h of surgery. After 5 d, resting energy expenditure returns to preoperative levels. Significant improvements in weight and growth occur within months after corrective surgery. However, limited postoperative recovery in nutritional status and growth occurs in infants with a low birth weight, intellectual deficit, or residual malformation. Further studies are needed to inform the timing of corrective cardiac surgery to maximize nutritional outcomes and to identify those infants who may benefit from aggressive preoperative nutrition support. © 2006 Elsevier Inc. All rights reserved.

## Keywords:

Basal metabolic rate; Cardiac surgery; Energy expenditure; Indirect calorimetry; Resting energy expenditure; Total energy expenditure

## Introduction

Energy is fundamental to basal metabolism, growth, and physical activity. Disturbance in energy balance is a major limiting factor for growth, and cognitive and motor development [1]. Because of a high metabolic rate and limited endogenous substrate reserves, children may rapidly develop energy deficiencies during episodes of acute illness or in chronic diseases. Infants with congenital heart disease (CHD) are particularly at risk of energy imbalance. Most infants with CHD have a normal weight for gestational age at birth but develop nutritional and growth problems in early infancy [2–6]. Weight tends to be more affected than height; even so, almost half (49%) of infants younger than 2 y are stunted [7].

A number of factors influence the development of mal-

nutrition in infants with CHD (Table 1) [8,9]. The relative contribution of each of these factors to the development of malnutrition in an individual patient depends on the type and severity of the cardiac lesion and associated disease conditions [10]. Infants with cyanotic heart lesions (tetralogy of Fallot, transposition of the great arteries) frequently have decreased weight and height compared with healthy infants [11]. The leptin-regulating axis is normal in patients who are cyanotic with CHD, suggesting that leptin does not contribute to cardiac cachexia [12]. Infants with acyanotic heart lesions and a large left-to-right shunt (patent ductus arteriosus, ventricular septal defect, atrial septal defect) have reduced weight gain but growth may be maintained during infancy [10,13]. However, in the presence of elevated pulmonary pressure severe growth failure frequently develops. Energy intake is often reduced in infants with CHD and is related to poor weight gain [14,15]. Associated genetic conditions such as Down syndrome and Turner's syndrome may also influence energy intake, gastrointestinal absorption, expenditure, and growth expectations [16].

Energy imbalance is a major factor contributing to mal-

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Table 1

Factors that may influence the development of malnutrition and growth failure in infants with congenital heart disease

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1. *Type and clinical impact of cardiac disease*
    - i. Cyanotic versus acyanotic defects
    - ii. Shunts
    - iii. Congestive cardiac failure
    - iv. Operative status
      - Age at time of surgery
      - Type of surgery
      - Complications
  2. *Disturbances in energy metabolism*
    - i. Increased energy expenditure
      - Cardiac hypertrophy
      - Abnormalities in body composition
      - Increased activity of sympathetic nervous system
      - Increased hematopoietic tissue
      - Increased basal temperature
      - Recurrent infections
      - Pharmacologic agents
  3. *Decreased energy intake*
    - i. Anorexia and early satiety
    - ii. Pharmacologic agents
    - iii. Decreased gastric volume caused by hepatomegaly
  4. *Disturbances in gastrointestinal function*
    - i. Malabsorption
      - edema and chronic hypoxia of the gut
      - interference with drugs
    - ii. Delayed gastrointestinal development
    - iii. Compressive hepatomegaly
      - Decreased gastric volume
      - Increased gastroesophageal reflux
  5. *Prenatal factors*
    - i. Chromosomal disorders
    - ii. Intrauterine factors
    - iii. Birth weight
- 

nutrition in infants with CHD. However, the published literature on energy metabolism in infants with CHD is difficult to interpret as studies generally involve small patient numbers with measurements undertaken in diverse patient groups, with respect to the type and severity of cardiac lesion, and genetic or prenatal factors. In addition, the lack of a control group and standardization in the timing and methods of energy measurements make comparability between studies problematic. Infants with CHD frequently have altered body composition, however, few studies express results of energy measurements with respect to body composition [17]. Considering these factors, it is not totally surprising that there are conflicting results between some studies of energy expenditure in infants with CHD [17]. In this review, we evaluate the published literature of energy metabolism in children with CHD with the specific aim to assess the impact of corrective cardiac surgery on energy metabolism in children with CHD.

## Materials and methods

A MEDLINE search was performed for all studies published from 1966 to December 2004 using the Medical

Subject Headings and keywords: *energy metabolism, congenital heart disease*, and “*all child (0-18 years)*”: data from all studies retrieved was collated into tables for comparison and presentation.

## Results

### *Energy expenditure in children with CHD*

There is an intimate relationship among energy intake, energy expenditure, nutritional status, and growth in infancy [6,7,9,15,18]. The energy available for metabolism (metabolizable energy) is the sum of total energy expenditure (TEE) and energy stored. TEE includes all energy expended in daily life including basal metabolic rate (BMR), thermoregulation, physical activity, and growth. The relative proportions of these components of TEE vary with age and body composition (Fig.1). BMR represents the major component of TEE and metabolizable energy intake (Fig.1). This energy is used for the maintenance of basic life functions such as heart function, breathing, and basic cellular function. The BMR of infants is almost twice that of adult based on a per kg body weight [19]. This reflects the difference in the relative proportion of body weight contributed by organs with a high metabolic rate, such as the brain, kidneys, liver, and heart [19]. It has been proposed that hypertrophic cardiac muscle in children with congestive heart failure may account for the increased BMR reported in some studies [20]. Although atrioventricular differences in energy metabolism have been observed in children with CHD, whether there is an impact on BMR in children with regional differences in cardiac muscle hypertrophy is not known [21]. Other explanations for increased BMR observed in infants with CHD include increased activity of the sympathetic nervous system, hematopoietic tissue, and respiratory muscles [20,22]. Infants with CHD are at risk of developing infections that may result in increased basal temperature and metabolic stress [23,24].

The measurement of resting energy expenditure (REE) involves the measurement of oxygen consumption and interpretation of results requires consideration of changes in body composition. Oxygen consumption (per kg/body weight) is increased in malnourished infants with CHD compared with well-nourished infants with CHD [5,25]. However, changes in the extent and proportion of the metabolically active body compartments, as occurs in infants with CHD, may alter interpretation of these results [16,26]. Infants with CHD have increased total body water (+7–8%) compared with healthy control subjects [17]. This may be a result of a relative decrease in fat mass, an increase in the hydration of the fat-free mass compartment, or both [17]. The relationship of BMR to fat-free mass is non-linear when used to compare individuals of different body sizes and alternative methods should be used to compare individuals with markedly different fat-free mass [27]. Increased

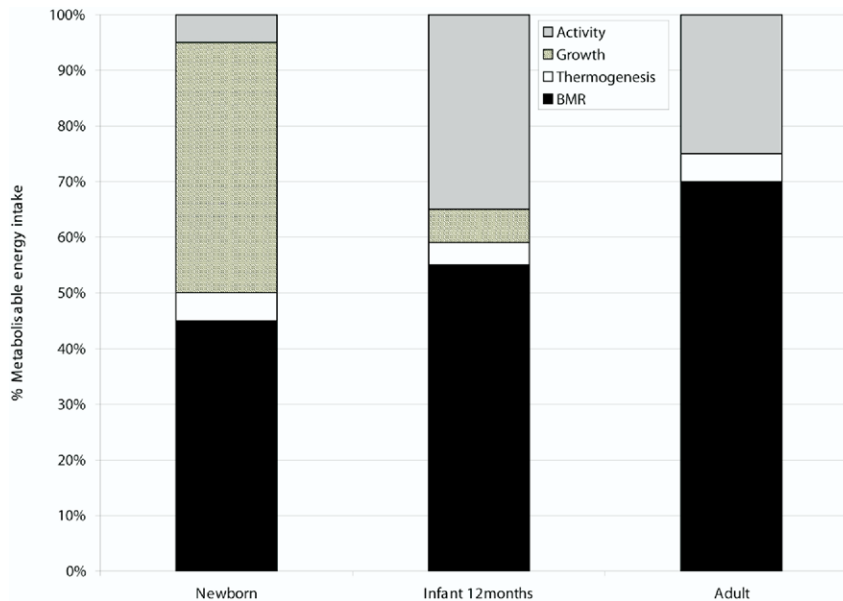


Fig. 1. Components of energy expenditure as percentage of metabolizable energy intake in newborns, infants, and adults (adapted [30]). BMR, basal metabolic rate.

REE reported in infants with CHD appears to be more closely correlated with the presence or absence of cardiac failure rather than with a specific type of cardiac lesion [28]. This relationship is not as clear in studies of TEE and may reflect small patient numbers, the influence of diuretics and fluid restriction, or both on interpretation of the doubly labeled water method for measurement of TEE. No significant differences in REE have been observed between infants with acyanotic and cyanotic cardiac lesions—although studies have been limited by small patient numbers (Table 2) [29].

The energy cost of growth is a specific consideration in infancy and includes energy put down in the new tissue and the energy cost of the synthesis of this new tissue. During the first year of life the energy cost of growth decreases precipitously from about one third of energy intake in the first 3 mo of life to only 4% of energy intake at 12 mo of age [19]. Failure to thrive and stunting in infants with CHD may result in a lower energy cost of growth than may be expected in a healthy infant of the same age [15].

In infants, physical activity–related energy expenditure increases from 5% of total metabolizable energy intake at 6 wk of age to 34% at 12 mo of age [30]. In late infancy, behavior contributes to physical activity and TEE, highlighting the pitfalls in predicting TEE based on body size alone [31]. A marked increase in TEE relative to REE has been reported in 3- to 5-mo-old infants with ventricular septal defect and a left-to-right shunt (Fig. 2) [16]. As these infants had deficits in weight and height at the time of study, it is unlikely that the increase in TEE was the result of increased energy cost of growth [16]. Increased TEE observed in infants with CHD has generally been attributed to the increased work of the heart, increased work of breath-

ing, diminished myocardial efficiency, and increased stimulation of the sympathetic nervous system [22]. Therefore, it would be expected that infants with CHD and congestive heart failure would have a higher TEE compared with infants with CHD without cardiac failure. Although a number of studies have suggested that TEE may be higher in infants with CHD and congestive cardiac failure this difference has not been shown to be statistically significant [16,17,28,32]. It has been proposed that diuretic therapy and fluid restriction may have restricted the hemodynamic abnormalities associated with cardiac failure in the infants studied [17].

#### *Energy metabolism in the perioperative period*

Nutritional status in infancy may influence decisions regarding the timing and type of corrective cardiac surgery [33]. Malnutrition is associated with increased surgical morbidity and mortality [34]. Factors contributing to this outcome may include the impact of macronutrient and micronutrient deficiencies on respiratory muscle function, immune responses, and wound healing [14,34–36]. Even in previously healthy children almost one-third will develop acute protein-energy malnutrition within 48 h of admission to an intensive care department [35,37]. This can contribute to metabolic instability and result in increased care requirements [37]. The type and severity of the underlying disease and the treatments required will influence the extent of disturbance in energy metabolism and substrate use [38]. Because of the nature of cardiac surgery the immediate postoperative period may be characterized by a hypermetabolic state and negative nitrogen balance [39]. The shift toward fat oxidation and either gluconeogenesis or impaired carbohydrate use observed after cardiac surgery may be a

Table 2  
Comparison of published literature

Author	Y	Age range (including n)	Preoperatively			Postoperatively			Controls			Study methodology	
			n	REE $\text{kJ} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ (kcal/kg/d)	TEE	n	REE $\text{kJ} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ (kcal/kg/d)	TEE	n	REE $\text{kJ} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ (kcal/kg/d)	TEE		
Gebara [40]	1992	2 mo–12 y (c = 20) (a = 6)				26	230 ± 33 (55 ± 8)				N/A		- Prospective, observational single- center study - REE postop only - No TEE, no controls
Mitchell [42]	1994	4–33 mo (c = 7) (a = 11)	18		487 ± 131 (116 ± 31)	17		315 ± 88 (75 ± 21)	18		467 ± 25 (112 ± 6)		- Prospective, single- center study - TEE pre and postop with controls - No REE
Barton [32]	1994	0.23–0.58 y (c = 2) (a = 6)	8		426 ± 12 (102 ± 3)	4		280 ± 60 (67 ± 14)			N/A		- Prospective, single- center study - TEE pre- and postop - No REE, no controls
Leitch [26]	1998	>35 wk (c = 10) (a = 0)	10 (2 wk)	242 ± 24 (58 ± 6)	304 ± 74 (73 ± 18)				12 (2 wk)	239 ± 41 (57–10)	250 ± 46 (60 ± 11)		- Longitudinal single- center study - REE and TEE preop only with controls
			10 (3 mo)	268 ± 69 (64 ± 16)	392 ± 97 (94 ± 23)				12 (3 mo)	234 ± 30 (56 ± 7)	302 ± 55 (72 ± 13)		
Ackerman [16]	1998	3–5 mo (c = 0) (a = 8)	8	198 ± 38 (47 ± 9)	433 ± 103 (103 ± 25)				10	238 ± 58 (57 ± 14)	350 ± 18 (84 ± 4)		- Prospective, single- center study - REE and TEE preop only, with controls
Leitch [44]	2000	5.7 ± 0.5 y (c = 7) (a = 0)				7	280 ± 32 (67 ± 8)	291 ± 60 (70 ± 14)	10	244 ± 32 (58 ± 8)	319 ± 37 (76 ± 9)		- Prospective, single- center study - REE and TEE postop only, with controls

(continued)

Table 2  
Comparison of published literature (Continued)

Author	Y	Age range (including n)	Preoperatively			Postoperatively			Controls			Study methodology
			n	REE kJ · kg <sup>-1</sup> · d <sup>-1</sup> (kcal/kg/d)	TEE	n	REE kJ · kg <sup>-1</sup> · d <sup>-1</sup> (kcal/kg/d)	TEE	n	REE kJ · kg <sup>-1</sup> · d <sup>-1</sup> (kcal/kg/d)	TEE	
Farrell [28]	2001	3–5 mo	Congestive heart failure:			13	184 ± 50 (44 ± 12)	255 ± 38 (61 ± 9)			- Prospective, single-center study - REE and TEE preop only, with controls	
		(c = 0) (a = 17)	10	218 ± 59 (52 ± 14)	385 ± 84 (92 ± 20)							
			Non-congestive heart failure:									
			7	184 ± 33 (44 ± 8)	322 ± 71 (77 ± 17)							
Avitzur [54]	2003	c = 13 (3.2 mo)	13 (c)	238 ± 54  (57 ± 13)		6 (c)	247 ± 42  (59 ± 10)		N/A		- Prospective, single-center study - REE pre and postop - No TEE, no controls	
		a = 13 (12.3 mo)	13 (a)	243 ± 38 (58 ± 9)		11 (a)	259 ± 42 (62 ± 10)					
van der Kuip [17]	2003	2–8 mo	11		381 ± 42				23	298 ± 36	- Prospective, observational two-center study, including meta-analysis	
		(c = 0) (a = 11)								(71 ± 9)	- TEE preop only, with controls - No REE	

a, acyanotic; c, cyanotic; n, number of patients; REE, resting energy expenditure; TEE, total energy expenditure; VSD, ventricular septal defect; DLW, doubly labeled water; preop, preoperatively; postop, postoperatively; N/A, not applicable.

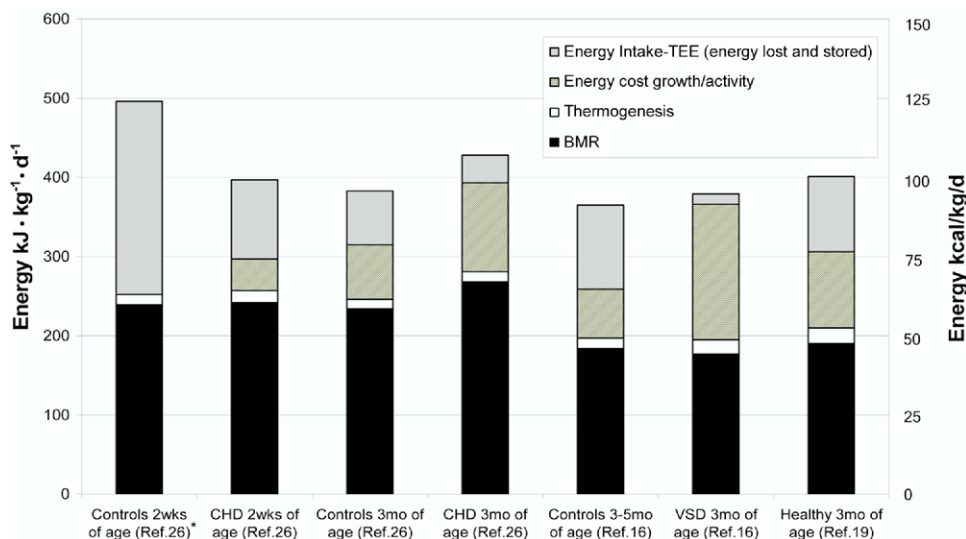


Fig. 2. Components of energy metabolism in infants with congenital heart disease (CHD). \*No contribution of energy cost growth/activity identified in study. BMR, basal metabolic rate; TEE, total energy expenditure; VSD, ventricular septal defect.

result of perioperative hormonal stress response and the therapeutic administration of catecholamines [40,41]. However, studies in infants with CHD have suggested lower TEE and REE within 24 h of surgery than that predicted in healthy age-matched infants [42]. It is unclear whether these results may reflect problems when measuring REE using indirect calorimetry in ventilated infants with uncuffed tubes or the effect of anesthetic gases, sedation, or medications or suggest that energy expenditure is modest during this period [43]. By postoperative day 3, a change to anabolic metabolism is signaled by a normalization of glucose levels and increase in insulin, glucagon, growth hormone, and thyroid hormone levels [41]. This response may be delayed in patients who were cyanotic before surgery [41]. REE in infants with cyanotic and acyanotic cardiac lesions returns to preoperative levels 5 days after corrective surgery [42].

#### Energy expenditure after corrective cardiac surgery

After successful correction of the cardiac lesion, energy expenditure returns to normal levels. By 5 y of age, or an average of 2.6 y after corrective cardiac surgery, TEE normalized in children with CHD who had increased TEE preoperatively [26,44]. This normalization of energy balance is mirrored by a recovery in nutritional status. Successful cardiac surgery is usually associated with improvements in weight within a few months of the procedure, however, it may take up to 1 y for height and head circumference to catch up to normal [45]. Significant improvements in weight gain, height, and head circumference is observed within 6 to 12 mo of surgical correction of a large ventricular septal defect and congestive heart failure in infants with a normal birth weight and surgical correction performed before 7 mo of age. Limited postoperative re-

covery in weight or length is observed in infants who had a low birth weight, small head circumference, intellectual deficit, or residual malformation [46]. Although obesity and premature cardiovascular disease have been observed in infants of very low birth weight after catch-up growth, this is unlikely to be a risk in CHD as most infants are normal weight at birth [2–6,47].

#### Evidence to support early operative correction

The age and time of corrective surgery affects the potential for nutritional recovery [18]. But the possible nutritional benefits must be weighed against increased intraoperative and postoperative risks of surgery in small, immature, and under-nourished infants. There are no published studies comparing the nutritional outcome of infants undergoing early versus late cardiac surgery. However, an association between myocardial lactate concentration and cyanosis and lower adenine nucleotide levels has been identified with increasing age [48]. Whether these factors may influence energy expenditure in older children with CHD has not yet been elucidated.

#### The role of nutrition support in improving postoperative outcome

Patients who are malnourished are prone to both infectious and non-infectious complications of their disease or therapy resulting in longer duration of hospital stay [49–51]. Meeting metabolic and nutritional needs during this period of medical instability by the provision of energy and nutritional substrates may assist in modifying the metabolic stress and contribute to improved outcome [52]. Providing nutrition support during the postoperative period until adequate voluntary intake can be reliably maintained is essen-

tial to minimize the contribution of malnutrition to metabolic stress and postoperative complications. Unfortunately, validated equations to predict energy requirements of infants with CHD during the perioperative period are limited [53]. Ideally, nutrition support should be provided by the enteral route unless there are contraindications to enteral feeding. Fluid restriction and the need to prioritize volumes available to provide essential drugs and blood products are a major barrier to effective nutrition support in the immediate postoperative period.

## Conclusions

Energy imbalance is a major contributing factor to failure to thrive in children with CHD and it influences the metabolic response to injury and outcome after corrective cardiac surgery. The published literature of studies of energy metabolism in children with CHD is difficult to interpret as studies generally involve small patient numbers with a diverse range of types and severity of cardiac lesions and genetic and/or prenatal factors. The age and time of corrective surgery affects the potential for nutritional recovery. Although the immediate postoperative period is characterized by a hypermetabolic state, low TEE and REE are reported within 24 h of surgery. REE returns to preoperative levels within days of surgery. Significant improvements in weight and growth occur within months after corrective surgery. However, limited postoperative recovery in nutritional status and growth occurs in infants with a low birth weight, intellectual deficit, or residual malformation. Further studies on energy metabolism are needed to inform the timing of corrective cardiac surgery to optimize nutritional outcomes and to identify those infants who may benefit from aggressive preoperative nutrition support. Not only will this help minimize risks associated with malnutrition in the perioperative period, but it will also support optimal growth and development as a platform to maximize the potential for catch-up growth in the postoperative phase.

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