Effect of infection on energy requirements of infants and children

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Abstract

This is a brief review of the effects of infection and other forms of stress on the energy needs of infants and young children. The results of studies estimating energy expenditure in infants and young children during illness and convalescence were evaluated. Expectations that energy expenditure is influenced by the severity of illness, nutritional status, the nature of the illness, the presence and intensity of 'catch-up growth,' and the stage of convalescence are generally supported by the literature. The qualitative or quantitative nature of responses, however, are not uniform for diverse illnesses in children in diverse planes of nutritional adequacy.

Introduction

Increases in energy requirements imposed by acute and chronic infections have not been studied extensively in infants and children. For this and other reasons reviewed briefly below, past estimates of energy requirements have not included quantitative, age-specific considerations of population disease burdens. The general difficulties that have precluded estimations of this type are most challenging for infancy because of anticipated complexities arising from interactions among the processes associated with normal and 'catch up' growth and development and responses to illness, and convalescence.

Quantitative predictions are made difficult because the effects of illness on energy needs likely depend on whether processes associated with growth and development are attenuated, maintained, or accelerated during acute phases of illness and convalescence, and in the post-convalescent period. Furthermore, energy needs are also affected by deficits accumulated during previous and index periods of illness and by the subject's pre-existing general plane of nutrition. Anorexia and increased metabolic demands that are likely to accompany illnesses and possible (depending on the nature of the illness) decreased absorption also influence accumulated deficits.

Insufficient data are available during illness, active convalescence, and post-convalescence to base estimates of energy requirements of infants and children on direct measurements of energy expenditure and growth. Disease-specific data for even single phases are often lacking. The paucity of information suggests that a factorial approach might be useful to estimate the theoretical needs of individuals during acute illness and/or convalescence. Theoretical requirements may be estimated by summing the energy costs of basal metabolism, possible faecal losses due to malabsorption, increased needs imposed by febrile and other responses to stress, and the costs of maintenance and discretionary activities. These estimates may be calculated most easily in the clinical setting. In the home or in the field, however, this becomes impractical.

Accounting for morbidity in assessing energy needs

Assessing the adequacy of energy intakes of populations or sub-groups, although also theoretically possible, is even more daunting. One can begin with a factorial approach analogous to that described briefly in the preceding paragraph and include population estimates of morbidity (type, frequency, duration, and severity). Unfortunately, required morbidity data are not available except, in part, for reportable diseases and usually these data are limited to general type of illness and incidence or rough estimates of prevalence. Accurate population figures for disease-specific duration of illness and for the various phases of convalescence are unavailable. In the end, one is left with an unsettling exercise of estimating needs from the sum of requirements of healthy populations and extrapolated estimates of additional needs imposed by 'endemic disease loads'. Thus qualitative inferences may be possible, but quantitative estimates for population applications are likely to be of limited value.

The most commonly quoted figure of the energy cost of illness is that of Du Bois[1], 13% increment in basal energy expenditure per degree Celsius of fever, and although this estimate generally is supported by more recent data, there are disagreements in the literature that are not explainable easily. Also it is clear that there is no consensus on objective estimates of intensity for other forms of 'illness' analogous to that provided by measurements of body temperature.

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Energy demands of infectious illness in infancy

Below are selected examples in the recent literature of the difficulties faced by attempts to quantitify the energy demands of illness in infancy. Among the more informative recent studies are those of Stettler et al.[2] These data are particularly valuable because they were obtained in a population clearly suffering from food insufficiency. They were collected in 19 Gambian children, 9 ± 4 years of age with a mean weight/height 86% of the expected NCHS[3] mean. Resting energy expenditure (REE) was measured at three times: period A, at the onset of a malarial crisis (mean axillary temperature (MAT), 39.2°C), period B, 3–4 days after therapy was initiated (MAT = 36.6°C) and, period C, 14–21 days after the onset of treatment (MAT = 36.7°C). REE measured during period C was 10 ± 6% lower than predicted by the Schofield[4] equations. Mean REE for periods A and B were 32 and 3%, respectively, greater than that measured during period C.

REE was elevated during febrile periods. The increase in REE was found to be proportional to the severity of the fever. The regression relating REE to body temperature has at least two interpretations. One is that the slope estimates the fraction of the REE increase explained by fever (i.e. a 6.9% increase in REE per degree Celsius) and that the 0 intercept estimates other metabolic costs (i.e. approximately 1/3 of the observed REE increment are due to processes not attributable directly to the febrile response). Alternatively, if all the REE increase is attributed to the febrile response, REE is expected to increase 11.7% per degree Celsius of fever, a figure close to that reported by Du Bois[1].

It is noteworthy that the elevation in energy expenditure was short lived. The most parsimonious explanation for this observation is that the hypermetabolic state associated with illness was relatively brief. Alternatively, if the REE measured during period C remained higher than 'usual' because of ongoing decrements in accumulated deficits the difference between REE in periods A and C would not be an accurate measure of the acute 'costs' of illness.

The relationship between resting metabolic rate (RMR) and the percentage of weight/height of the NCHS[3] mean also is of interest. The study reported a significantly positive relationship ($r = 0.54$, $P < 0.05$) between the increment in energy expenditure due to fever and percentage of mean weight/height, thus less wasting was associated with greater increases in energy expenditure in response to fever. The likely net long-term effect of the increased RMR during illness, however, is difficult to ascertain because of compensatory decreases in activity and, as mentioned briefly above, the expected anorectic responses likely to accompany febrile and other illnesses.

This study suggested that at least in older children with malaria the REE was significantly elevated in the acute phase, that with treatment this increase was relatively short lived, that RMR during convalescence remained below basal metabolic rates (BMR) predicted by the Schofield[4] equations, and that the response to fever was dampened by pre-existing wasting.

In contrast to these findings, Duggan et al.[5] found no increment in REE during the acute, febrile phase of measles. These observations were made on 17 children, 13–60 months of age, and weight/length Z-scores that ranged from 0.06 to −3.60. Only one child had a Z-score above 0, seven had Z-scores between −1 and −2, seven had Z-scores between −2 and −3, and one had a Z-score below −3. Initial measurements were obtained at the time of admission to hospital with acute measles. Children were readmitted for follow-up studies after 'full recovery'. All children were febrile during the initial period (the mean rectal temperature was 38.8°C). The mean REE during acute illness was $254 ± 40\,\mathrm{kJ\,kg^{-1}}$ per 24 hour and $274 ± 35\,\mathrm{kJ\,kg^{-1}}$ per 24 hour at follow-up. The lack of an increment in REE is difficult to explain unless we assume that the nature of the illness, the children's younger ages, and/or the children's wasted condition resulted in blunted responses to the infection, and/or that significant catch-up growth was underway during the follow-up measurements. Although the intervals between initial and final measurements are not given, the group's mean weight gain between measurements was 1.2 kg, or over 10% of the group's mean initial body weight (10.2 kg). This increment in body weight suggests that the accelerated metabolic activity associated with catch up growth may account for these observations.

McIntyre and Hull[6] also found no increment in REE in febrile infants. They studied 12 febrile (MAT = 37.5°C) infants (mean age 3.7 months, range 1.4–6.5 months). Measurements were obtained on admission ($227 ± 40\,\mathrm{kJ\,kg^{-1}}$ per 24 hour) and at recovery (before discharge when all infants were afebrile ($207 ± 31\,\mathrm{kJ\,kg^{-1}}$ per 24 hour). The sample size and variability of measurements permitted the investigators to detect a 20% increment in REE with a power of 0.9 at a P-value of 0.05. Neither age (i.e. there was an equivalent number of infants younger and older than 3 months and the two groups responded similarly) nor type of infection (i.e. no differences were seen in infants with viral illnesses or bacterial meningitis) appeared to predict whether REE remained stable or increased in response to fever. No data were presented to suggest that any of the infants were wasted. The mean REE measured was approximately 8% below the BMR predicted by the Schofied[4] equations. Again, although the possibility of accelerated growth in the convalescent period is a potential confounder, the lower than predicted REE in an apparently well-nourished group during convalescence makes this explanation highly unlikely. However, since the mean increment was approximately 10% above baseline, it is difficult to discount the role of insufficient power to detect

increments at or lower than 10%, a possible outcome given the mean relatively low intensity of fever reported by the investigators.

Energy demands of other forms of stress

These studies represent the two extremes of possible outcomes, i.e. 0–30% increments in energy expenditure due to a wide variety of parasitic, viral, and bacterial infections, but, what about other forms of stress? Cuthbertson[7] was among the first to report increased metabolic rates following trauma. It is thus potentially instructive to assess energy expenditure by children undergoing forms of stress other than that presented by infectious illness.

Jones et al.[8] studied 19 young infants (mean age 29.16 days). Their weight ranged from 2 to 5 kg. Five underwent minor surgery. The surgery in the remaining 14 was classified as major according to an operative stress score (OSS) based principally on the nature of the surgery. The mean increment in REE was 15% above baseline. REE increased by 2–4 hours postoperatively and returned to baseline by 12–24 hours. Neither age nor weight explained any of the variation in postoperative REE. When infants were grouped according to the surgery's severity, REE was observed to increase by approximately 20% in those undergoing major surgery and 5% in those undergoing minor procedures.

Chwals et al.[9] studied slightly older infants undergoing various surgical procedures. They included 12 infants. Their mean age was 47 days. They were studied after two surgical procedures separated by at least 8 days. Children were stratified by a stress index based on the level of post-operative serum C-reactive protein. The mean age of infants undergoing 'high stress' procedures was 33 days and those undergoing 'low stress' procedures, 67 days. The 'high' stress group's REE was approximately 30% higher on day 2 than day 8 following surgery. The 'low' stress group's REE was approximately 30% lower on day 2 than day 8. The group explained their findings by suggesting that growth was restricted for a longer duration in the 'high' stress group and thus ascribed the 'low' stress group's heightened REE on day 8 to the increased metabolic activity associated with catch up growth.

Winthrop et al.[10] also studied older children post-operatively. Results were obtained in 19 children whose age ranged from 3.5 to 16 years. Children were studied within 48 hours of traumatic physical injury, 3–5 days after the initial injury, and after discharge. Not all children were studied at any of the two follow-up periods. These investigators found that increases in BMR were related to the severity of injury. The peak value was 14% above baseline.

Goran et al.[11] reported REE in burned children. They examined data from 127 measurements obtained in 56 children (85 from males and 42 in females). The subjects'

mean age was 9 ± 5 years. No evidence was provided that any were wasted. The mean 3° burn size was 57 ± 24% of body surface area. All measurements were treated independently of each other and no effort was made to control 'for standardising conditions with respect to fever, infection, antibiotics, pain medication, etc.' These investigators found that the most powerful predictor of measured REE was basal energy expenditure predicted (PBEE) by the equations of Harris and Benedict,[12] that REE was predicted best by multiplying PBEE by 1.29 and that energy needs including maintenance could be met, on average, by multiplying PBEE by 1.55. Furthermore, Goran et al.[11] estimated that the energy needs of 95% of the children undergoing similar stress would be met by multiplying PBEE by 2. This estimate would cover both maintenance and increased REE.

Summary

Clearly, increases in REE have been found to be related to stress severity, but neither the qualitative nor quantitative nature of the responses has been uniform. Expectations that energy expenditure would be influenced by the severity of illness, the infant's nutritional plane, possibly the nature of illness, the presence and intensity of catch-up growth, and the stage of convalescence generally are supported by the available literature. Published studies have concluded that REE remains stable, increases minimally or is raised up to 30% above baseline and that this range of responses is due to the variable effects of factors that have been outlined briefly in this review.

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