Growth Outcome: Nutritionist Perspective

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Abstract

Increasing evidence points to a fundamental role of early nutrition on rates of growth and development, and later health. We may identify three major fields of scientific interest and clinical application. (1) In developing countries poor growth is associated with greater risk of morbidity and mortality from infectious diseases, mainly lower respiratory infections and diarrhea. In these settings, failure to promote compensatory growth may have negative short-term consequences, and the nutritionist’s task is the primary prevention of nutrient deficiencies to promote the full expression of the individual genetic potential, while allowing for recovery of early secondary functional deficiencies. (2) A second challenge for nutritionists is represented by the approach to growth impairments in rare disorders, ranging from congenital disorders to chronic infections. Most disorders are favorably influenced by improved nutritional status and better growth, and patients may satisfactorily reach adolescence, pubertal and reproductive age, up to ageing. Even for the less positive conditions, an improvement in the quality of life for families is in any case a rewarding aim. (3) A third challenge is represented by the definition of the role of nutrition on growth in physiological conditions for all individuals. Concern has been raised about the potential adverse long-term consequences of accelerated child growth rates, possibly resulting in a predisposition to develop non-communicable chronic diseases in the adult age. Accordingly, this hypothesis might explain the benefits of breastfeeding in terms of slower early growth, and the fetal origins hypothesis in terms of adverse postnatal catch-up growth in infants born small. Therefore, growth as viewed by a pediatric nutritionist perspective is a complex matter, ranging from the early stages of intrauterine development up to adult ages and ageing processes. Cost/benefit analyses of interventions on growth such as cost per DALYs (disability-adjusted life years) or QALYs (quality-adjusted life years) should be expanded on population basis and extended also to congenital and invalidating disorders to identify the most effective and economic sustainable strategies of action.

Introduction: Why Evaluating Growth

Infant’s growth pattern may be particularly relevant starting as early as the first months of life, since it may be associated with later health outcomes. Different studies have shown a reduced growth in infants with symptomatic allergy to cow’s milk (expressed
with atopic eczema) during the first year of life. Differences in weight and length progression between atopic infants and healthy children are significant from the second month of age onward, and become marked in the second 6 months of life. The growth faltering starts even before the clinical expression of the disease, maybe indicating a more general unbalance in energy metabolism and disposal [1]. No adverse long-term effect on anthropometric development up to age 10 years was found for infants fed partially hydrolyzed whey, extensively hydrolyzed whey, extensively hydrolyzed casein, or cow-milk formula, whether comparisons were made between formula groups or with respect to breastfed children [2]. Temporary limited delays in growth achievements have been found with the use of extensively hydrolyzed formulas, and either taste characteristics or intrinsic characteristics of absorption and nutrient utilization have been advocated to explain these observations [3]. Even more clear growth delays before the appearance of clinical symptoms have been found in infants born to HIV-seropositive mothers [4]. Early symptomatic showed impairments in growth progression starting as early as 2 months of age [5]. Differences towards noninfected counterparts through the first year of life were evident for later symptomatic versus noninfected ones too. In this last subgroup, at two years of age negative differences in length achievement versus infant born to non-infected mothers were found [6]. The issue has been recently reviewed, with the recommendations that timely growth monitoring should be used to improve the clinical course and the quality of life of these children [7].

From these two examples we may therefore derive that growth is a general indicator of health status in any case, and even more sensitive than previously believed in children. Since growth (besides genetics and ethnic backgrounds) is also closely connected to nutrition patterns, we may easily derive that nutrition, growth and health outcomes are closely connected in children.

**Growth Quality and Health Outcomes**

The primary role of adequate nutrition in the perspective of health outcomes is the immediate threat to children in resource-poor environments in developing countries where child morbidity and mortality remain high. Children with evidence of poor prior growth are at greater risk of morbidity and mortality from common infectious diseases, including lower respiratory infections and diarrhea. In these settings, failure to promote compensatory growth may have negative short-term consequences. Within this context the nutritionist’s task is the prevention of deficiencies, on order to leave the individual the full possibility of expression of its genetic potential, while allowing for recovery of early secondary functional deficiencies. Combined interventions have the greatest chance of success. At the same time, the rapid passage to better economic conditions has generated contrasting situations. In transitional countries, stunting (shortness for age) and micronutrient deficiencies (iron, vitamin A, and zinc) in children coexist with obesity and noncommunicable disorders originating
the double burden of nutritional disease [8, 9]. Specific patterns of prenatal and post-natal growth are also potential contributors, and intervention strategies to prevent malnutrition should emphasize improvements in linear growth in the first 2–3 years of life rather than aim at gaining weight. In any case, in considering the costs and benefits of promoting catch-up growth, we must not lose sight of the immediate health threats to children in resource-poor environments [10]. The positive effects of compensatory growth are associated with improvements in neurocognitive development and intellectual achievements. Nutrition interventions aimed at women and children under 2 years are among the key strategies for the millennium development goal of universal primary education by 2015 [11].

Therefore, health outcomes in developing and transition country are immediate (survival vs. infections and acute diseases), intermediate (neurocognitive achievement) and long term (prevention of the early manifestations of noncommunicable disorders).

A second challenge for nutritionists is represented by the approach to growth impairments in rare disorders, ranging from congenital disorders to chronic infections. With the improvement of the treatment of primary diseases, new needs and requirements have been defined together with the best way to deliver them. The concept of quality of life has entered the pediatric clinical practice in this area, and most disorders are favorably influenced by improved nutritional status and better growth. The so-called rare disorders are greatly benefitted by this relatively new attitude, posing the pediatric nutritionist in front of new challenges, such as attaining adolescence, pubertal age, successful pregnancy, and even prevention of the early involution of brain function in most favorable disorders and cases [12]. The progress in technical solutions (by providing natural, enteral and parenteral nutrition), the improved knowledge on energy and dietary needs not just disease by disease, but also patient per patient, the creation of dedicated nutrition teams has resulted in improved nutrition status, better growth and, once again, in parallel, better growth and intellectual achievement. The population affected by Rett syndrome represents a significant example of progresses in this field [13, 14]. In the least favorable situations, an improvement in the quality of life for patients and families is an acceptable rewarding aim.

Therefore, for rare and invalidating diseases, health outcomes of growth are the patients' and their families' quality of life. In some cases, this translates into a full-life span effect, inclusive of pregnancy and reproduction, higher school achievements, and a satisfactory private life.

Finally, a third challenge is represented by the definition of the role of nutrition on growth in physiological conditions for all individuals. Based on recent evidence, concern has been raised about the potential adverse long-term consequences of rapid child growth. Accordingly, rapid early weight gain in childhood is associated with the increased likelihood of being overweight or obese later during the life-span, with the progressive development of insulin resistance, dyslipidemc conditions and elevated blood pressure [15]. This concept is actually expressed by the postnatal growth
acceleration hypothesis [16]. The hypothesis is consistent with the observations of a lower risk of future noncommunicable disorders in breastfed infants, since breastfeeding is associated with a slower growth rate compared to other types of early feeding [17]. The concept matches also the observations of increased prevalence of the early symptoms of the metabolic syndrome in those born small for gestational age (growth-restricted, thrifty phenotype hypothesis) [18]. Finally, this interpretation is fully consistent with the increasingly and alarming prevalence of chronic-degenerative disorders and their prodromic signs (obesity, high blood pressure, insulin resistance) in developing and transition countries, mentioned before [8, 9]. Indeed, rapidly improved economic conditions could allow for an easier availability of energy-dense food and rapid gains in growth, mainly weight (instead than just compensatory height gain).

In other words, the event of rapid early weight gain should be the starting point, in either those born at term and adequate for gestational age, or those who have been growth restricted. Understanding these mechanisms has an enormous preventive potential, given the major public health implications, including opportunities for an effective primary prevention of adult diseases. A possible problem in this field is represented by the outcome measures of accelerated growth, investigated through some biochemical markers, or indicators, also called 'surrogates', since they cannot stand for the overt disease [19]. Recently, techniques allowing for the detection of early anatomical and functional changes have shown possible higher degrees of associations with the possible disease conditions [20]. In this setting, possibly interesting all individuals, the focus of growth outcomes is to maximize the positive genetic potential while preventing, even in those that are predisposed, the appearance of symptoms of non-communicable disorders.

**The Future: A Nutrieconomic Approach to Growth Outcomes?**

Economic constraints in all countries, in some of them further exacerbated by the present crisis, require the use of cost/benefit analyses for all the interventions performed at the stadium of preventive medicine. Optimistically, this type of analysis would help in selecting the best diagnostic-therapeutic approaches in terms of health gain and costs, while optimizing the interventions on conditions recognized ‘at high risk’. In the last decade DALYs (disability-adjusted life years) or QALYs (quality-adjusted life years) have been widely used to measure the overall impact on health of interventions and thus to identify the most favorable approaches in terms of costs and outcome [21].

Cost-utility, the technique using a summative indicator incorporating quality of life or disability and mortality, has progressively been used in all subspecialties of pediatrics, and, within this context, the field of nutrition has been the object of re-appraisal in either developed or underdeveloped countries [22]. The prevention and
treatment of malnutrition on the one hand, and population programmes for the prevention of overweight and obesity on the other, have been the first to be considered. Programmes of home food fortification by the addition of Sprinkles (micronutrients) have been evaluated, considering that only the combined supplementation of multiple micronutrients with lipid-based supplements improves growth in young children [23]. In any case, home fortification of complementary foods reduces the prevalence of anemia in infancy, and zinc supplementation is associated with a reduction in diarrhea and respiratory disease morbidity while improving linear growth. Also vitamin A supplementation decreases the incidence of diarrhea and measles. For these interventions, economic measures were estimated: the cost per death averted, the cost per DALYs saved and the gain in earnings due to higher cognitive functioning for each dollar spent. The estimated cost per death averted is USD 406 (273–3,248), the cost per DALY saved is USD 12.2 (8–97) and the present value of the gain in earnings is USD 37 (18–51) for each dollar spent on the Sprinkles program [24]. Clearly, these estimates are produced for a low-income country such as Pakistan (GDP per capita = dollars 417) where high infant mortality rates (IMR = 83/1000), high prevalence of anemia (93%), and high mean longitudinal prevalence of diarrhea (17%) take place. At the other extreme there are studies investigating the most cost-effective ways to prevent overweight and obesity, and the related consequences in terms of prevention of obesity-related complications. Within a 2-year controlled community-based obesity prevention initiative, for instance, it has been calculated that the cost per kilogram of weight gain prevented over the 2 years of the intervention was NZD 1,708 in 7-year-old children (average weight gain prevented of 0.75 kg) and NZD 664 in 13-year-old children (average weight gain prevented 1.93 kg). The value of NZD 1 is around EUR 0.63, to date [25].

On the whole, a systematic review of the routine monitoring of growth in children of primary school age to identify growth-related conditions has been carried out, with the objectives of clarifying the role of growth monitoring in primary school children, including obesity, and the cost-effectiveness of the intervention. From 31 studies, growth monitoring has been found associated with health improvements at incremental costs per QALY gained of GBP 9,500 and the statistical analysis shows that this monitoring intervention is certainly below the willingness to pay threshold of GBP 30,000 per QALY used by the NICE (National Institute for Health and Clinical Excellence) in England and Wales. Therefore, the authors concluded that identification of effective interventions for the treatment of obesity is likely to be considered a prerequisite to any move from monitoring to a screening programme. Similarly, further long-term studies of the predictors of obesity-related co-morbidities in adulthood are warranted [26].

In this setting, interesting all individuals, the focus of outcomes of growth is to individualize cost and benefits of any intervention, with a common expression in terms of QALYs and DALYs, as a sort of common exchange – in a way similar to z-scores for the evaluation of anthropometric indices.
Conclusions

From this brief revision, we may summarize some fundamental outcomes of growth. Growth is an indicator of health status, and improvement of short-term growth may have a relevant impact on survival in developing countries. Short-term growth may have positive effects on the neurodevelopment of children in developing countries and LBW infants, respectively. Unfavorable long-term effects of accelerated growth in the early stages need to be prevented (through follow-up measures, and referring to functional and/or anatomic indicators). Cost/benefit analyses of interventions on growth such as cost per DALYs and cost per QALYs should be expanded on a population basis and extended also to congenital and invalidating disorders to identify the most effective and economic sustainable strategies of action.

References


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