Growth and Health: A General Perspective

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Growth is a key biological attribute that distinguishes the pediatric from adult population. It is the traditional measure of nutritional status and a large literature describes its measurement and its derangement in disease. However, a new focus is its association with lifetime health and, in animals, senescence – an area providing new insights into developmental biology, early origins of adult health, and primary prevention of disease.

Programming

Central to this field is ‘programming’ – the broader concept that a stimulus or insult, at a critical early period can have long-term or lifetime effects. In 1961 McCance first showed manipulation of litter size in rats, which affected early growth and programmed body size. Now, numerous animal studies show manipulation of early nutrition or growth programs later fatness, blood pressure, cholesterol metabolism, insulin resistance, atherosclerosis, bone health, immune health, learning, behavior and lifespan. Observational studies and, importantly, randomized trials (RCTs, that can establish causation) show corresponding effects in humans, with major public health implications.

Growth is fuelled by nutrition, making it difficult to extricate these two influential early factors for later health; yet, a central programming influence of growth itself is suggested in numerous species including butterflies, fish, rodents and primates.

Complex coupling and epigenetic mechanisms linking growth to later outcomes are emerging. Early programming of hormonal coupling systems including insulin-like growth factors and leptin, theoretically provide future potential to modulate the programming cascade pharmacologically.
Programming of Obesity and Cardiovascular Disease

Numerous animal and human studies, including RCTs, show early manipulations that increase early growth rate, adversely program later fatness, blood pressure, insulin resistance and LDL cholesterol – classical risk factors for cardiovascular disease (CVD). Thus in 2004 Singhal and Lucas proposed the postnatal growth acceleration hypothesis – that rapid early growth (upward centile crossing) programs obesity and CVD. This explains the benefits in breastfed infants for later obesity and CVD risk, in terms of their slower early growth, and is consistent with adverse later effects of fast early growth across species.

The postnatal origins concept is supported by 50 years of robust research; but more recently, the fetal origins of adult disease hypothesis was introduced to explain the retrospective association between low birthweight (a marker of reduced fetal growth) and later CVD. However stronger evidence now suggests the risk for low birthweight infants is not principally prior adverse fetal programming, but their tendency to subsequent catch-up growth, emphasizing the major window for cardiovascular programming is postnatal.

Programming of the Brain

Conversely, the period prior to full term is most influential for the impact of nutrition and/or growth on long-term brain development. Preterm infants nutritionally fuelled to gain weight at 18 (versus 13–15) g/kg per day had major advantages in subsequent verbal IQ, incidence of motor or mental impairment, educational skills, and associated changes in brain structure. In monozygous twins discordant for birthweight, a major deficit in later verbal IQ emerged in the slower growing twin (unpublished). Conversely, postnatal nutrition and growth appear to have less dramatic effects.

Future Perspectives

The new understanding of the impact of growth on health raises key research questions on critical programming stimuli, windows and mechanisms. Current assessment of an individual’s growth itself, using reference charts, is conceptually flawed, since such charts do not identify ‘desirable’ growth in terms of health outcomes – they do not grade individual growth trajectories according to CVD risk, or decelerating
head growth according to later cognitive potential. We also know little about what *aspects* of growth and related body composition best predict health outcomes. These issues have major relevance to public health.