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Nutrition, size, and tempo

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Abstract

Nutrition is a prerequisite, but not a regulator of growth. Growth is defined as increase in size over time. The understanding of growth includes an understanding of the binary concept of physical time and individual *tempo.* Excess food causes *tempo* acceleration. Food restriction delays *tempo*. *Tempo* reflects the pace of life. It is a dynamic physical response to a broad spectrum of social, economic, political, and emotional (SEPE) factors and can affect life expectancy. Variations in *tempo* create distortions of the z-score patterns of height and weight. Illness or intermediate food shortage lead to intermediate halts in development and create short dips in the z-score patterns. Children who develop throughout life at delayed pace usually run at lower z-scores for height and weight, and show a characteristic adolescent trough; children who develop throughout life at faster than average pace usually run at higher z-scores and show a characteristic adolescent peak in their z-score patterns. During adolescence, almost half of the height variance is due to *tempo* variation. There is not one *tempo* for the whole body. Different organ systems grow and mature at different pace.

Take-home message for students Nutrition is a prerequisite, but not a regulator of growth. Nutrition influences the developmental *tempo*. *Tempo* reflects the pace of life, and is a dynamic physical response not only to food supply, but to a broad spectrum of social, economic, political, and emotional (SEPE) factors.

Abbreviations

ADHD Attention-Deficit/Hyperactivity Disorder
BDI-II Beck's Depression Inventory II
bmi-z BMI-for-age z-score
C1 Cohort 1
GHRHR GH Releasing Hormone Receptor
OROS Osmotic-Release Oral System (OROS)
MPH Methylphenidate Hydrochloride
P Centile

Table 1 Average weight of newborns is related to body weight of women in labor. Data from (Gassner 1862)

N	weight of woman in labor (kg)	weight of newborn (kg)
7	45-50	2.835
23	50-55	2.995
56	55-60	3.203
70	60-65	3.260
49	65-70	3.416
27	70-75	3.541
6	75-80	3.677

Introduction

Nutrition is a prerequisite of growth. This general biological principle is long known, and also applies to the human species from conception to adulthood. Severe maternal starvation is associated with smaller size already at birth – multiple historic birth weight data support this association, with data from the siege of Leningrad (Antonov 1947) and the Dutch hunger winter during World War II (Rooij et al. 2010). On the other side, maternal overweight and obesity are associated with larger neonatal weights. Table 1 exemplifies observations of the mid-19th century (Gassner 1862). Yet, this association is deceptive. Growth is sensitive to food shortages and food excess (Brix et al. 2020; Li et al. 2017), but food is not the regulator of growth and final height in the proper sense. Neither tall stature nor short stature mirror food supply. Short stature is not a synonym of malnutrition (Scheffler and Hermanussen 2022b; Scheffler et al. 2019).

Growth is defined as increase in size over time. But whereas size is easily expressible in measures of length and volume, the commensurability of time is ambiguous. Physical time is measurable with clocks and calendars, but growth demands for an understanding of the *pace of life (POL)* (Dammhahn et al. 2018; Hermanussen and Meigen 2007; Réale et al. 2010). The POL differs between species and between individuals of the same species. The day length of the fruit fly differs in its meaning from the day length of the tortoise. Fruit fly and tortoise differ in POL, they live at different speed and differ in developmental *tempo*. So do humans. When most of the 6th and 7th grade school girls have started to exhibit the obvious signs of sexual maturity, most of their male classmates are still pre-pubertal. Even though girls and boys do not differ in calendar age, girls mature at faster pace than boys. Skeletal age (bone age (Greulich and Pyle 1959; Tanner et al. 1991)) that has become the gold standard for determining the state of maturity (Serinelli et al. 2011) clearly shows the differences between the sexes, and also the variation of maturity within the same sex (table 2). The same is true for dentition. Assessing the dental state is less accurate, but may serve as a radiation-free alternative for estimating the state of maturity in pre-pubertal children (Boeker et al. 2022; Almonaitiene et al. 2012; Lewis 1991).

The aim of this review is to highlight the association between nutrition and the developmental *tempo*. Excess food causes *tempo* acceleration. Food restriction delays *tempo*.

The binary concept of time *tempo*

An understanding of the binary concept of physical time and individual *tempo* is essential for the understanding of growth.

Tempo varies throughout life. Some people mature at slower, others at faster than average pace. Illness, stress, intermediate food shortage and other adverse environmental impacts, may lead to additional halts or periods of deceleration in the development of a child. In many cases, subsequent catch-up compensates for those halts: for a while, children may grow faster than normal. Yet, catch-up may not be complete. Periods of developmental delay may accumulate and in the long run decelerate an individual's developmental pace. *Tempo* deceleration affects z-score patterns. Short developmental halts create short dips in the z-scores. Children who permanently mature at delayed or accelerated pace, show characteristic z-score patterns.

Children with delayed growth appear younger than documented in their passports, they are on average shorter and lighter than their classmates of the same age, and tend to grow at low z-scores for height and weight. At pubertal age their height and weight z-scores further decrease forming a V-shape trough, and thereafter rise to final size (Hermanussen 2010). Children with accelerated growth appear older, they are taller and heavier than their calendar age suggests. They tend to grow at high z-scores with a pubertal peak. Absolute height at a certain age depends on *tempo*, but height also depends on the prospective "true" size. "Truly" tall, but developmentally delayed children may appear normal in size, whereas a developmentally accelerated child may temporarily appear tall and mature early, but will finally end up normal in height (Llop-Viñolas et al. 2004). For better describing the "true" size in the sense of final outcome, the term *amplitude* has become established for many years. In analogy to the sine function – the sine value depends on both phase and *amplitude* – the term *tempo* refers to phase, that is the speed of development and to the state of maturity at a given calendar age; the term *amplitude* describes the maximum extension.

Table 2 Standard deviation (SD) of skeletal age in months found among healthy American children aged 2 to 17 years. Data from (Greulich and Pyle 1959)

	SD of skeletal age in month	
Age (years)	Boys	girls
2	4	4
3	6	5.6
4	7	7.2
5	8.4	8.6
6	9.3	9
7	10.1	8.3
8	10.8	8.8
9	11	9.3
10	11.4	10.8
11	10.5	12.3
12	10.4	14
13	11.1	14.6
14	12	12.6
15	14.2	11.2
16	15.1	na
17	15.4	na

Tempo varies considerably among healthy individuals as reflected by the standard deviation of skeletal age in American children (Greulich and Pyle 1959) (table 2). It significantly contributes to the variation in momentary size. During adolescence, almost half of the height variance is due to *tempo* variation (Hermanussen and Meigen 2007). Thus, when talking about variation in growth velocity, we need to carefully consider calendar versus biological age, and to clearly distinguish between the aspects of *amplitude* and *tempo* of the growth process.

The inter-individual variability of *tempo* and its sensitivity to nutrition has caused much confusion. Overfeeding causes mild developmental acceleration. For many years child obesity has been related with tall stature, and was even specifically termed as "Adiposogigantismus" in German literature (Joppich et al. 1975). Meanwhile, the spurious association between food excess and *tempo* acceleration has been recognized well (Brix et al. 2020; Li et al. 2017). Nowadays, nobody would propagate to treat tall stature by means of diet anymore, but this is much less obvious in the case of short stature and food restriction.

The clinical audience is still wedded to the idea that short stature, called stunting, is caused by malnutritional (Scheffler and Hermanussen 2022b; Scheffler et al. 2019; Hermanussen et al. 2019; Scheffler and Hermanussen 2022a). Also, among the nutrition community, there is "…convergence on the use of length-for-age as the indicator of choice in monitoring the long-term impact of chronic nutritional deficiency" (Lartey 2015). Food restriction delays *tempo*. Schlesinger (1919) wrote: "The difficult living conditions in the last years of the war [World War I] might even more often cause the *delay of the increase in growth* during puberty," and: "The whole growth disturbance described here is also to be regarded as a simple inhibition; the growth type, the growth curve, did not undergo any significant change in its form, apart from the occasionally observed slight delay of the puberty drive, the onset of puberty increase". The fact of inhibition of the longitudinal growth of children during the last years of the war is of more scientific interest than practical importance for the above-mentioned reason of the expected reparative capacity; it is an indication of the intensity of the general malnutrition of children. Schlesinger considered the "whole growth disturbance" as a "simple inhibition" that does not affect the form of the growth curve. He also mentioned "expected reparative capacity", that is *catch-up growth* in modern terminology.

Catch-up growth

The term *catch-up growth* (Wit et al. 2013) insinuates catch-up in *amplitude*. But this is not the case. *Catch-up growth* describes the compensatory and transitory *tempo* acceleration following a preceding deceleration in *tempo*. Catch-up in "growth" is in fact catch-up in *tempo*. *Catch-up growth* is cause-specific and characterized by height velocity above the limits of normal for a certain age. It follows a removal of previous biological or psychosocial growth-inhibiting conditions and may occur already within a few days. *Catch-up growth* is an immediate dynamic physical response and a sensitive indicator of preceding developmental malfunction (Scheffler et al. 2021; Scheffler et al. 2020).

The historic perspective

The sensitivity of *tempo* is not restricted to nutrition. *Tempo* is sensitive to a broad spectrum of social, economic, political, and emotional (SEPE) factors (Bogin 2021a; Bogin 2021b). Historic growth data obtained in boarding school boys in 18th century Germany (Komlos et al. 1992) illustrate the social and political impact on developmental *tempo*. Adolescents of high aristocratic background are not only taller, but they enter puberty some two years earlier than their non-aristocratic classmates. In the second half of the 19th century, Kotelmann (1879) studied male students of a Latin school in Hamburg. The boys increased in height velocity from 2.17cm per year in the 9th to 10th year of age to a maximum of 7.46 cm in the 15th to 16th year of

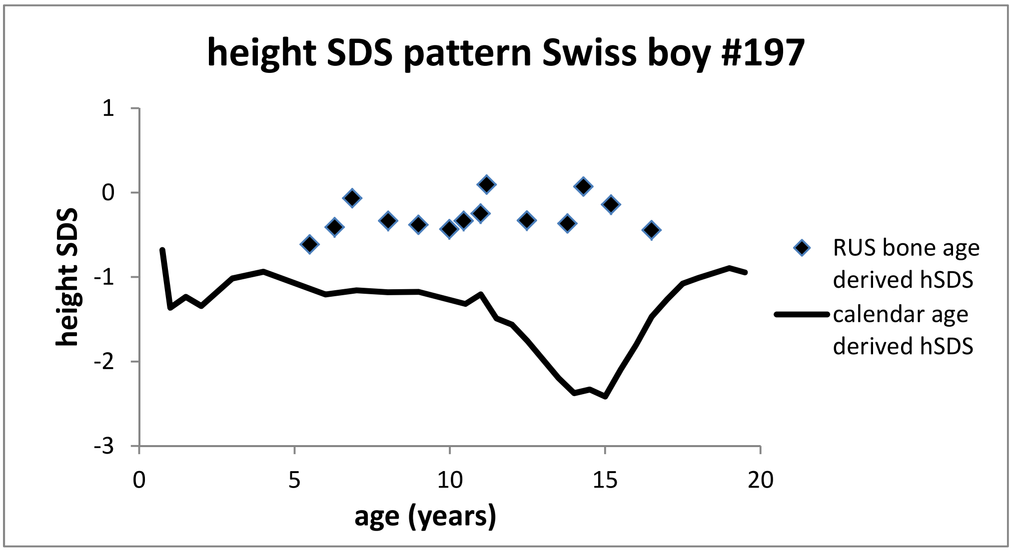

Figure 2 Height z-score pattern of the Swiss boy #197 (see Figure 1). Through line: Z-score pattern based on calendar age. The significant distortion of this z-score pattern with its characteristic adolescent trough coincides with the delay in bone age maturation. Rectangles: Z-score pattern based on RUS (radius, ulnar, small bones) bone age (Tanner et al. 1991). This pattern adjusts for tempo and lacks the adolescent trough as it refers to skeletal maturity

age, i.e. they experienced their adolescent growth spurt some 2–3 years later than modern boys. Similarly, late adolescent growth was repeatedly reported throughout the second half of the 19th century and also in the rural areas in the first half of the 20th century. Further evidence for the sensitivity of *tempo* to environmental stimuli was provided by studies of menarcheal age. First menstrual bleedings occurred at a surprising 4–5 year delay in the mid-19th century compared with modern European girls. We assume that social networking and the collective inhibition of sexuality in the 19th century bourgeoisie was responsible for this "collective social amenorrhea" that, by far, exceeded the delay in growth and physical development of the girls (Hermanussen et al. 2012).

Pace of life (POL)

The POL (Dammhahn et al. 2018; Réale et al. 2010) as reflected in the concept of *tempo* in human growth is not restricted to early development. Factors that affect *tempo* tend to persist throughout life. Caloric restriction as one of the most obvious modulators of developmental *tempo* can extend mean and maximal lifespan. This was first shown in rats (McCay et al. 1935), and thereafter in many other species. The studies contributed essential pieces of knowledge for our understanding of the mechanisms of ageing (McDonald and Ramsey 2010). Thompson et al. showed that humans who grow fastest have the highest hazard of death, and the shortest life expectancy.

These data question modern notions of "optima" and "maxima" in nutrition and height. We appreciate superabundant choices of food in supermarkets and tall and fast-growing children, but we must be increasingly cautious when linking maxima and optima. There is increasing evidence that optimum nutrition rather propends to what we may call "mild caloric restriction". The association between *tempo* and life expectancy on the one side – the latter being one of the most frequently used health status indicators (Health status – life expectancy at birth – OECD Data 2022) – and nutritional supply on the other side, suggests modesty in our recommendations and warrens serious contemplation when linking shortness in stature and any necessity of nutrition interventions.

Both *tempo* and *amplitude* are dynamic physical responses to environmental circumstances. The wide margin within which both parameters can vary suggests that life-history trade-offs and the plasticity of *tempo* and *amplitude* have been most advantageous traits in the bio-cultural evolution of our species.

Many years ago, Jim Tanner [personal communication 1988] borrowed a picture from the world of music: *tempo* does not change the number of notes or harmonies within a particular piece of music. Yet, it makes an essential difference whether you play this piece of music *largo*, *adagio*, or *presto*.

The Swiss boy #197 (First Zürich Growth Study (Prader et al. 1989)) Figure 2 illustrates height z-score patterns of the Swiss boy #197. Z-scores are usually based on calendar age. Calendar age-based z-scores of the Swiss boy #197 (through line) are low between the age of 1 and 2 years, recover at early childhood and again decrease at the age of 15 years. The pattern exemplifies the characteristic z-score distortion of developmentally delayed children and adolescents. Developmental delay in growth coincides with delay in bone age maturation. When instead of referring to calendar age, z-scores are based on bone age, the pattern changes (rectangles). Z-scores based on bone age lack the characteristics of delayed development, and rather appear horizontal imitating growth at average *tempo*. The figure highlights the necessity of recognizing the concept of *tempo* for the understanding of growth.

The effect of *tempo* on z-score patterns

It has become common practice to depict anthropometric variables on centile curves, or to transform the raw measurement values into z-scores (standard deviation scores, SDS), and thereby relating individual measurements to a reference population of the same sex and the same calendar age (Cole and Green 1992). Z-scores are most appropriate for describing patterns of human growth.

Z-scores depict both *amplitude* and *tempo*. But whereas taller than average *amplitude* results in positive, and smaller than average *amplitude* in negative z-scores, variations in *tempo* result in the distortion of the z-score pattern. Children who develop at delayed pace with late onset pubertal growth show an adolescent trough in their z-score pattern (Figure 1, center row), children who develop at faster than average pace temporarily increase in z-scores with an adolescent peak (Figure 1, bottom row).

The Gambian males (Prentice et al. 2013) Similar distortions of z-score patterns can occur in entire populations. In 2013, Prentice et al. (Prentice et al. 2013) published semi-longitudinal data on growth collected between 1951 and 2006 in rural Gambia, and plotted height-for-age z-scores against the UK 1990 reference (Figure 3). The authors were aware of the "artefact arising from their later entry into puberty", but most modern researches are not. The current literature is full of speculations linking z-score patterns to food supply and demands for nutrition interventions when height z-scores deviate from horizontal patterns (Hermanussen 2010). Many are indicative for *tempo* deceleration at the population level independent of food supply.

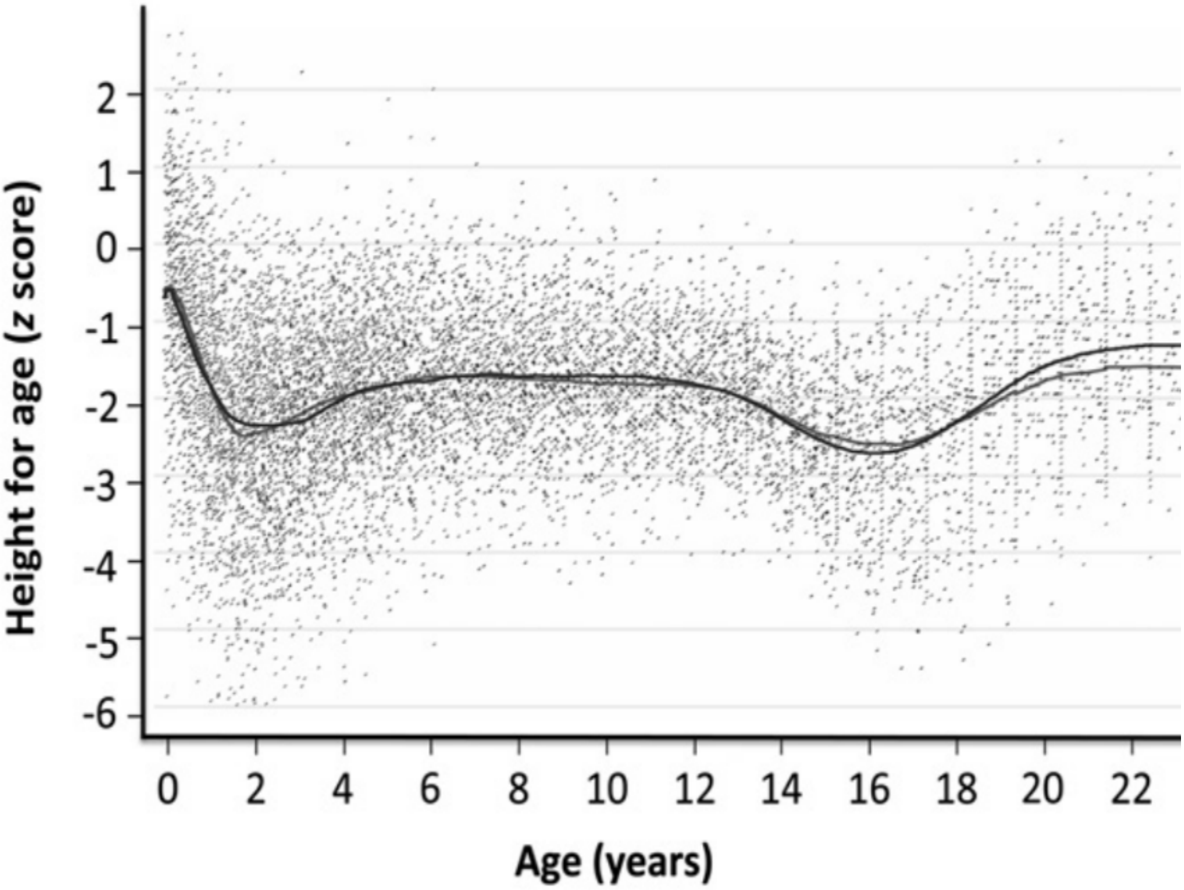

Figure 3 LOWESS-fitted curves applied to semi-longitudinal data on growth collected between 1951 and 2006 in rural Gambian males. Height-for-age z scores were calculated against the UK 1990 reference. The slightly higher lines in adulthood are the post-1970 data (Prentice et al. 2013). The height-for-age z-score pattern resembles the pattern in Figure 2 suggesting tempo delay of the Gambian male population (reprinted with kind permission of Oxford University Press, November 30th 2020).

Allometry

There is not one *tempo* for the whole body. Allometry describes the growth of body parts and organ systems at different pace, resulting in changes of proportions. Even the sequence of organ maturation may vary within the body. The maturation of the endocrine system may uncouple from the *tempo* at which the skeletal maturation proceeds as illustrated in growth studies of girls adopted from orphanages in India or Bangladesh into high-income Scandinavian households (Teilmann et al. 2006; Kuzawa and Bragg 2012). Proos (2009) reported that adopted Indian girls tended to start pubertal development already at age 11.6 (range of 7.3 –14.6) years which was much earlier than Swedish (13.0 years) and wealthy Indian girls (12.4 –12.9 years). The degree to which maturation was sped up in these girls depended on their age of adoption: girls adopted at older ages who spent more time in less favorable conditions, entered puberty earliest upon environmental improvement (Proos et al. 1991). The premature onset of the endocrine regulation seriously interfered with skeletal maturation, and impaired the adolescent growth component. The adolescent growth spurt, though normal in duration and magnitude, was on average 1.5 years earlier, started at shorter height, with final height being reduced to 154 cm. 8% of the adopted Indian girls remained 145 cm or shorter. Several studies from India (Datta Banik 2022b) and Mexico (Datta Banik 2022a) refer to the effect of nutrition and unfavorable living conditions on relative leg length and body proportion.

Conclusion

Nutrition is a prerequisite, but not a regulator of growth in the sense of final outcome in height or weight (amplitude). Nutrition influences the developmental *tempo*. Excess food causes acceleration, food restriction delays *tempo*. *Tempo* acceleration makes children mature at faster pace, and makes them temporarily appear taller than their age mates. Delay in tempo makes children appear short, but it is temporary shortness. Narrowing the view on calendar age leads to the delusion that it is the food that regulates growth. Yet this is deceptive. *Tempo* reflects the pace of life (POL), and is a dynamic physical response to a broad spectrum also of stressful social, economic, political, and emotional (SEPE) factors. Slowing down *tempo* e.g. by mild starvation retards the pace of life and thereby, can even extend life expectancy. *Tempo* is organ specific. Different organ systems grow and mature at different pace.

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Appendix

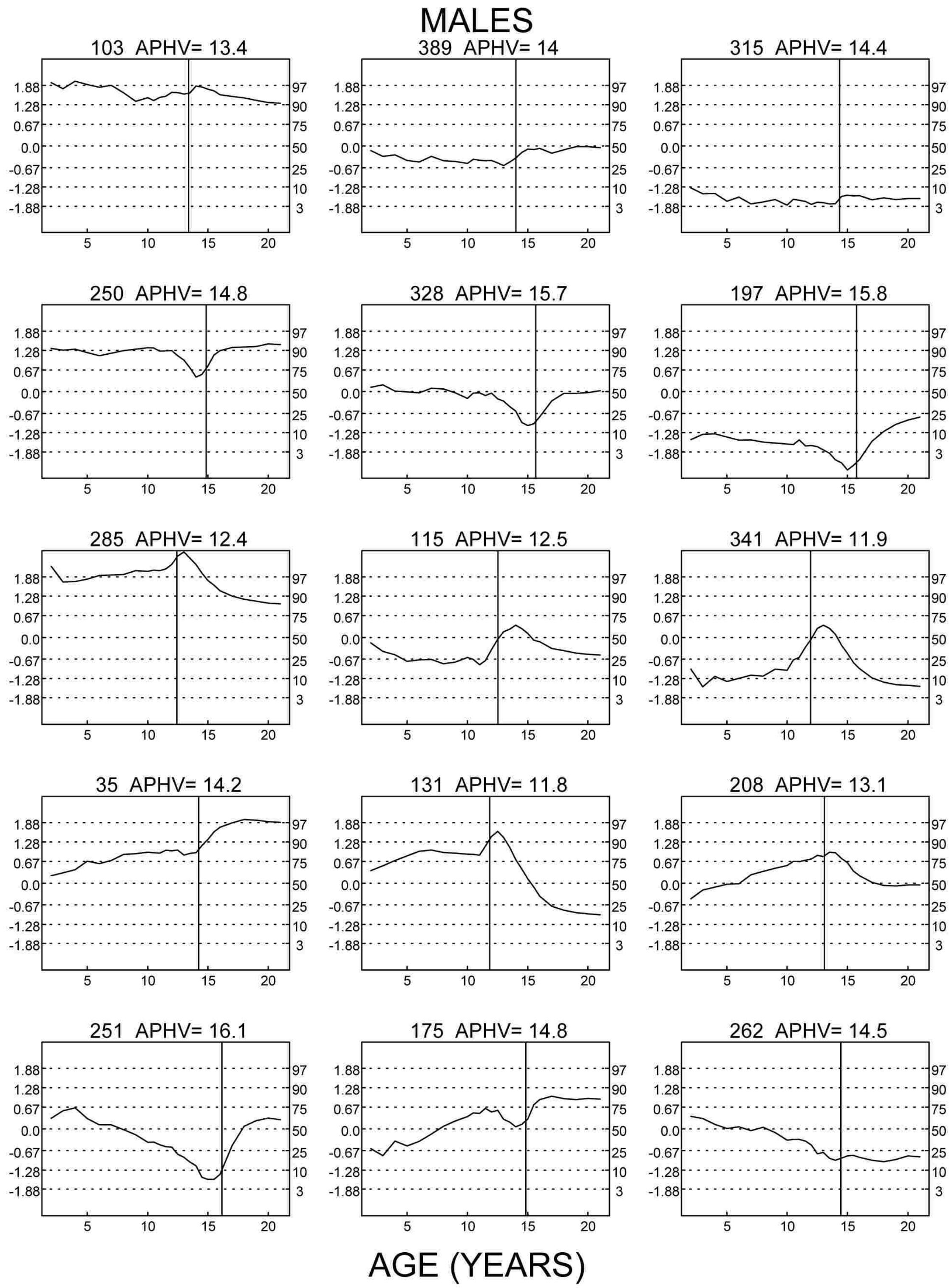

Figure 1 Z-scores for height (centiles for height on the right margins) of nine exemplarily chosen boys of the Swiss longitudinal growth study (Prader et al. 1989) aged 2 to 19 years. Numbers refer to the original numbering of the studied children. APHV indicates age at peak height velocity. Left column: three tall boys, center column: three average height boys, right column: three short boys. Top row: Z-score patterns of children who grow at average tempo (APHV 13.4 to 14.4 years) tend to be horizontal. Center row: Z-score patterns of delayed children (APHV 14.8 to 15.8 years) show an adolescent trough. Bottom row: Z-score patterns of accelerated children (APHV 11.9 to 12.5 years) show an adolescent peak.