Adolescent Growth: Genes, Hormones and the Peer Group. Proceedings of the 20th Aschauer Soiree, held at Glücksburg castle, Germany, 15th to 17th November 2013.

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Abstract

The association between poverty, malnutrition, illness and poor socioeconomic conditions on the one side, and poor growth and short adult stature on the other side, is well recognized. Yet, the simple assumption by implication that poor growth and short stature result from poor living conditions, should be questioned. Recent evidence on the impact of the social network on adolescent growth and adult height further challenges the traditional concept of growth being a mirror of health. Twenty-nine scientists met at Glücksburg castle, Northern Germany, November 15th - 17th 2013, to discuss genetic, endocrine, mathematical and psychological aspects and related issues, of child and adolescent growth and final height.

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Thomas Meitinger summarized genetic aspects on height. Several genes cause large effects on height, particularly duplications or deletions of the growth hormone gene, the SHOX gene, and defects in the fibrillin1 gene that are associated with Marfan syndrome, and in the FGF receptor 3 gene that are associated with achondroplasia and hypochondroplasia. In a recent large-scale screening of candidate genes Wang et al. (1) identified 4928 genetic variants in 1077 genes that were present in case patients but not in control subjects. Of those, 1349 variants were novel. The authors identified 3 individuals with known pathogenic variants in PTPN11 causing undiagnosed Noonan syndrome. In genome-wide association studies DNA is compared between people with, and control people without the disease. Genome wide association studies investigate the entire genome. Samples of DNA are obtained from all persons and screened for genetic variants. SNPs that are more frequently observed in people with the disease, are considered to be associated with that disease.

Johannes D. Veldhuis discussed growth hormone (GH) regulation.(2,3) GH controls skeletal growth, organ size, body composition, intermediary metabolism, muscle strength, bone mass and possibly neurocognitive function. Various clinical factors modulate the primarily (>85%) pulsatile mode of fasting GH secretion.(4) Foremost determinants are age, puberty, sex steroids, body composition, glucose, free fatty acids, amino acids, exercise, fasting, food intake, core body temperature, thyroxine, IGF-I and GH itself via autofeedback. Local and systemic factors are believed to regulate pulsatile GH secretion by way of three principal hypothalamic-pituitary peptides, viz., GH-releasing hormone (GHRH), GH-releasing peptide (GHRP, of which the endogenous prototype is ghrelin), and somatostatin (SST, an inhibitor of GH release, but not synthesis). A major conceptual issue is how these potent GH-regulating peptides interact together and with sex steroids in the control of GH secretion.

Malcolm J Low focussed on the contribution of hypothalamic neuropeptides and dopamine to the regulation of growth hormone secretion in genetically engineered mice. Pulsatile growth hormone (GH) secretion is directly shaped by a combination of three neuropeptides, growth hormone releasing hormone (GHRH), somatostatin (SST) and ghrelin, which activate their cognate G-protein coupled receptors on the somatotroph plasma membrane.(Figure 1) Low and colleagues used mutant mouse models to interrogate the specific contributions of SST and hypothalamic dopamine to GH production and release. Targeted deletion of the Sst gene did not affect weight gain, naso-anal length or sexually dimorphic body sizes of mice from birth through early adulthood.(5) However, intensive random sampling of plasma GH showed that SST-deficient mice of both sexes had elevated median and almost no undetectable values, compared to wildtype males. mRNA expression analyses in liver of male SST-deficient mice revealed that most normally male-biased genes were repressed, while normally female-biased genes were activated. These data, together with preliminary serial plasma GH measurements obtained from cannulated mice, indicate that the primary physiological action of SST is a phasic suppression of GH secretion in males resulting in the characteristic sexually dimorphic patterns of both GH levels and hepatic gene expression. In contrast, the absence of dopamine signalling through the D2 receptor (D2R) produces moderate dwarfism in constitutive Drd2 knockout mice, secondary to a marked reduction in pituitary somatotroph number and reduced GH secretion between ages 3-6 wk.(6) This effect was recapitulated in mice with a conditional deletion of Drd2 in all neurons, but not specifically in SST neurons or in pituitary lactotrophs. (7) Therefore, hypothalamic dopamine signalling, via the inhibitory D2R, is required for the normal adolescent expansion of somatotroph cell mass and GH secretion by facilitating GHRH synthesis and release from hypothalamic arcuate neurons. The specific neuronal target of dopamine responsible for this effect has yet to be identified.

Roland Pfäffle discussed the interaction between psychological make-up and growth. Talbot and co-workers (8) first observed the association between short stature in healthy children and emotional, nutritional and endocrine disturbances. Later Powell and co-workers (9) showed the similarity between growth in emotional deprivation

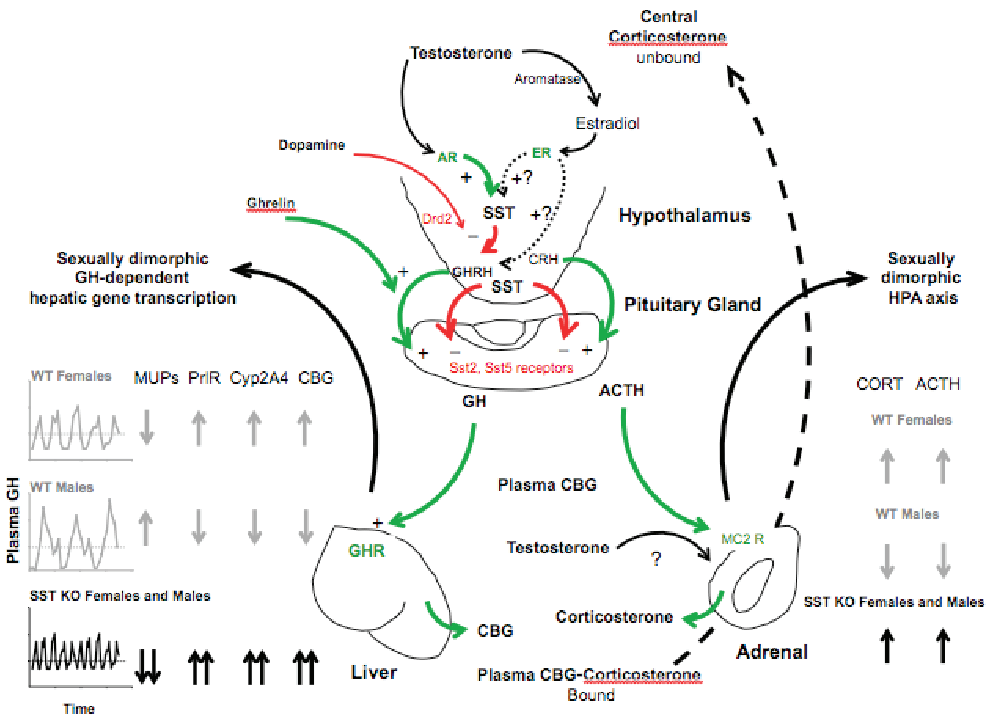

Figure 1: *Growth hormone regulation*

and growth in idiopathic hypopituitarism. Denholm and co-workers (10) studied the long term outcome of childhood experiences of maltreatment and household dysfunction in the 1958 British birth cohort and showed that with a higher neglect score by age 7, children grew more slowly, with deficits up to adulthood, and they also found that deficits associated with early life neglect and household dysfunction might have implications for adult cardiovascular disease risks. Wales and co-workers (11) first showed disproportionate growth in psychosocial short stature. Psychological deprivation is associated with impaired growth, psychological short stature is associated with a blunted GH secretion that can be reversed within a relatively short time period after withdrawal of the „stress“. Pfäffle pointed out that psychological short stature is most probably still under-diagnosed.

Kaspar Staub and Radoslaw Panczak reported on development and socioeconomic/regional differences in height and weight in Swiss conscripts 2004-2012. They showed national trends, regional and socioeconomic differences in BMI on regional (district and ZIP-code) levels. Staub and Panczak showed associations of weight and height of conscripts across set of individual- and ecological-level contextual variables. One of the explanatory factors was an area based measure of socioeconomic position (Swiss Neighbourhood Index of Socioeconomic Position,Swiss-SEP), based on census 2000 data, calculated for 1.3 million Swiss neighbourhoods, capturing the domains of education, employment, housing conditions and income.(12) There was no obvious association between socioeconomic position and body height particularly in the alpine areas of Switzerland, and on the other hand, the similarity of height in neighbouring districts. These and historic Swiss data were used to further studying the association between socioeconomic characteristics of conscripts and areas of their residence and development of BMI in the period 2004-2012 as well as regional variation in height.

Michael Hermanussen and Detlef Groth presented new modelling approaches suggesting an independent regulation of adolescent growth and final height. They formed a geographic network of Switzerland consisting of 169 nodes (district capitals) and 335 connecting edges (direct road connections), and investigated military conscript data obtained between 2004 and 2009(13).(Figure 2) It was shown that conscripts from first order neighbouring districts (district capitals connected by direct roads) were more similar in height than expected. Short stature districts tend to have short, tall stature districts tend to have tall neighbours. Significant correlations in body height existed between 1st (r=0.58), 2nd (r=0.64), 3rd (r=0.45) and even 4th order neighbours (r=0.42). It appears that tall stature communities generate tall people, short stature communities generate short people, and migrants orientate towards the new height target of their host population

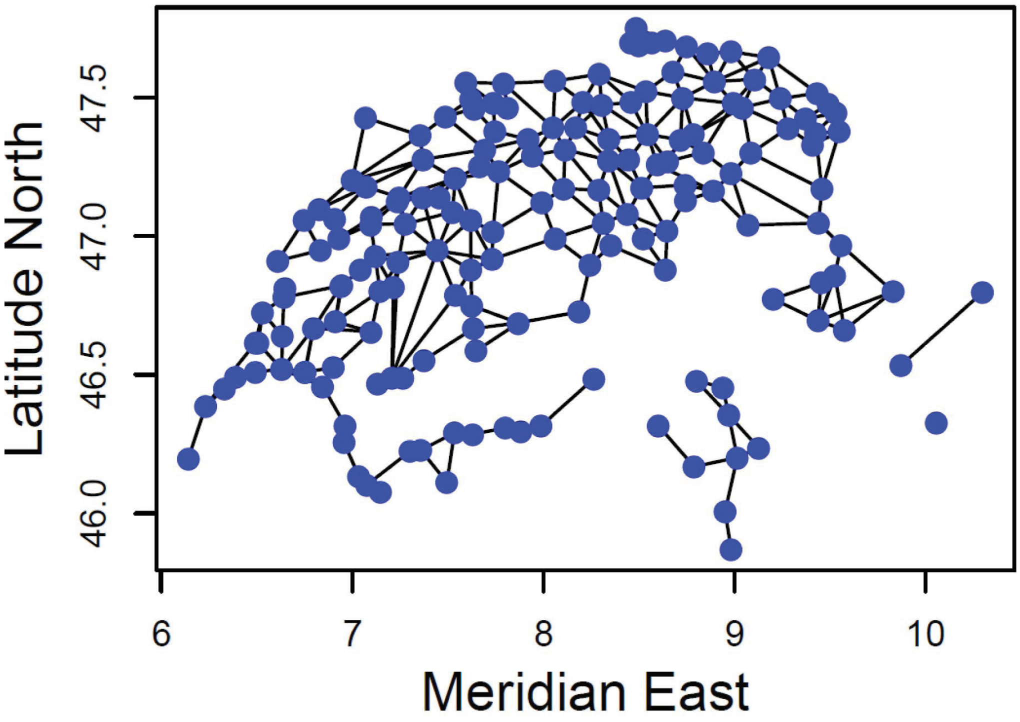

Figure 2: *The geographic network of Switzerland consisting of 169 nodes (district capitals) and 335 connecting edges (direct road connections).*

(community effect on growth (14)) quite regardless of the current personal socioeconomic condition. The concept strongly challenges the traditional concept of growth being a mirror of health.(15)

Marek Brabec performed a spatial analysis of the same historical Swiss height data (13). He showed results of a formalized statistical analysis of the Swiss height and BMI data using two alternative methodological approaches:

- conditional autoregressive modelling based on Bayesian simulations, and
- generalized additive modelling with Gaussian Markov random field spatial autocorrelation structure.

Using this framework, he focussed on the spatio-temporal height trends and changes of the spatial autocorrelation over time (changes of smoothness of the height field over time). The results are interesting both theoretically and practically, since they illustrate in detail the process of “spatial homogenization” of heights across the Swiss territory which is quite consistent with previous findings obtained in other parts of the word and via different methodology. He also analysed the possible influence of various available covariates, both in modern time and in the history. The analysis utilized the Bayesian paradigm and computational MCMC methodology. Quite surprisingly, most of the available spatially-varying covariates do not explain much height variation. This is probably related to the degree of aggregation level of the data (district or “Bezirk” level).

Maria von Salisch discussed peer-relationships in adolescence. Studies on youth development indicate that the average time adolescents spend with their peers increases over the course of adolescence. The study on peers in networks (PIN) examines the social support within different types of peer relationships in a sample of N = 299 adolescents who filled in questionnaires and a network interview (LueNIK) after a school transition in the beginning of grade 7 (age 12-14 years), at the end of grade 7 and again at the end of grade 9 (age 14-16 years). Repeated measures MANOVAs of the PIN-study suggest that peer networks grow in size from about 8 peers to about 10 peers over the 30 months of the study. Girls’ networks tend to be larger than boys’ networks. The decreasing proportions of out-of-school peer relationships suggest that adolescents tend to focus on the peers they spend time with in school. Decreasing proportions of unilateral friendships in school indicate that adolescents get to know each other and nominate fewer peers as friends who do not count them among their friends. Growing proportions of reciprocal friendships (after the end of grade 7) suggest that adolescents increasingly nominate peers as friends who also nominate them as friends. These mutually supportive friendships can help adolescents in coping with their developmental tasks, such as coming to terms with puberty, their gender-role, changing

	Groningen (20th y)		Amsterdam (20th y)		Russian part of Poland (21st y)		
Year of conscription	Jewish	non-Jewish	Jewish	non-Jewish	Jewish	Peasants	Small towns
1850*			156.5	158.5			
1866 -1876	160.6	164.3			160.6	163.1	162.5
1900	164.0	169.6	162.9	169.4	162.3	165.8	165.1

* average age 19 years

Table 1: *In the last decades of the nineteenth century there was a general process of convergence in the biological standard of living. During this period however, Jewish conscripts did not have the same increase in stature as their non-Jewish counterparts.*

relationships with parents, finding a job perspective and developing an identity.

Chung-Ping Loh reported on a study on the peer effects on adolescent bodyweight (BMI). Peer influence has been suggested as a possible determinant of individual weight gain. Possible pathways of peer influence may include peers affecting a person's norms about acceptable weight or weight-related behaviors such as food consumption and exercise. He investigated adolescent bodyweight (BMI) in a rural sample of the wave 2000 of the China Health and Nutrition Survey. The small-community characteristics of the rural sample allowed to define plausible peer groups which include both friends and no-friend acquaintances but not strangers. An instrumental variable approach was applied to control for potential reverse-causality between an adolescent's and his/her peer group's average BMI. In addition to individual and household characteristics, the regression also controlled for community level covariates, including the price of food, access to fast food restaurants, availability of public gyms, and average community income. Placebo tests were employed to check the robustness of our results to uncontrolled community level confounding factors. Loh found that the peer effect was around 0.3 with slight variation between alternative peer definitions. Conditional quantile regressions showed that the peer effect in weight gain was mainly present at or below the median in the conditional BMI distribution for girls, and at the higher end of the BMI distribution for boys. In addition, he found that same gender peers have greater influence on girls than on boys. The presence of peer effect implies that policies targeted at changing bodyweight can have enhanced effectiveness through a multiplier effect.

Vincent Tassenaar investigated the changes in stature of Jewish and Non-Jewish conscripts in Amsterdam (Northern Holland) and Groningen (Groningen) during the second half of the nineteenth century. In the middle of the nineteenth century the position of the Jewish population was rather weak from an economic perspective. In the last decades of the nineteenth century there was a general process of convergence in the biological standard of living (height). During this period however, Jewish conscripts in Amsterdam, in Groningen, the centre of agricultural trade, and in the parts of Russian Poland did not have the same increase in stature as there non-Jewish counterparts. **(Table 1)** What caused this striking divergence is rather puzzling. An aspect might be that Jewish conscripts were highly underrepresented in booming economic sectors such as transport, construction and civil service. An explanation could also be that the prices of food products which were allowed by the Jewish food laws did not decrease in the same pace as other foods. Furthermore, non-Jewish conscripts gained less in stature because their morbidity rates declined less than the non-Jewish population. As a result of their religious rules of hygiene they had in the middle of the nineteenth century a relatively low morbidity level.

Christiane Scheffler discussed the influence of modern living conditions on the skeleton in childhood. In the last years the modern life style caused a lower level of physical activity as well as physical abilities in children and adolescents. The daily physical activity (steps per time unit) has a significant positive correlation to skeleton breadth measurement.(16) A re-analyse of skeletal measurements (breadth of pelvic, shoulder, elbow, thorax; thoracic depth and height) of some 52,000 3-18 years old children and adolescents of different anthropometric studies between 1980 and 2012 in Germany shows a significant decrease in bipedal locomotion induced breadths measures of the pelvis, the shoulder, and the elbow. In contrast height and thoracic index did not change over time. The slimmer bodies of children are not explained by change of shape of body type based on secular trend; they can be explained by the lack of utilisations of muscle load on skeleton. The present investigation underscores a typical example of cost and benefit in a biological context. Since the early hunters and gatherers the biomechanical requirements of the upright bipedal locomotion closely parallel the evolutionary changes of the human skeleton. Humans are persistent in walking and can easily hike more than 30 km per day.

Rebekka Mumm presented the effect of maturation on BMI in adolescents. She re-analyzed height and weight data of 3776 girls and 3956 boys obtained from the German KiGGs study (17,18) in view of the state of maturity. On average, post-menarcheal girls are 5.3 cm taller, 9.7 kg heavier, and their BMI is 2.9 kg/m² higher than in pre-menarcheal girls of the same calendar age. Analogous results were obtained in boys between the age of 12 and 14 years. After voice mutation boys are on average 12 cm taller and 12 kg heavier, and their BMI is 1 to 2 kg/m² higher than boys of the same calendar age before mutation.

Elena Godina conceptualized some new perspectives in the secular trend in Russia. In the previous decades it was noted that young people in Russia were becoming more leptosomic (narrow shaped): the same height but smaller weight, BMI, some circumferences and diameters. It was a typical trend at the turn of the century, particularly among girls in the big cities, interpreted not only as a result of worsening of living conditions in the 1990's but also in terms of changing stereotypes – "from Matreshka to Barbie".(19) However the situation is changing. Three successive longitudinal studies of Moscow children (1960–69, 1982–91, 2003–12) documented a significant increase in height, weight and chest circumference.(20) In the latest growth survey of children and adolescents of Archangelsk, the trend towards increase in weight, BMI and fat mass was obvious in both sexes. Central (abdominal) distribution of fat, together with shorter leg length indicate unfavourable growth conditions in this area.

Andreas Lehmann presented the concept of social amenorrhea.(21) Growth and developmental tempo are influenced by health, nutrition, and socioeconomic factors, but under certain circumstances and particularly in the historical context, physical maturation and the onset of fertility appear to dissociate. Age at menarche is far more delayed than other markers of physical maturity such as peak height velocity. The term social amenorrhea has been coined to describe the delay in menarcheal age and/or suppression of menstrual bleedings due to psychosocial circumstances, in otherwise healthy, normally developed girls. Lindgren (22) and Hoshi and Kouchi (23) suggest that menarche may occur independently from the general physical development.

Janina Tutkuviene and Simona Gervickaite focussed on peer group effects on menarche and the menstrual cycle, reviewed variation in menarcheal age at different regions, districts and schools in Lithuania, and compared the worldwide variation in menarcheal age and its possible environmental factors. The onset of maturation, in particular, menarcheal age can be influenced by inherited, genetic and epigenetic, environmental factors. The mean menarcheal age varies widely, and is a sensitive indicator for various characteristics of population including socioeconomic situation, nutritional status, style of life, stress level, special local conditions, etc.(24,25,26) Synchrony and suppression of menstruation also occurs among women living together in a college dormitory suggesting that social interaction can have a strong effect on their menstrual cycles (27) though this phenomenon is not ubiquitously found (e.g. 28,29, and others). For a long time, the decline in the menarcheal age had been related to improving social and economic conditions, better nutrition and health. However recently, early menarche was linked to the risk of obesity and metabolic syndrome. According to one of the evolutionary hypotheses, unpredictable environmental conditions, early stressful rearing environment, characterized by family conflicts, and insecurity lead to more offspring – hence to mature early.(30) Moreover, girls raised in urban environments often have earlier menarcheal age than girls from rural environments. To date, the effects of socio-endocrinology on pubertal timing are poorly understood,(31) though even in 1980s it was stated that women who begin living together in close proximity before long experience their menstruation more or less at the same time as pheromones might cause menstrual cycle synchronization.(27) Later the other researchers began reporting the failure to find menstrual synchrony in women.(28,32) Whether peer group effects might somehow influence menarcheal age – that is unexplored phenomenon. Three studies (1985-1986; 2000-2002; 2010-2011) on menarcheal age in Lithuanian girls from different towns, districts and schools were analyzed and compared. Menarcheal age of 41 countries during the last decade (Figure 3) was analysed in relation to economic, demographic indicators, food consumption, as well as geographic location and climatic factors of the corresponding country – factor analysis (principal component) was applied. Menarcheal age, to some extend, was still related to girls ethnicity, countries' geographic location, climatic and demographic indicators (the higher the altitude and the more northern the region – the later menarche; the bigger the territorial density, the higher the temperature, rainfalls and sunshine – the earlier the menarche). Urbanization level, gross domestic product (per capita) and food consumption indicators were also related to menarcheal age, but these interactions are poorly understood.

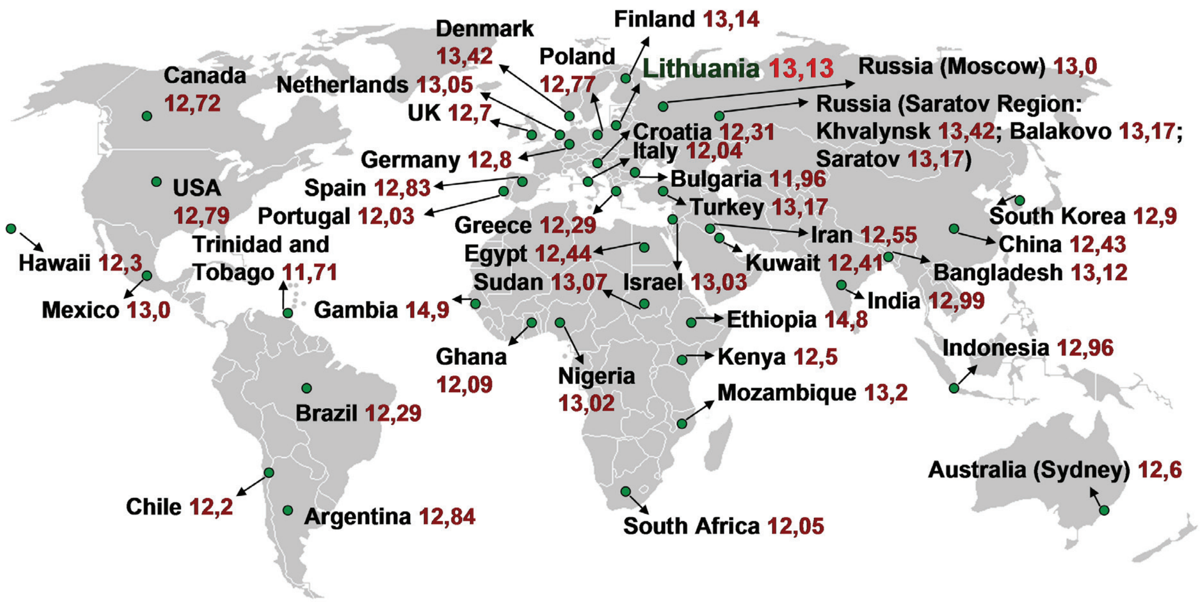

Figure 3: *Menarcheal age of 41 countries during the last decade.*
Argentina (Orden et al., 2011), Australia (Tam et al., 2006), Bangladesh (Hossaina et al., 2010), Brazil (Silva & Padez, 2006), Bulgaria (Tomova et al., 2009), Kanada (Al-Sahab et al., 2010), Chile (Amigo et al., 2012), China (Sun et al., 2012), Croatia (Veček et al., 2012), Denmark (Juul et al., 2006), Egypt (Hosny et al., 2005), Ethiopia (Zegeye et al., 2009), Finland (Pouta et al., 2005), Gambia (Prentice et al., 2010), Germany (Bau et al., 2009), Ghana (Richmond et al., 2011), Greece (Papadimitriou et al., 2008), Hawaii (Epplein et al., 2010), India (Rokade & Mane, 2009), Indonesia (Batubara et al., 2010), Iran (Rabbani et al., 2010), Israel (Chodick et al., 2005), Italy (Rigon et al., 2010), Kenya (Ogeng'o et al., 2011), Kuwait (Al-Awadhi et al., 2013), Lithuania (Tutkuviene et al., 2011), Mexico (Malina et al., 2004), Mozambique (Padez, 2003), Netherlands (Talma et al., 2013), Nigeria (Goon et al., 2010), Poland (Saczuk & Wasiluk, 2010), Portugal (Padez & Rocha, 2003), Russia (Godina et al., 2005), South Africa (Jones et al., 2009), South Korea (Cho et al., 2010), Spain (Cabanes et al., 2009), Sudan (Ali et al., 2011), Trinidad and Tobago (Uche-Nwachi et al., 2007), Turkey (Adali & Koc, 2011), UK (Morris et al., 2011), USA (Matchock & Susman, 2006).

Andreas Nierop presented the new QEPS model describing growth from fetal life to adult height including maturation/biological tempo (33). The model characterizes individual growth with six key parameters expressing height in height SD scores and in cm. Longitudinal height was modelled on the cohort from the Swedish growth reference (born 1974, n=3650). The growth values were described as a sum of four growth functions: Quadratic (Q), exponential (E), pubertal (P) and stopping (S).(Figure 4) The model was tested on 712 girls and 727 boys from a cohort born in 1990. Systematic non-parallel growth in SD-scores was classified by non overlapping 90% confidence intervals in SD scores. In the prepubertal period 10% (11%) of the girls (boys) had non-parallel growth in SD scores before age 2 and 19% (20%) after age 2 years. For the pubertal period we adjusted the SD scores for the individual timing of puberty and still found 25% (20%) of the girls (boys) having pubertal non-parallel growth. Evaluating over the total growth period 55% (53%) of the girls (boys) had non-parallel growth. The QEPS model precisely describes a wide variety of growth curves in SD scores of healthy individuals. More than half of the individuals appear to have systematic non-parallel growth in SD scores.

Anton Holmgren further elucidated the QEPS model for describing and comparing the pubertal growth between different groups and for individuals, and showed confidence intervals (CI) for the variables at individual level as a measurement of quality of the growth data.(34,35) He analyzed measurements for onset, mid and end of puberty together with duration of puberty and pubertal gain. Onset of puberty was defined as the age at minimal height velocity with 10.78 (0.98) years for boys and 9.26 (1.04) years for girls. The age at which 5% of the pubertal part of the growth curve had passed was 11.81 (0.97) in boys and 9.86 (0.98) years in girls. He calculated age at PHV of the total curve (AgeTPHV) with 13.65 years for boys, and 11.84 years for girls. Good correlation existed between age at PHV from the original ICP-manuscripts and the ages obtained by the QEPS model. End of puberty was defined as the age where height velocity has decreased to 1cm per year. The age at which 95% of the pubertal part was reached was 16.13 (0.98) years in boys and 14.67 (0.97) years in girls. The duration of puberty between that age at which 5% and 95% of pubertal growth had taken place was 4.32 (0.22) years in boys and 4.80 (0.23) years in girls. The total area under the

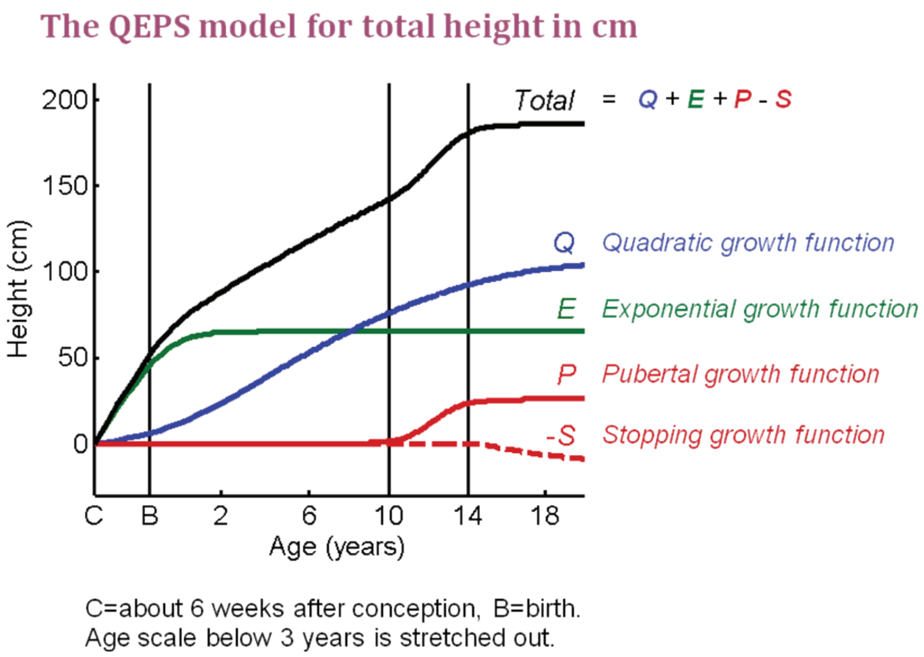

Figure 4: *Growth as the sum of four growth functions: Quadratic (Q), exponential (E), pubertal (P) and stopping (S).*

pubertal curve, i.e. the pubertal gain was 35.68 (4.94) cm in boys and 31.04 (5.36) cm in girls. The QEPS model can mathematically delineate the specific pubertal parts of the total growth curve.

Christian Aßmann presented a statistical comparison of human growth modelling. The variety of modelling approaches towards human height has largely increased during last decades. Beginning with the work of Preece and Baines (36) suggesting a deterministic trend characterization for human growth, several alternatives concerning the characterization of time trending behaviour of human growth are at hand. To decide which statistical modelling approach serves best in terms of model fit, forecasting performance or a combination of both, statistical techniques for nonnested model comparison are required. Forecast based or decision theoretic approaches are natural choices to discriminate between different nonnested model alternatives. Further, the inevitable occurrence of missing values within longitudinal data makes the use of a Bayesian estimation approach attractive allowing for dealing with missing values via data augmentation. In the Bayesian context the Marginal Likelihood as discussed by Kass and Raftery (37) is one possibility to discriminate between different model specifications. Using simulated data and a forecast based measure embedded within a cross validation approach for benchmark comparison, the marginal likelihood shows promising discriminating power between different trend characterizations of human growth. Next steps involve explicit consideration of missing values and their effect on the possibility of discriminating between different model specifications.

Stef van Buuren worked on predicting individual growth curves through matching. In practice, the health professional is often confronted with questions like: Given what I know of the child, how will it develop in the future? How certain am I of the child's future growth? If I do not intervene, will development be normal? Longitudinal growth data are valuable to answer such questions. Curve matching is a new statistical technique to improve prediction of future growth of an individual child. The key idea is to find existing children in existing databases that are similar to the current child. The growth patterns of the matched children suggest how the current child might evolve in future. Curve matching easily connects to current practice, puts existing data to a new use, can portray of the uncertainty prediction, and can indicate the future effect of prospective treatments. In this way, the intelligent re-use of 'old' clinical data may be used to extend the capabilities of the health professional. A demo can be found at http://vps.stefvanbuuren.nl:3838/frisodemo/.

Sławomir Kozieł and Elżbieta Żądzińska focussed on parental smoking during pregnancy and assessed the effect of parental (mother and/or father) smoking on relative leg length in school children. The study was performed in 2001/2002 and included 495 boys and 339 girls at the age of 7-10 years. Information concerning the birth weight of child was obtained from the health records of the women. Information about smoking habits of mother and father during pregnancy and mother's education level were obtained from questionnaire. In order to estimate the influence of parental smoking on relative leg length, controlling for age, sex, birth weight and mother's education, as a proxy measure of socioeconomic status, analysis of covariance was used. The relative leg length was dependent variable, smoking and sex were independent variables and birth weight and mother's education were covariates. Separated analyses were run for three modes of smoking habits during pregnancy: mother or father smoked and both parents smoked. Only parental smoking showed significant effect on relative leg length of children. The interaction between sex and parental smoking was not significant. Probably fetal hypoxia cased by carbon oxygen in smoke decelerated growth of long bones of foetuses.

Ines Varela-Silva presented details of the Portuguese national obesity study. Portuguese children showed no stunting, no underweight, children were taller and heavier than the references up to 8-9 years, but were shorter legged at all ages. More than a quarter of the national sample was either overweight or obese. Protective factors against childhood overweight/obesity were being male; having been breastfed; having been born from mothers who did not smoke during pregnancy; engaging in little sedentary behaviours performing, at least, 1 hour of moderate physical activity every day; and having parents with higher educational levels and BMI within the healthy ranges. In a subsample of 16,788 children parents self-reported their height and weight. It was found that too many parents underestimate their child's body weight. Parental underestimation increases with the child's age. Older children tended to be more frequently underestimated by their parents than younger children. The question remains how do we tell parents they are wrong about their child's nutritional status?

Jana Vignerová compared the growth of Czech breastfed children with the WHO standards. A total of 960 breastfed infants were selected for the study with similar criteria utilized in the WHO Multicentre Growth Reference Study (38) (e.g., good socioeconomic status, exclusive or predominant breastfeeding for a minimum of 4 months, nonsmoking mother, ≥ high-school degree). Anthropometric measurements were recorded at all visits to the pediatrician (11 visits for each infant up to 18 months). Czech infants were longer and head circumference was greater at all percentiles compared to the WHO standards. The length and head circumference values were nearly identical to the Czech growth references.(39,40) The percentile weigh-for-age and weight-for-length values of Czech infants (≤ 6 months) were higher, and lower (6-12 months) compared to the WHO standards. Vignerová concluded that the growth of Czech breastfed children differed somewhat from the current national references (infants with all types of feeding were included in their construction) as well, these discrepancies were less significant than the differences in relation to the WHO standards. The study also confirms that the growth of breastfed infants is specific and different from the growth of formula fed infants. Thus, it is critical that paediatricians are aware of the relative decrease in weight gain among breastfed infants around the age of 3 months in order to avoid premature introduction of supplemental feeding at this critical time. In the Czech Republic, the results of the study of breastfed children have led to a development of new growth assessment guidelines that have been already provided to pediatricians across the country in order to optimize feeding recommendations for Czech infants. The adoption of the WHO standards in the Czech Republic is not recommended.

Emad Salama studied the nutritional status of children living in El-Farafra Oasis in Egypt. In the developing countries, children are at high risk of goiter, vitamin A deficiency, and iron deficiency anemia (IDA).(41) IDA interferes with the thyroidal metabolism of iodine and may reduce the efficiency of iodine prophylaxis. Vitamin A deficiency may impair iron metabolism and aggravate anemia. This study aimed to assess nutritional status as regard goiter, anemia and vitamin A deficiency in children of El-Farafra oasis – New Valley, Egypt which is known to be endemic for goiter and to evaluate adequacy of salt iodization program in this area. This small scale study was conducted in 2012 in El-Farafra which is a remote isolated community, lies 600 km to the south west of Cairo and more than 1000 km south to sea shore. The total number of the population in 2002 was 5000. The study included 180 children, their age ranged from 1.5 to 13 years. Children were examined clinically for the presence of goiter according to WHO classification. 30 cases were found to have thyroid enlargement (goiterous). Weight and height were recorded for the 30 goiterous cases (16.6%) and 29 of non goiterous cases. Laboratory analysis included hemoglobin level, vitamin A level and urinary iodine for the 30 goiterous cases. The study revealed that wasting was present in 6.7%, stunting in 10%, IDA in 24%, decreased urinary iodine in 32% and vitamin A deficiency in 92% of goiterous children. Mean BMI was significantly lower in the goiterous (15.6 kg/m^2) than in the non-goiterous children (19.3 kg/m^2). We concluded that the prevalence of iodine deficiency goiter is still high despite the implementation of universal salt iodization program since 1996. We recommend strengthening a monitoring system for the salt iodization program to ensure regular quality control, conducting a periodic survey on a representative sample, and international education should be undertaken to promote community awareness of the importance of the use of iodized salt.(42) Adequate other micronutrients supplementation such as vitamin A and iron together with protein and energy are mandatory to improve iodine status and to reduce goiter prevalence.

Mortada El-Shabrawi and Mona Elhusseini showed data on rickets in Egyptian infants and very young children in 2013. Rickets is inadequate mineralization of the newly-formed growing bones. Vitamin D (VD) deficiency is the major cause of rickets, osteopenia and growth failure in infants and children. Serum levels of cholecalciferol (25-hydroxyvitamin D or 25(OH)D) are the best available biomarker for VD status. Levels less than 30 ng per ml (75 nmol per L) indicate insufficiency; and 20 ng per mL (50 nmol per L) deficiency. Infants and children in Egypt are at risk of VD deficiency and insufficiency, owing to their limited exposure to direct ultraviolet B sunlight and the low levels of VD in breast milk. The weaning foods are mostly cereals, grains and yoghurt, which are poor in VD. Most Egyptians, also, have dark skin. Mohamed and Al-Shehri (43) reported that 25(OH)D was lower in Egyptian infants who developed acute lower respiratory infections compared with those who did not ($p<0.0001$). Noussa El Basha, Mona Mohsen, Marwa Kamal, and Dina Mehaney conducted a case–control study at Cairo University Children Hospital (Cairo; Egypt) to investigate whether VD deficiency is a risk factor for severe pneumonia in 81 infants and very young children (<5 years) comparing them to 89 matched "apparently healthy" controls. In this cohort, 67 (82.7%) patients and surprisingly 53 (59.6%) "controls" had low serum 25(OH)D. Breastfeeding was found to provide significant protective effect against severe pneumonia compared to bottle feeding (p value 0.04); however VD deficiency was significantly higher in breast-fed babies (65.1%) compared to bottle-fed (34.9%) with a p of 0.04. Although Egypt has abundant sunlight, infants and very young children in 2013 may not benefit from it, developing rickets with its major health consequences, partially due to cultural or lifestyle reasons (excessive wrapping of babies in winter as well as in summer) and probably also due to air pollution.

Alisa Hujić presented the relation between δ15N in primary dentin, long bone length und other proxies for nutrient supply during childhood in prehistoric adult individuals from a Linear Pottery Culture site Viesenhäußer Hof, Stuttgart-Mühlhausen. The work is based on the proposal that body height may be considered a substitute measure of welfare in times when proxies like GDP (gross domestic product) are not reliable or not available. The concept "Biological Standard of Living" assumes that adult body height is a proxy for net nutrition – i.e. intake minus expenses for body warmth, fighting of diseases etc. – especially in protein during childhood and youth. As body height is closely correlated with long bone length, archaeological adult skeletal data can be used to apply this concept in prehistory. The relationship between the nitrogen isotope ratio in primary tooth dentin, the long bone lengths and the microscopically visible health status indicators on teeth and bones were analyzed in adult Linear Pottery Culture individuals to obtain information about the trophic level and the nutritional status during childhood. δ15N and body height in women increased at the transition from older to middle/younger Linear Pottery Culture. δ15N and body height in males decrease at the transition from older to the middle/younger Linear Pottery Culture. This may be due to heavy agricultural workload or violent conflicts. There seems to be a positive correlation between body height and dietary proteins, but only in connection with carbohydrates or fat. The study suggests that not only proteins, but also energy are important prerequisites for growth.

Takashi Satake, Toshie Hirohara and Komei Hattori showed age-related change in body proportion in Japanese child using a Body Proportion Method. He analysed information about body proportion changes during adolescence in Japanese both in average and in individual growth by using longitudinal data from the first grade of elementary school through the 3rd grade of high school.(44) The data were extracted from serial annual school health records. The study focused on lower body-upper body segment ratio (LUR). In average growth, the mean values of the LUR at every age group constantly increased from 6.5 years of age and reached peak value and then decreased to the terminal age in both sexes. Ages at the maximum LUR were 13.5 years of age in boys and 12.5 years of age in girls, respectively. Almost all correlation coefficients between the LUR at the terminal age with the LURs at the other ages were significantly higher in girls than in boys. Age changes of the correlation coefficients showed similar patterns in both sexes. However, the correlation coefficients increased sharply in boys compared with girls. These results suggested that the body proportion in girls should approach the terminal body proportion earlier than that in boys. The LUR increased gradually and reached the maximum value during adolescence in average growth. However, in individual growth, there were several children in both sexes who reached the maximum LUR at 6.5 years of age and after that the value fluctuated. There was a wide variation in age change of body proportion in both sexes. Using a Body Proportion Chart (45) for each individual, we could observe simultaneously age changes of stature, sitting height, lower limb length and sitting height besides the LUR for each individual, and individual variation of age change of the body proportion could become clearer.

Barry Bogin and Dejana Nikitovic (46) showed that sexual size dimorphism, the difference in height between males

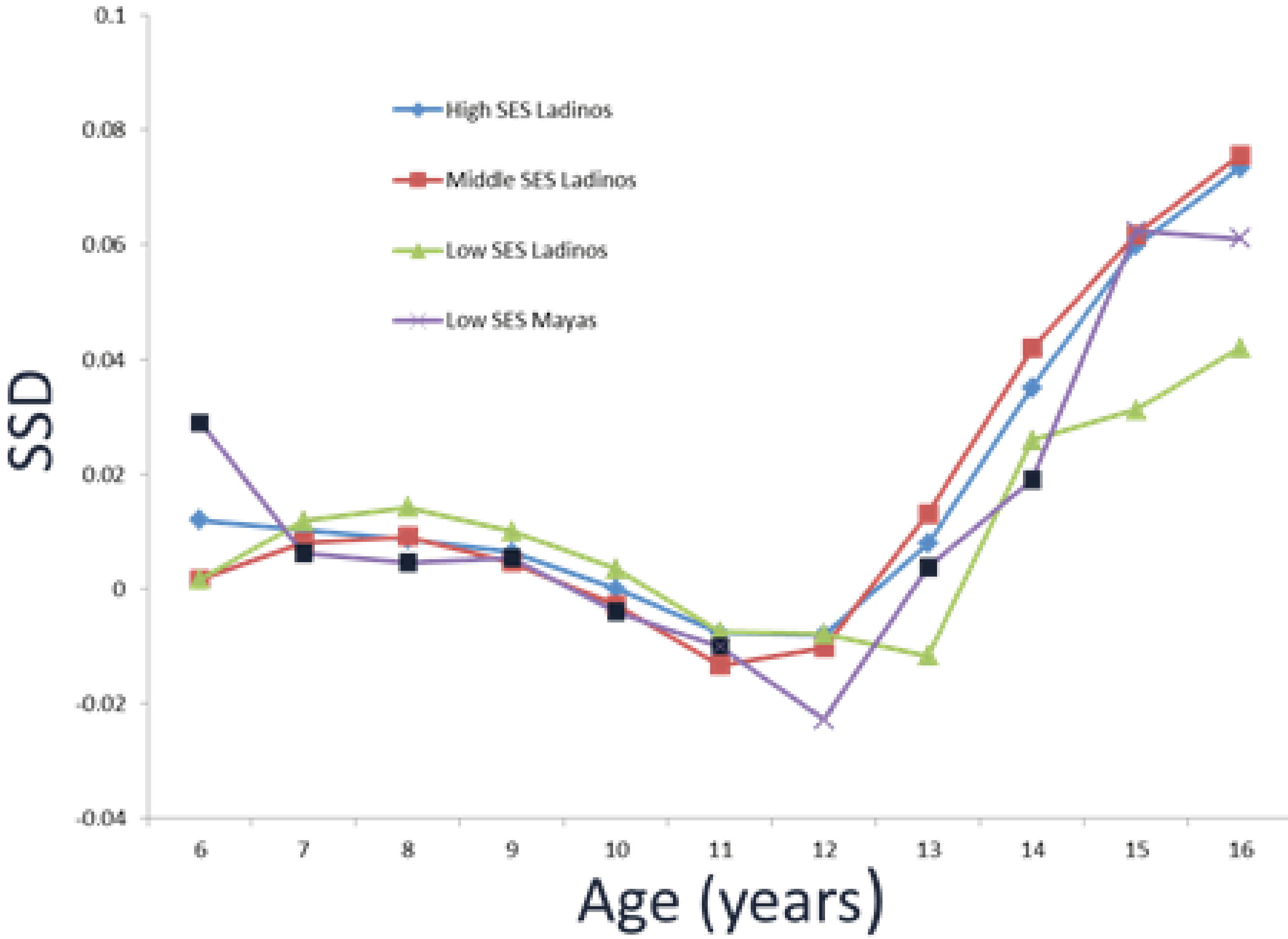

Figure 5: *Sexual size dimorphism (SSD) values differed between ethnic groups*

and females of the same species, may be used as a measure of environmental quality in Guatemalan children. Human growth data from Guatemalan school children (6 to 16.99 years of age) were analyzed to test the hypothesis that the degree of sexual size dimorphism (SSD) in height is greater for children and adolescents living under better overall environmental quality. The study sample consisted of two major Guatemalan ethnic groups, Maya and Ladino, distributed into high, middle and low socioeconomic status (SES) groups (data from the Longitudinal Study of Child Development, by the Universidad del Valle de Guatemala). Significance of SSD was tested within each age category for Maya, and Ladinos from high, middle and low SES. Groups were then compared for each age category to determine if the SSD values were significantly different between groups. Ladinos from high and middle SES groups expressed height SSD that was statistically significant for most of the age groups. Ladinos from low SES had significant SSD at only ages 7, 8 and 9 years. Very low SES Maya had no significant differences in SSD. All groups exhibited similar age changes in the pattern of SSD, with a gentle decline in the level of SSD between 6 and 12 years of age and then a more pronounced increase after age 12 years.(Figure 5) Bogin and Nikitovic concluded that age-related changes in the pattern of SSD values during growth may be a human species characteristic, while the amount of SSD at any age is an indicator of environmental quality.

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