

Nutrition and puberty

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Abstract

Nutrition plays an important role in the growth, development and puberty of children. Adequate nutrition is very important for the normal development of the child during the various stages of childhood and into puberty. Unfortunately, we note the spread of fast food and the adoption of wrong methods in feeding the child, such as making them watch TV to motivate them to eat a larger amount of food etc. This has led to the spread of obesity and overweight among children. Overweight or obese children are more likely to enter puberty early. Some evidence suggests that obesity can accelerate the onset of puberty in girls and this is a major reason why girls begin puberty at an earlier age compared to past decades while overweight or obesity may delay the onset of puberty in boys. On the other hand, severe primary or secondary malnutrition also can delay the onset and progression of puberty.

The aim of our article is to shed light on the relation between nutrition and puberty and to focus on the importance of adequate nutrition to create a healthy child with a normal development.

Key words: Nutrition, children, puberty

Introduction

Nutritional status in childhood is very important because it has a profound effect on biological, physical, and psychological development of children. Nutrition can affect as much as 25% of pubertal timing variation. Over-nutrition and obesity seem to trigger pubertal onset. Neonatal shortness and thinness are associated with earlier pubertal maturation [1].

Puberty parameters are mainly, height, weight, Tanner staging and breast development.

Most girls enter puberty between ages 8 and 13 years, while boys enter puberty from age 10 to 15 years. Strong associations were found between all pubertal timing parameters on the one hand and BMI and percentage of body fat on the other hand. Increased consumption of processed, high-fat foods may be blamed for this phenomenon [2,3,4]. Some controversy exists about the effect of obesity on pubertal onset in males. An expert panel reviewing existing American pubertal data from boys in 2005 could not confirm a secular trend in male pubertal timing[5]. National Health and Nutrition Examination Survey III findings reported a mean age of 10.4 years for Caucasian boys entering Tanner stage G2 [6].

Progression of puberty has been shown to be affected by prepubertal body composition in healthy boys and girls in a longitudinal study. Higher prepubertal BMI and fat mass resulted in earlier attainment of pubertal stages. Both clearly predicted the age at peak height velocity (APHV) and puberty duration in both sexes and age at menarche in girls [7,8].

Growth in children

Proper growth is the most important factor in health assessment of children and adolescents. Growth can be presented as an increase in height and an increase in body weight. Postnatal linear growth is controlled by genetic, endocrine and nutrition factors.

Most girls enter puberty between age 8 and 13 years, while boys enter puberty from age 10 to 15 years. For pubertal development and menstrual function in girls, it is essential to achieve a certain minimum weight or percentage of body fat (PBF): the “critical weight hypothesis”(8,9). A secular trend for earlier age at menarche associated with an increase in the prevalence of overweight and obesity has been reported (10). An accelerated growth rate in overweight children accompanied by early appearance of pubertal signs may raise the concern of hormonal abnormalities such as precocious puberty.

Careful assessment of pubertal status and bone age determination are important for growth assessment in children and adolescents. For better sensitivity in the initial assessment and sequential follow-up of nutritional status, body composition evaluation could be considered in routine clinical practice (11).

Nutritional status from fetal to childhood and onset of puberty:

Nutritional imbalances during pregnancy may be implicated in the programming of the fetal metabolism, including the setting of the hypothalamic-pituitary axis(12) on the one hand, and of insulin resistance and body composition on the other hand, which could, in turn, trigger subsequent hormonal changes affecting pubertal timing(13). To date, evidence linking prenatal nutritional imbalances to the timing of puberty is only indirect, using birth weight as a marker of the intrauterine environment. Nutritional factors during pregnancy that have been discussed in relation to an influence on birth weight range from malnourishment(14) to deficiencies in micronutrients vitamin B12, or docosahexaenoic acid intake(15). A recent study has suggested maternal vitamin D status in early pregnancy may play a role in both birth weight and subsequent growth velocity(16). With respect to the timing of puberty, a lower birth weight has been related to an earlier menarche(17,–18). The DONALD Study confirmed this association for other pubertal markers (ATO and APHV) in both boys and girls (21).

It has been suggested that the postnatal nutritional environment will, to some extent, override prenatal nutritional influences (e.g., prepubertal nutritional deprivation will result in delayed sexual maturity, irrespective of prenatal influences) (14). On the other hand, lower birth weight predisposes to rapid weight gain among those who encounter – in contrast to what they had “anticipated” in the uterus – a sufficient or even excessive nutrient supply (mismatch theory) (20). Rapid weight gain during infancy and early childhood has, in turn, repeatedly been linked to a notably earlier onset of menarche(218,–22) and other early and late pubertal

markers.(23,–24) pre- and postnatal genetic/intrauterine and nutritional influences appear to interact; i.e., infants with a lower birth weight and subsequent rapid weight gain during childhood will experience the earliest puberty onset(17,–25).

Nutrition during early life might also play an important role in the timing of puberty. Direct evidence for such a link is largely confined to studies investigating the association of breastfeeding with pubertal timing. Prospective studies have not, however, found an independent association of breastfeeding with age at menarche,(26,–27) ATO, or APHV(21). In line with this is the observation from the DONALD Study that protein intake in early childhood (1–2 years) is not critical for the timing of early and late pubertal markers(28).

Prepubertal attainment of a critical body weight and/or fat mass (FM) has been thought to have a noticeable role in the start of sexual maturation whereas underfeeding and malnutrition in humans has been related to delayed pubertal onset [29,30,31,32]. In a large population-based study done in Sweden, large growth data showed that an increase of one BMI unit between ages 2 and 8 was associated with an average of 0.11 years earlier for peak height velocity. In addition children with higher changes in BMI had significantly earlier timing of pubertal onset. This suggests that over-nutrition in early childhood can result in an earlier onset of puberty in both sexes [33]. Girls with a higher percentage of body fat and BMI at age 5 and 7 had significantly earlier pubertal development at or by age 9. A strong correlation was reported between percentage body fat at age 7 and breast development at age 9 [33,34].

Nutrition–hormone interaction during critical periods of growth plays an essential role in the control and prediction of metabolic adaptation and pubertal development later in life [19]. Rapid early weight gain leads to taller childhood stature and higher insulin-like growth factor I (IGF-I) levels, possibly through early induction of growth hormone (GH) receptor numbers, and such children are also at risk of childhood obesity [35]. In the Avon Longitudinal Study of Parents and Children, rapid infancy weight gain was associated with increased risk of obesity at 5 and 8 years, with evidence of insulin resistance, exaggerated adrenarche and reduced levels of sex hormone binding globulin (SHBG). Theoretically the increased IGF-I and adrenal androgen levels can increase aromatase activity and free sex steroid levels which consequently can early arouse the GnRH pulse generator. Besides, obese infants and children have higher leptin levels with a proven permissive factor in initiating LH pulsatility [36,37,38,12,39].

Obesity and its effect on puberty:

A three years follow-up study of 8–12-year-old pupils in China [41] demonstrated that the incidence of menarche in obese children of all age groups was higher than in the normal-weight group, while the incidence of first spermatorrhea in obese children was lower than that in normal-weight group. Another cohort in Sweden [42]

involving 1901 children defined the pubertal development by childhood pubertal height growth, in which the result suggests that onset of puberty reached for girls/boys was 3.5/2.5 months earlier in the overweight and obese group than the normal-weight and underweight group.

Two included cohort studies [43,53] comprising 788 girls and 776 girls respectively, all showed that girls with a higher BMI at younger age had significantly earlier menarche compared with those with lower BMI, which is consistent with St. George [49] and one case-control study [44] conducted in Korea with 144 girls, demonstrating an inverse association between body fat and age at pubertal onset in girls.

As for the number of girls with menarche, the pooled estimates showed that obesity is a risk factor for early menarche, which was in agreement with Frisch [45], who proposed that the onset of the female adolescent growth spurt and menarche require a critical weight of 47.8 kg, and that increased body fat can lead to early height spurt start age and menarche age in puberty [45,46].

Only one cohort [52] studies have evaluated the association between obesity and the timing of genitalia development in boys in our systematic review, which showed that boys with higher BMI trajectory were more likely to be later mature compared with lower BMI trajectory, which is consistent with cross-sectional studies conducted by Lee [50] and Wang [51], where boys with a higher BMI were more likely to be classified as late maturers. However, another cohort based on 1060 boys [47] reported that BMI-for-age z score at 5 years were positively associated with pubic hair development, which is consistent with the results in girls. It is hard to draw a definite conclusion that obesity led to early puberty timing in boys due to the limited number of studies with small sample size in this meta-analysis. Compared with the study of girls, there are few studies on boys; the reason may be that data can be even more difficult to interpret in boys considering that early staging of genitalia and subsequent progression through puberty (without assessment of testicular volume) is more subjective, with no easily identified event like menarche in girls [48,40].

Malnutrition

Under-nutrition, chronic diseases and pubertal growth: Under-nutrition is the most important cause of growth retardation worldwide. Poverty in the poor countries and self-induced food restriction in the rich countries or malabsorption and chronic systemic

diseases are the main causes. Primary or secondary malnutrition leads to serious consequences including impaired growth, osteopenia, anemia, and different syndromes caused by deficiency of vitamins, minerals, essential fatty acids and amino acids, and trace elements [54,55,56,57].

Chronic primary malnutrition during childhood modulates the timing of adolescent sexual development in both sexes and is associated with later age of menarche (as well as secondary amenorrhea) [57,58,59].

Patients suffering from secondary malnutrition due to chronic diseases also have delayed onset of puberty and a reduced pubertal growth spurt. Although the etiology of abnormal puberty in these patients is multifactorial, nutritional deficiency largely contributes to their growth and pubertal delay [60,61]. Insufficient food supply due to decreased appetite, eating disorders and/or malabsorption of nutrients can be observed in these patients. Moreover, increased energy expenditure is another mechanism of hastening malnutrition in these children [62]. More specific factors due to the disease itself may be involved in growth and puberty disorders. Abnormalities of the growth hormone (GH-IGF-1) axis and gonadotrophin secretion have been described in patients with chronic renal failure, cystic fibrosis and Crohn's disease [63,64,65].

More recently, it has been shown that cytokines produced during chronic diseases such as juvenile idiopathic arthritis and CF may affect the GH-IGF-1 axis. The associated medication, namely corticosteroids, which are often given to these patients, also contribute to delayed puberty and poor pubertal growth [66,67].

Endocrine disruptor (EDs) and pubertal development: EDs accumulate in the environment in the long term and are introduced into the human body through water, air, foodstuffs, or through equipment used in the office and home. Human studies have shown that several EDs including DDT/dichlorodiphenyldichloroethylene (DDE), PCBs, polybrominated biphenyls (PBB), hexachlorobenzene, endosulfan, dioxins, heavy metals and phthalates affect puberty in humans. A significant relationship has been found between intrauterine exposure to high doses of PBB pesticides and early thelarche and pubarche in girls. In addition, an association between serum DDT/DDE concentrations and early menarche was reported in textile workers. Exposure to phthalate esters (used as plastic softeners and in some cosmetic products, shampoo, and perfumes) has been linked with early thelarche. A bisphenol A (BPA) (found in huge amounts in baby feeding bottles), has also been suggested to have estrogenic effects causing precocious puberty. Heavy metal exposure especially to lead was associated with delayed pubarche and menarche. Avoiding different methods of exposure to these EDs should be enforced to avoid abnormalities of pubertal development and reproduction [68,69,70,71].

Conclusion

In summary, nutritional condition can affect pubertal development and we will outline it in a few points:

- Increased adiposity during childhood, advances puberty in girl and delays puberty in boys.
- Nutrition during early life might also play an important role in the timing of puberty.
- Rapid growth during infancy was related to early pubertal maturation
- Higher prepubertal BMI and fat mass resulted in earlier attainment of pubertal stages.
- Malnutrition during childhood modulates the timing of adolescent sexual development in both sexes.
- Likelihood that timing of puberty (menarche) may be set in utero or early in life, even though it can be modified by changes in nutrition, body size and composition in childhood.

References

1. Karlberg J. Secular trends in pubertal development. *Horm Res.* 2002;57(Suppl 2):S19–30. [PubMed] [Google Scholar]
2. Biro FM, Greenspan LC, Galvez MP, Pinney SM, Teitelbaum S, Windham GC, et al. Onset of breast development in a longitudinal cohort. *Pediatrics.* 2013;132:1019–27. [PMC free article] [PubMed] [Google Scholar]
3. Castilho SD, Pinheiro CD, Bento CA, Barros-Filho Ade A, Cocetti M. Secular trends in age at menarche in relation to body mass index. *Arq Bras Endocrinol Metab.* 2012;56:195–200. [PubMed] [Google Scholar]
4. Huang B, Biro FM, Dorn LD. Determination of relative timing of pubertal maturation through ordinal logistic modeling: Evaluation of growth and timing parameters. *J Adolesc Health.* 2009;45:383–8. [PMC free article] [PubMed] [Google Scholar]
5. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. Full report. [Last accessed on 2012 Oct 02]. Available from: http://www.nhlbi.nih.gov/guidelines/cvd_ped/peds_guidelines_full.pdf. [PMC free article] [PubMed]
6. Buyken AE, Bolzenius K, Karaolis-Danckert N, Günther AL, Kroke A. Body composition trajectories into adolescence according to age at pubertal growth spurt. *Am J Hum Biol.* 2011;23:216–24. [PubMed] [Google Scholar]
7. Tinggaard J, Mieritz MG, Sørensen K, Mouritsen A, Hagen CP, Aksglaede L, et al. The physiology and timing of male puberty. *Curr Opin Endocrinol Diabetes Obes.* 2012;19:197–203. [PubMed] [Google Scholar]
8. Kaplowitz PB. Link between body fat and the timing of puberty. *Pediatrics.* 2008;121(Suppl 3):S208–17. doi: 10.1542/peds.2007-1813F. [PubMed] [CrossRef] [Google Scholar]
9. Frisch RE, Revelle R. Height and weight at menarche and a hypothesis of menarche. *Arch Dis Child.* 1971;46:695–701. doi: 10.1136/adc.46.249.695. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
10. Euling SY, Herman-Giddens ME, Lee PA, Selevan SG, Juul A, Sørensen TI, et al. Examination of US puberty-timing data from 1940 to 1994 for secular trends: panel findings. *Pediatrics.* 2008;121(Suppl 3):S172–91. doi: 10.1542/peds.2007-1813D. [PubMed] [CrossRef] [Google Scholar]
11. Thibault R, Pichard C. The evaluation of body composition: a useful tool for clinical practice. *Ann Nutr*
12. Ud Din Z, Emmett P, Steer C, Emond A. Growth outcomes of weight faltering in infancy in ALSPAC. *Pediatrics.* 2013;131:e843–9. [PubMed] [Google Scholar]
13. Dunger DB, Ahmed ML, Ong KK. Early and late weight gain and the timing of puberty. *Mol Cell Endocrinol.* 2006;254–255:140–145. Google Scholar Crossref Search ADS PubMed
14. Mishra GD, Cooper R, Tom SE, et al. Early life circumstances and their impact on menarche and menopause. *Womens Health (Lond Engl).* 2009;5:175–190. Google Scholar Crossref Search ADS
15. Muthayya S. Maternal nutrition & low birth weight – what is really important? *Indian J Med Res.* 2009;130:600–608. Google Scholar PubMed OpenURL Placeholder Text
16. Leffelaar ER, Vrijkotte TG, van Eijsden M. Maternal early pregnancy vitamin D status in relation to fetal and neonatal growth: results of the multi-ethnic Amsterdam Born Children and their development cohort. *Br J Nutr.* 2010;104:108–117. Google Scholar Crossref Search ADS PubMed
17. Cooper C, Kuh D, Egger P, et al. Childhood growth and age at menarche. *Br J Obstet Gynaecol.* 1996;103:814–817. Google Scholar Crossref Search ADS PubMed Metab. 2012;60:6–16. doi: 10.1159/000334879. [PubMed] [CrossRef] [Google Scholar]
18. Terry MB, Ferris JS, Tehranifar P, et al. Birth weight, postnatal growth, and age at menarche. *Am J Epidemiol.* 2009;170:72–79. Google Scholar Crossref Search ADS PubMed
19. O'Connor DM, Blache D, Hoggard N, Brookes E, Wooding FB, Fowden AL, et al. Developmental control of plasma leptin and adipose leptin messenger ribonucleic acid in the ovine fetus during late gestation: Role of glucocorticoids and thyroid hormones. *Endocrinology.* 2007;148:3750–7. [PubMed] [Google Scholar]
20. Gluckman PD, Hanson MA. Evolution, development and timing of puberty. *Trends Endocrinol Metab.* 2006;17:7–12. Google Scholar Crossref Search ADS PubMed
21. Karaolis-Danckert N, Buyken AE, Sonntag A, et al. Birth and early life influences on the timing of puberty onset: results from the DONALD (Dortmund Nutritional and Anthropometric Longitudinally Designed) Study. *Am J Clin Nutr.* 2009;90:1559–1565. Google Scholar Crossref Search ADS PubMed
22. dos Santos Silva I, De Stavola BL, Mann V, et al. Prenatal factors, childhood growth trajectories and age at menarche. *Int J Epidemiol.* 2002;31:405–412. Google Scholar Crossref Search ADS PubMed
23. Boyne MS, Thame M, Osmond C, et al. Growth, body composition, and the onset of puberty: longitudinal observations in Afro-Caribbean children. *J Clin Endocrinol Metab.* 2010;95:3194–3200. Google Scholar Crossref Search ADS

24. Lee JM, Appugliese D, Kaciroti N, et al., Weight status in young girls and the onset of puberty. *Pediatrics*. 2007;119:e624–e630. Google Scholar Crossref Search ADS PubMed
25. Ong KK, Potaun N, Petry CJ, et al. Opposing influences of prenatal and postnatal weight gain on adrenarche in normal boys and girls. *J Clin Endocrinol Metab*. 2004;89:2647–2651. Google Scholar Crossref Search ADS PubMed
26. Merzenich H, Boeing H, Wahrendorf J. Dietary fat and sports activity as determinants for age at menarche. *Am J Epidemiol*. 1993;138:217–224. Google Scholar Crossref Search ADS PubMed
27. Blell M, Pollard TM, Pearce MS. Predictors of age at menarche in the Newcastle Thousand Families Study. *J Biosoc Sci*. 2008;40:563–575. Google Scholar Crossref Search ADS PubMed
28. Günther AL, Karaolis-Danckert N, Kroke A, et al. Dietary protein intake throughout childhood is associated with the timing of puberty. *J Nutr*. 2010;140:565–571. Google Scholar Crossref Search ADS PubMed
29. Dewey KG, Peerson JM, Brown KH, Krebs NF, Michaelsen KF, Persson LA, et al. Growth of breast-fed infants deviates from current reference data: A pooled analysis of US, Canadian, and European data sets. *Pediatrics*. 1995;96:495–503. [PubMed] [Google Scholar]
30. Bluher S, Mantzoros CS. Leptin in reproduction. *Curr Opin Endocrinol Diabetes Obes*. 2007;14:458–64. [PubMed] [Google Scholar]
31. He Q, Karlberg J. BMI gain in childhood and its association with height gain, timing of puberty, and final height. *Pediatr Res*. 2001;49:244–51. [PubMed] [Google Scholar]
32. Davison KK, Susman EJ, Birch LL. Percent body fat at age 5 predicts earlier pubertal development among girls at age 9. *Pediatrics*. 2003;111(4 pt 1):815–21. [PMC free article] [PubMed] [Google Scholar]
33. Lee JM, Appugliese D, Kaciroti N, Corwyn RF, Bradley RH, Lumeng JC. Weight status in young girls and the onset of puberty. *Pediatrics*. 2007;119:e624–30. [PubMed] [Google Scholar]
34. Tanner JM. Normal growth and techniques of growth assessment. *Clin Endocrinol Metab*. 1986;15:411–51. [PubMed] [Google Scholar]
35. Riumallo J, Durnin JV. Changes in body composition in adolescent boys. *Eur J Clin Nutr*. 1988;42:107–12. [PubMed] [Google Scholar]
36. Fraser A, Macdonald-Wallis C, Tilling K, Boyd A, Golding J, Davey Smith G, et al. Cohort Profile: The Avon Longitudinal Study of Parents and Children: ALSPAC mothers cohort. *Int J Epidemiol*. 2013;42:97–110. [PMC free article] [PubMed] [Google Scholar]
37. Marcovecchio ML, Chiarelli F. Obesity and growth during childhood and puberty. *World Rev Nutr Diet*. 2013;106:135–41. [PubMed] [Google Scholar]
38. Reinehr T, de Sousa G, Wabitsch M. Relationships of IGF-I and androgens to skeletal maturation in obese children and adolescents. *J Pediatr Endocrinol Metab*. 2006;19:1133–40. [PubMed] [Google Scholar]
39. Mann DR, Johnson AO, Gimpel T, Castracane VD. Changes in circulating leptin, leptin receptor, and gonadal hormones from infancy until advanced age in humans. *J Clin Endocrinol Metab*. 2003;88:3339–45. [PubMed] [Google Scholar]
40. Nielsen C.T., Skakkebaek N.E., Richardson D.W., Darling J.A., Hunter W.M., Jørgensen M., Nielsen A., Ingerslev O., Keiding N., Müller J. Onset of the release of spermatozoa (spermarche) in boys in relation to age, testicular growth, pubic hair, and height. *J Clin. Endocrinol. Metab*. 1986;62:532–535. doi: 10.1210/jcem-62-3-532. [PubMed] [CrossRef] [Google Scholar]
41. Qiang M., Sun M., Liu Z., Xing Y., Zhao S. Effects of childhood obesity on early puberty: A follow-up study. *Chin. J. Publ. Health*. 1997;13:409–410. [Google Scholar]
42. Holmgren A., Niklasson A., Nierop A.F., Gelerander L., Aronson A.S., Sjöberg A., Lissner L., Albertsson-Wikland K. Pubertal height gain is inversely related to peak BMI in childhood. *Pediatr. Res*. 2017;81:448–454. doi: 10.1038/pr.2016.253. [PubMed] [CrossRef] [Google Scholar]
43. Flom J.D., Cohn B.A., Tehranifar P., Houghton L.C., Wei Y., Protacio A., Cirillo P., Michels K.B., Terry M.B. Earlier age at menarche in girls with rapid early life growth: Cohort and within sibling analyses. *Ann. Epidemiol*. 2017;27:187–193. doi: 10.1016/j.annepidem.2017.01.004. [PubMed] [CrossRef] [Google Scholar]
44. Oh C.M., Oh I.H., Choi K.S., Choe B.K., Yoon T.Y., Choi J.M. Relationship between body mass index and early menarche of adolescent girls in Seoul. *J. Prev. Med. Public Health*. 2012;45:227–234. doi: 10.3961/jpmph.2012.45.4.227. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
45. Frisch R.E., Revelle R. Height and weight at menarche and a hypothesis of critical body weights and adolescent events. *Science*. 1970;169:397–399. doi: 10.1126/science.169.3943.397. [PubMed] [CrossRef] [Google Scholar]
46. Frisch R.E., Revelle R. The height and weight of girls and boys at the time of initiation of the adolescent growth spurt in height and weight and the relationship to menarche. *J. Hum. Biol*. 1971;43:140–159. [PubMed] [Google Scholar]
47. Lundeen E.A., Norris S.A., Martorell R., Suchdev P.S., Mehta N.K., Richter L.M., Stein A.D. Early Life Growth Predicts Pubertal Development in South African Adolescents. *J. Nutr*. 2016;146:622–629. doi: 10.3945/jn.115.222000. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
48. Ahmed M.L., Ong K.K., Dunger D.B. Childhood obesity and the timing of puberty. *J. Trends Endocrinol. Metab*. 2009;20:237–242. doi: 10.1016/j.tem.2009.02.004. [PubMed] [CrossRef] [Google Scholar]
49. St. George I.M., Williams S., Silva P.A. Body size and the menarche: The Dunedin Study. *J. Adolesc. Health*. 1994;15:573–576. doi: 10.1016/1054-139X(94)90141-O. [PubMed] [CrossRef] [Google Scholar]
50. Lee J.M., Wasserman R., Kaciroti N., Gebremariam A., Steffes J., Dowshen S., Harris D., Serwint J., Abney D., Smitherman L., et al. Timing of Puberty in Overweight Versus Obese Boys. *Pediatrics*. 2016;137:e20150164. doi: 10.1542/peds.2015-0164. [PubMed] [CrossRef] [Google Scholar]

51. Wang Y. Is obesity associated with early sexual maturation? A comparison of the association in American boys versus girls. *J. Pediatrics*. 2002;110:903–910. doi: 10.1542/peds.110.5.903. [PubMed] [CrossRef] [Google Scholar]
52. Lee J.M., Kaciroti N., Appugliese D., Corwyn R.F., Bradley R.H., Lumeng J.C. Body mass index and timing of pubertal initiation in boys. *Arch. Pediatr. Adolesc. Med.* 2010;164:139–144. doi: 10.1001/archpediatrics.2009.258. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
53. Sloboda D.M., Hart R., Doherty D.A., Pennell C.E., Hickey M. Age at menarche: Influences of prenatal and postnatal growth. *J. Clin. Endocrinol. Metab.* 2007;92:46–50. doi: 10.1210/jc.2006-1378. [PubMed] [CrossRef] [Google Scholar]
54. Burt Solorzano CM, McCartney CR. Obesity and the pubertal transition in girls and boys. *Reproduction*. 2010;140:399–410. [PMC free article] [PubMed] [Google Scholar]
55. Rogol AD, Roemmich JN, Clark PA. Growth at puberty. *J Adolescent Health*. 2002;31:192–200. [PubMed] [Google Scholar]
56. Epstein LH, Wing RR, Valaski A. Childhood obesity. *Pediatr Clin North Am.* 1985;32:363–79. [PubMed] [Google Scholar]
57. Forbes GB. Influence of nutrition. In: Forbes GB, editor. *Human body composition: Growth, aging, nutrition and activity*. New York: Springer-Verlag; 1987. pp. 209–47. [Google Scholar]
58. Kulin HE, Bwibo N, Mutie D, Santner S. The effect of chronic childhood malnutrition on pubertal growth and development. *Am J Clin Nutr.* 1982;36:527–36. [PubMed] [Google Scholar]
59. Sogbanmu MO, Aregbesola YA. Menarchal age in Nigerian schoolgirls: Its relationship to their height, weight and menstrual profile. *Int J Gynaecol Obstet.* 1979;16:39–40. [PubMed] [Google Scholar]
60. Satyanarayana K, Nadamuni Naidu A, Narasinga Rao BS. Adolescent growth spurt among rural Indian boys in relation to their nutritional status in early childhood. *An Hum Biol.* 1980;7:359–65. [PubMed] [Google Scholar]
61. Simon D. Puberty in chronically diseased patients. *Horm Res.* 2002;57(Suppl 2):S53–6. [PubMed] [Google Scholar]
62. Arrigo T, Rulli I, Sferlazzas C, De Luca F. Pubertal development in cystic fibrosis: An overview. *J Pediatr Endocrinol Metab.* 2000;16(Suppl 2):S267–70. [PubMed] [Google Scholar]
63. Utaka S, Avesani CM, Draibe SA, Kamimura MA, Andreoni S, Cuppari L. Inflammation is associated with increased energy expenditure in patients with chronic kidney disease. *Am J Clin Nutr.* 2005;82:801–5. [PubMed] [Google Scholar]
64. Street ME, Ziveri MA, Spaggiari C, Viani I, Volta C, Grzincich GL, et al. Inflammation is a modulator of the insulin-like growth factor (IGF)/IGF-binding protein system inducing reduced bioactivity of IGFs in cystic fibrosis. *Eur J Endocrinol.* 2006;154:47–52. [PubMed] [Google Scholar]
65. Gianotti L, Lanfranco F, Ramunni J, Destefanis S, Ghigo E, Arvat E. GH/IGF-I axis in anorexia nervosa. *Eat Weight Disord.* 2002;7:94–105. [PubMed] [Google Scholar]
66. Tomova A, Makker K, Kirilov G, Agarwal A, Kumanov P. Disturbances in gonadal axis in women with anorexia nervosa. *Eat Weight Disord.* 2007;12:e92–7. [PubMed] [Google Scholar]
67. AUWong SC, Macrae VE, McGrogan P, Ahmed SF. The role of pro-inflammatory cytokines in inflammatory bowel disease growth retardation. *SOJ Pediatr Gastroenterol Nutr.* 2006;43:144. [PubMed] [Google Scholar]
68. Giannini C, Mohn A, Chiarelli F. Growth abnormalities in children with type 1 diabetes, juvenile chronic arthritis, and asthma. *Int J Endocrinol* 2014. 2014 265954. [PMC free article] [PubMed] [Google Scholar]
69. Gladen BC, Ragan NB, Rogan WJ. Pubertal growth and development and prenatal and lactational exposure to polychlorinated biphenyls and dichlorodiphenyl dichloroethene. *J Pediatr.* 2000;136:490–6. [PubMed] [Google Scholar]
70. Ouyang F, Perry MJ, Venners SA, Chen C, Wang B, Yang F, et al. Serum DDT, age at menarche, and abnormal menstrual cycle length. *Occup Environ Med.* 2005;62:878–84. [PMC free article] [PubMed] [Google Scholar]
71. Özen S, Darcan S. Effects of environmental endocrine disruptors on pubertal development. *J Clin Res Pediatr Endocrinol.* 2011;3:1–6. [PMC free article] [PubMed] [Google Scholar]