NUTRITION REVIEWS 70 YEARS 1942-2012

Lead Article

Beyond overweight: nutrition as an important lifestyle factor influencing timing of puberty

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Early onset of puberty may confer adverse health consequences. Thus, modifiable factors influencing the timing of puberty are of public health interest. Childhood overweight as a factor in the earlier onset of menarche has been supported by prospective evidence; nonetheless, its overall contribution may have been overemphasized, since secular trends toward a younger age at menarche have not been a universal finding during the recent obesity epidemic. Current observational studies suggest notable associations between dietary intakes and pubertal timing beyond contributions to an energy imbalance: children with the highest intakes of vegetable protein or animal protein experience pubertal onset up to 7 months later or 7 months earlier, respectively. Furthermore, girls with high isoflavone intakes may experience the onset of breast development and peak height velocity approximately 7–8 months later. These effect sizes are on the order of those observed for potentially neuroactive steroid hormones. Thus, dietary patterns characterized by higher intakes of vegetable protein and isoflavones and lower intakes of animal protein may contribute to a lower risk of breast cancer or a lower total mortality.

INTRODUCTION

Early onset of puberty is considered an intermediary factor on the life-course path to a number of diseases in adulthood, including hormone-related cancers,[1–5] a higher risk of all-cause mortality,[6,7] metabolic syndrome, and cardiovascular disease.[8,9] In view of these potentially adverse consequences for health in later life, modifiable factors influencing the timing of puberty are of endocrinological and public health relevance. So far, attention has largely focused on secular increases in childhood overweight and their relevance for secular changes in the timing of puberty. These two secular trends coincide to some extent in the United States and developing countries, but not in most European countries. Hence, nutritional factors beyond overweight in the years preceding pubertal onset as well as during prenatal and early postnatal life may be of interest.

The purpose of this review, therefore, is to briefly compare more recent secular trends in childhood overweight with those in the timing of puberty and to summarize the available evidence regarding the role of other nutritional factors in pubertal timing.

OVERWEIGHT AND THE ONSET OF PUBERTY

Secular trends in overweight and the timing of menarche since 1960–1970

Since the increased prevalence of childhood overweight is a relatively recent finding,[10] this review focuses in

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Key words: hormone, nutrition, timing of puberty

doi:10.1111/j.1753-4887.2011.00461.x

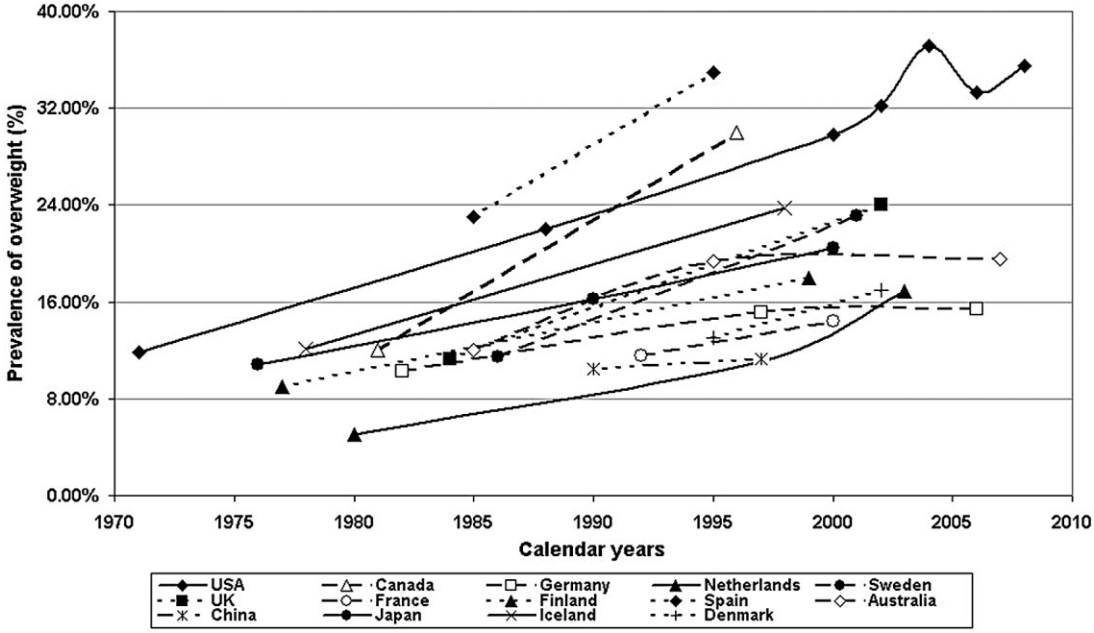

Figure 1 **Secular changes in the prevalence of overweight among children aged 4–12 years (data from[13,120–140]).**

particular on secular trends in childhood overweight and the timing of puberty since 1960–1970. A limiting factor for comparing secular changes in the timing of puberty across different studies lies in the use of different markers to characterize the timing of puberty. Furthermore, to date, no comparable international data are available on secular changes in the timing of puberty, as characterized by the various Tanner stages. Therefore, only evidence relating to age at menarche as an appropriately comparable marker of pubertal timing is presented.

Data from nationally representative surveys of US children shows that the prevalence of overweight increased dramatically from 1976–1980 to 1999–2004.[11–13] A recent review of secular trends in the number of overweight children concluded that the prevalence of childhood overweight has doubled or tripled between the early 1970s and the late 1990s in Australia, Canada, Finland, France, Germany, the United Kingdom, and the United States[14] (Figure 1). In addition, childhood overweight is becoming an increasing problem in many developing countries[14] (Figure 1).

Between the mid-19th and the mid-20th centuries, the average age at menarche decreased remarkably in both Western Europe and in the United States.[15,16] This trend paralleled increases in adult height in most European countries, with rates of around 10–30 mm per decade.[17] Since 1960–1970, i.e., before overweight emerged as a major health concern in children, this decrease in menarcheal age has leveled off, come to a halt, or even been reversed in European countries (Figure 2A). In the Netherlands, the median age at menarche decreased rapidly between 1955 and 1965, followed by a decelerated decrease in 1980.[18] Examination of menarcheal age in Denmark between 1965–1966 and 1982–1983 revealed a decrease;[19] however, a subsequent study in 1996 demonstrated a halt in the secular trend toward earlier menarche.[20] In line with this finding, no secular trend toward earlier menarche was found from a nationwide representative sample of Finnish girls evaluated from 1979 to 1989.[21] Similarly, between 1965 and 1980, the mean age at menarche remained stable in Iceland, at around 13.5 years.[22] Furthermore, in the Netherlands, the median age at menarche remained unchanged from 1980 to 1997.[23] On the other hand, in the United Kingdom, the trend toward a younger age at menarche came to an end in girls in the 1950s, and a subsequently modest increase in the age at menarche was seen.[24] Similarly, in Belgium, the secular trend toward increasing age at menarche seems to have stopped in the early 1960s, even though a modest increase has been observed since then.[25,26] Furthermore, the trend toward a later age of menarche was recorded from 1977 to 1991 in Croatia.[27] In Sweden, a modest increase of 0.1 year per decade in mean age at menarche between 1986 and 2001 has been observed.[28]

Among white girls in the United States, a slight decrease (approximately −0.12 years/decade)[29–31] or a substantial halt[32–36] in the mean age at menarche was observed since the 1960s. It is of interest that this halt or decrease in mean menarcheal age occurred during a period when the prevalence of overweight had just begun to increase.

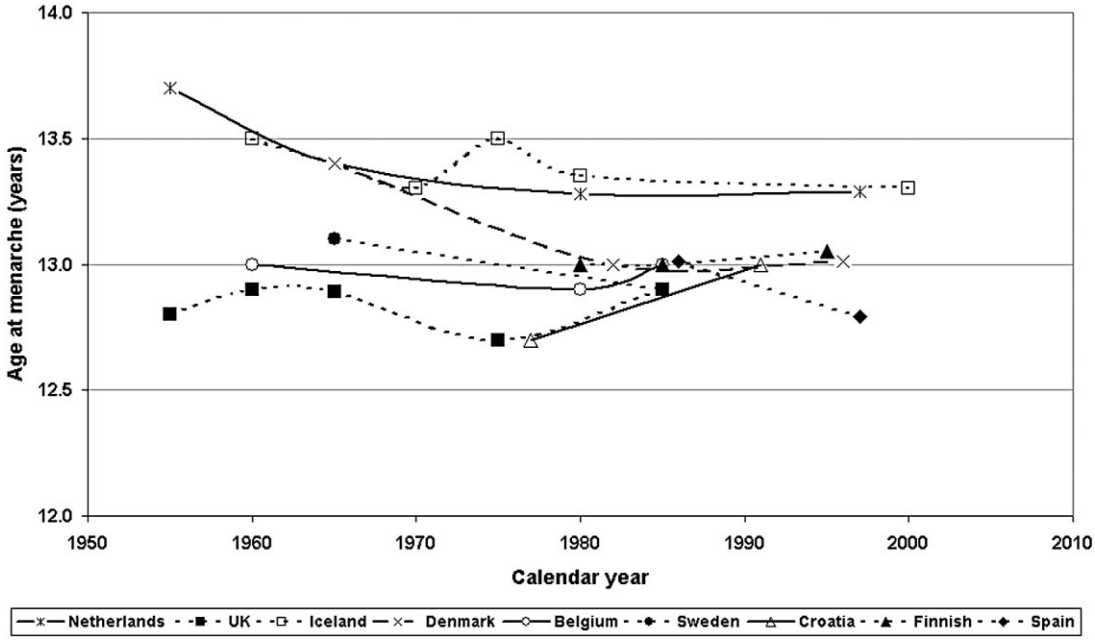

Figure 2A **Secular changes in the age at menarche in countries without consistent decline (data from[18–28,141,142]).**

During the same period, the secular trend toward a decrease in mean menarcheal age in the United States continued in black girls, from 12.48 years in 1963–1970 to 12.14 years in 1988–1994.[30,33] Similarly, secular trends towards an earlier menarcheal age were also observed in the following developing countries: Hong Kong,[37] Japan,[38] India,[39] and China[40] (Figure 2B). Since 1970–1980, the prevalence of childhood overweight has increased markedly in these countries. However, concurrent improvements in living standards, hygiene, nutrition, and health care, which are also considered to result in earlier sexual maturation,[41] suggest that the increased prevalence of childhood overweight may not be the sole contributor to the decreased age of menarche observed in these developing countries.

In conclusion, the commonly implied parallel between an increase in the prevalence of overweight and a secular trend toward earlier timing of puberty is not a

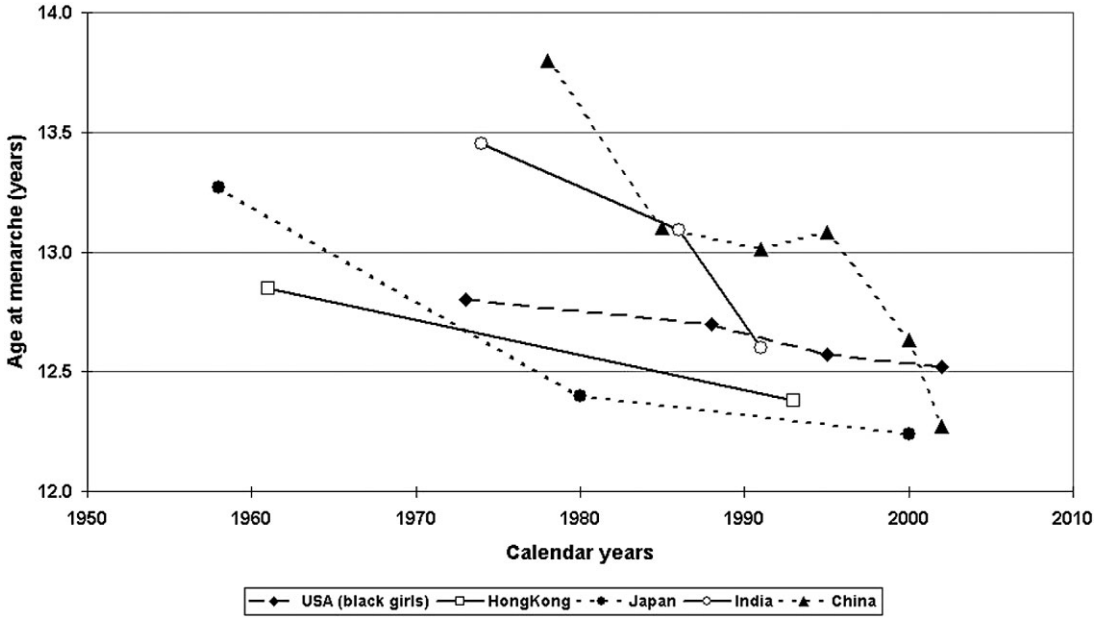

Figure 2B **Secular changes in the age at menarche in countries with consistent decline (data from[29–31,33–39,143,144]).**

universal finding, at least with regard to menarcheal age. This suggests that the contribution of childhood overweight to the timing of puberty may have been somewhat overemphasized.

Prepubertal body composition and the onset of puberty: longitudinal evidence

Conclusions about the contribution of prepubertal body composition to the timing of puberty can only be drawn from longitudinal observational studies in humans. To date, a number of such studies have addressed this issue. However, most were conducted primarily in girls,[8,42–46] and only the onset of menarche, a relatively late stage of pubertal development, was addressed. These studies showed that higher levels of prepubertal body mass in girls are related to an earlier menarche. Table 1 presents all of the longitudinal studies that investigated the potential association of prepubertal body composition with pubertal timing in both boys and girls, or in boys only.

For both boys and girls, five longitudinal analyses[47–51] have demonstrated a role of body composition during prepuberty in the timing of puberty. Two of these studies focused on secondary sexual characteristics to characterize earlier (age at pubarche/thelarche,[48] Tanner stage 2 for genital and breast development[51]) and later (age at menarche,[48] advanced Tanner stages[48,51]) stages of pubertal development. In a retrospective analysis of 2,897 Australian adults, Mamun et al.[51] suggested a positive association between higher body mass index (BMI) at age 5 years and advanced pubertal stages at age 14 years. Using data from 259 Afro-Caribbean children, Boyne et al.[48] indicated that increased BMI/height during childhood was related to earlier age at pubarche, and higher fat mass at age 8 years was associated with a more advanced pubertal development. Two further studies used growth-related markers to determine the timing of puberty and to characterize earlier (age at take-off [ATO][47]) and later (age at peak height velocity [APHV][47,50]) pubertal stages. In 2001, He and Karlberg[50] showed that higher BMI in childhood was related to earlier APHV in 3,650 Swedish children. Similarly, Aksglaede et al.[47] examined 156,835 Danish children and found that higher prepubertal BMI was associated with earlier ATO and APHV. In addition, an analysis of 215 children in the DONALD (DOrtmund Nutritional and Anthropometric Longitudinally Designed) Study by Buyken et al.[49] considered both sexual- and growth-related pubertal markers to characterize earlier (ATO) and later (APHV and age at menarche) stages of pubertal development. In that study, prepubertal body composition in both genders was critical for later pubertal markers (APHV and age at menarche) but not for the initiation of puberty (ATO), i.e., higher prepubertal BMI or fat mass index (FMI) was related to a shorter duration of puberty.

An association between higher prepubertal body mass and earlier timing of puberty was also suggested in two further longitudinal studies that included boys only: a higher prepubertal BMI was associated with an earlier age at voice break (assessed by the same experienced otorhinolaryngologist) in 463 Danish choir boys[52] or with an earlier APHV in a retrospective analysis of 1,520 British men.[53] By contrast, a recent prospective analysis by Lee et al.[54] has shown that boys with a higher BMI z-score trajectory during childhood experience their pubertal onset at a later age, which indicates that the association of prepubertal body mass with pubertal timing might not be the same in boys as it is in girls.

In summary, evidence regarding the association between prepubertal body composition and the timing of puberty consistently suggests that girls with higher body mass have an earlier timing of puberty with respect to both sexual-related maturation markers and the later growth-related markers, whereas the onset of the pubertal growth spurt was not influenced consistently. It is thus not clear whether the influence of prepubertal body composition is more relevant to onset-of-puberty markers in general or to puberty duration. Although, to date, most studies suggested similar associations in girls and boys, it cannot be precluded that the relevance of body composition in prepuberty for pubertal timing might differ for boys.

Potential mechanisms underlying the influences of body composition on the timing of puberty

Body fat mass is an important indicator of nutritional status and is determined by genetic as well as pre- and postnatal environmental factors. Body fat- or body size-related peripheral hormones, such as leptin,[55] insulin,[56] and insulin-like growth factor 1 (IGF-1),[56,57] may mediate the body-composition-dependent variations of pubertal timing in the following ways: deprivation of IGF-1 (e.g., in malnutrition) delays the onset of puberty and slows the tempo of pubertal progression[58]; insulin resistance in obese subjects is associated with compensatory hyperinsulinemia and decreased levels of sex-hormone-binding globulin, resulting in increased sex steroid bioavailability[59]; and while leptin has been proposed to play a permissive role in the acceleration of puberty onset, it does not appear to be the central element or "trigger" in the timing of puberty.[60] In addition, aromatase, an enzyme largely expressed in adipose tissues, converts adrenal androgens to estrogenic sex hormones.[61] Although various determinants of the pubertal process and their network-like interrelations have yet to be identified and

Table 1 **Longitudinal data on prepubertal body composition and the timing of puberty.**

Reference	Study type; no. of participants	Predictors	Outcomes	Covariables	Results	Conclusion
Studies including both boys and girls – multiple pubertal markers evaluated						
Aksglaede et al. (2009)[47]	Prospective study; 156,835 Danish children (135,223 girls and 21,612 boys)	Categories of BMI-SDS at age 7 years (<–0.75, –0.75 to –0.25, –0.25 to +0.25, +0.25 to +0.75, >+0.75)	Pubertal growth spurt (ATO), PHV, puberty duration (PHV-ATO), and no menarche	Unspecified	Higher prepubertal BMI was significantly associated with earlier ATO and earlier age at PHV	The heavier the children were at age 7 years, the earlier they entered puberty. Difference between sexes: no
Boyne et al. (2010)[48]	Prospective study; 259 Afro-Caribbean children (140 girls and 119 boys)	Birth size; height, weight, and BMI at ages 0.5, 2, 8, and 11 years; fat mass and lean mass at ages 8 and 11 years	Age at thelarche and pubarche (Tanner staging), age at menarche, and testicular volume (orchidometry performed every 6 months starting at age 8 years)	Unspecified	Higher BMI from birth to 6 months was associated with earlier pubarche ($r = 0.15$, $P < 0.05$). Higher height from 2 to 8 years was associated with earlier pubarche ($r = 0.15$, $P < 0.05$). Higher fat mass at age 8 years was associated with a more advanced puberty at age 11 years ($P < 0.05$).No association with age at menarche was found	Faster growth throughout childhood, especially with fat mass accretion, is associated with a more advanced puberty. Difference between sexes: no
Buyken et al. (2009)[49]	Prospective study; 215 German children (107 girls and 108 boys)	z-scores of BMI, FMI, and FFMI 1 and 2 years before ATO	ATO, APHV, puberty duration (APHV-ATO), and age at menarche	Birth weight, gestational age, birth year, being firstborn, breastfeeding status, rapid weight gain, maternal overweight status, high maternal educational status, maternal age at birth, and smoking in the household	Girls with higher prepubertal BMI and FMI tended to have an earlier ATO (P for trend = 0.1 and 0.05, respectively). Prepubertal FFMI was not related to ATO. Higher prepubertal BMI and FMI were clearly associated with earlier APHV and shorter puberty duration in both sexes, and with earlier age at menarche in girls (girls: P for trend < 0.0001–0.03; boys: $P = 0.01$–0.046)	Prepubertal body composition in boys and girls may not be critical for the initiation of the pubertal growth spurt but instead affects the progression of pubertal development, which results in earlier attainment of later pubertal stages. Difference between sexes: no

Table 1 **Continued**

Reference	Study type; no. of participants	Predictors	Outcomes	Covariables	Results	Conclusion
Mamun et al. (2009)[51]	Retrospective study; 2,897 Australian adults (1,391 women and 1,506 men)	BMI z-score and overweight at age 5 years	Pubertal stages (Tanner staging of genital and breast development, and pubic hair) at 14 years, BMI and its categories at 21 years, no menarche	Maternal age at pregnancy, maternal educational attainment, birth weight, maternal prepregnancy BMI, maternal tobacco consumption during pregnancy, and breastfeeding Mediators:child's nutritional status, family meal patterns, TV watching and sports involvement at age 14 years	Higher BMI z-score at age 5 years was positively associated with more advanced stages of puberty at age 14 years (OR 1.88, 95%CI 1.53–2.31). Children who were overweight at age 5 years had a more than twofold greater risk to be in Tanner stage 5 at age 14 years than normal-weight children (OR 2.32, 95%CI 1.32–4.05)	Higher BMI and overweight at age 5 years predict more advanced pubertal stages at age 14 years. Difference between sexes: no
Studies including both boys and girls – single pubertal marker evaluated						
He and Karlberg (2001)[50]	Prospective study; 3,650 Swedish children (1,796 girls and 1,854 boys)	BMI at age 2 years, BMI at age 8 years, and BMI change between 2 and 8 years	APHV, no menarche	Midparental height	In both sexes, higher BMI gain in childhood was inversely related to APHV ($-0.13 \leq ß \leq -0.08$, $P < 0.05$). BMI at age 2 years and BMI at age 8 years were inversely associated with APHV for boys only ($ß = -0.05$, $P < 0.05$)	Faster growth in childhood is related to earlier timing of puberty. Difference between sexes: no (consistent difference)
Studies including boys only – single pubertal marker evaluated						
Juul et al. (2007)[52]	Prospective study; 463 Danish choir boys	BMI-SDS at age 8 years	Timing of voice break (assessed by the same experienced otorhinolaryngologist)	Year of admission	Boys with the highest BMI-SDS at age 8 years had an increased risk of early voice break (RR 1.74 [95%CI 1.14–2.65]) compared with boys with the lowest BMI-SDS	Boys with higher prepubertal BMI experienced voice break at an earlier age
Lee et al. (2010)[54]	Prospective study; 401 US boys	BMI trajectory created from BMI z-score at ages 2, 3, 4.5, 7, 9, 9.5, 10.5, and 11.5 years	Pubertal stage at age 11.5 years (Tanner stage)	Income-to-needs ratio at age 2, race	Boys in the highest BMI trajectory had a greater relative risk of later puberty onset compared with boys in the lowest BMI trajectory (RR 2.63 [95%CI 1.05–6.61], $P = 0.04$)	In boys, a higher BMI z-score trajectory during childhood was associated with later puberty onset, which indicated that the relationship between body fat and timing of pubertal onset is not the same in boys as it is in girls
Sandhu et al. (2006)[53]	Retrospective study; 1,520 British men	Prepubertal BMI	APHV	Birth year	A higher prepubertal BMI was related to an earlier APHV (per SD increase in child BMI: −0.31 years, 95%CI −0.23 to −0.39, $P < 0.001$)	Boys with a higher prepubertal BMI experienced puberty at an earlier age

Abbreviations: APHV, age at peak height velocity, ATO, age at take-off; BMI, body mass index; BMI-SDS, body mass index standard deviation score; FFMI, fat-free mass index; FMI, fat mass index; OR, odds ratio; PHV, peak height velocity.

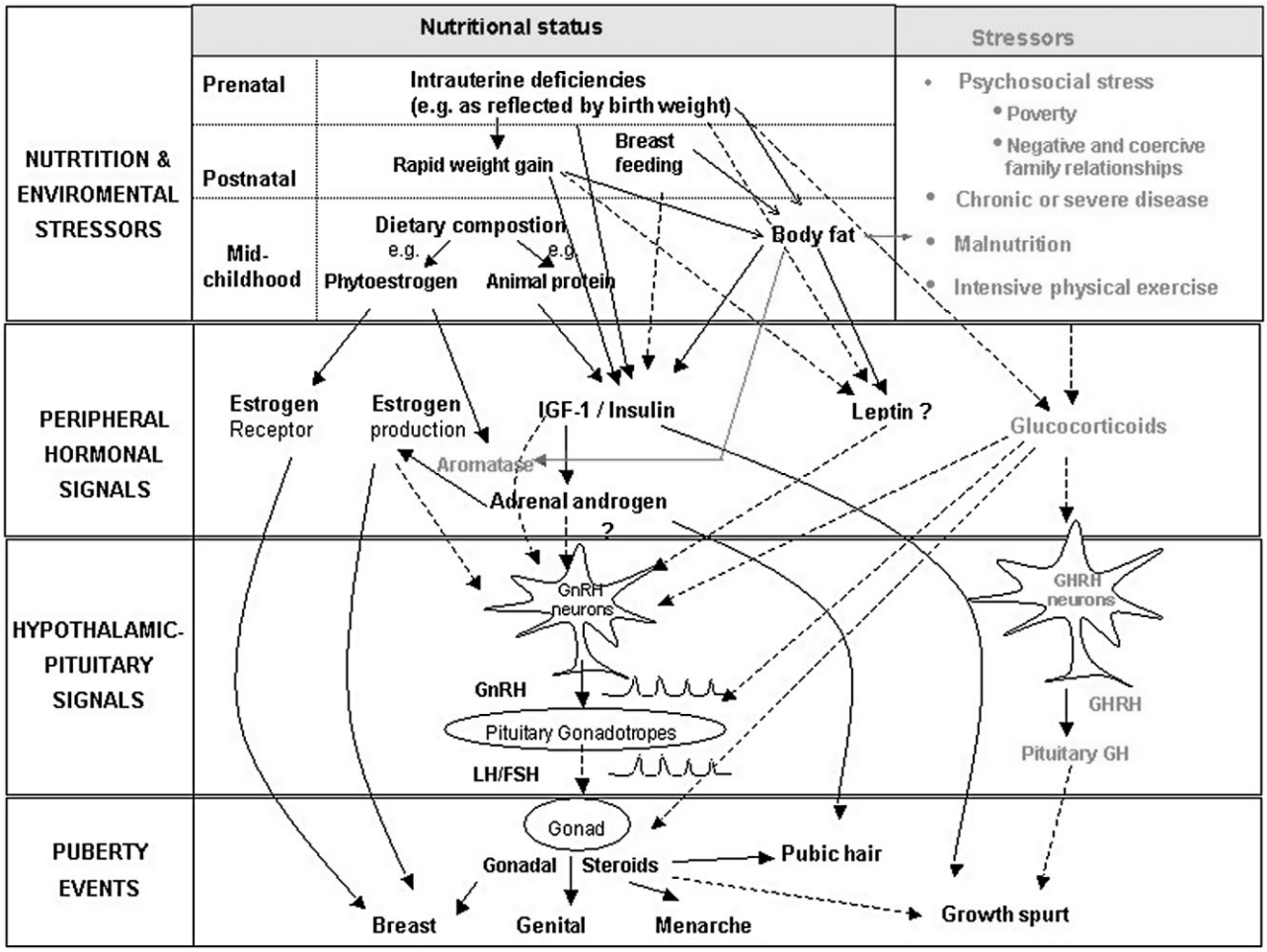

Figure 3 **Schematic illustration of potential pathways via peripheral hormonal and hypothalamic signaling through which nutritional and environmental stressors may influence pubertal markers.**

specified, it is clear that the amplification of pulsatile gonadotropin-releasing hormone (GnRH) secretion in the central nervous system is one of the key elements required for the onset of puberty.[62,63] In vitro and in vivo experiments suggest that IGF-1, insulin, leptin, and sex steroids may exert their effects on the reproductive axis through influences on the secretion and the expression of GnRH by hypothalamic neurons (Figure 3).

NUTRITION AND TIMING OF PUBERTY

Besides body composition, the role of nutrition, which is an important lifestyle factor, in the timing of puberty has been acknowledged increasingly. The influence of nutrition in midchildhood on the onset of puberty has been addressed variously. Furthermore, both pre- and perinatal exposures have been identified as potential determinants of pubertal timing in a number of studies.

Nutrition in midchildhood

To date, a number of prospective observational studies have investigated the potential association of different nutrient/food intakes in midchildhood with the timing of puberty. These studies are summarized in Table 2 and reviewed in the following section. Only four[64–67] of the above studies have prospectively analyzed the relevance of nutrition in midchildhood for the timing of puberty in both boys and girls. The other studies[68–78] were conducted in girls only, and most[70–78] of them focused on only one pubertal marker, the timing of menarche, which represents a relatively late stage of reproductive development. In addition, the prepubertal time window of 9–15 years of age analyzed in many studies[68–77] may have actually encompassed the onset of early pubertal signs.

Energy intake (girls only). Since excess body fat mass results from long-term energy imbalance, the role of

Table 2 **Prospective data on prepubertal nutrition and the timing of puberty.**

Reference	Study type; no. of participants	Predictors	Outcomes	Assessment method	Covariables	Results	Conclusion
Studies including both boys and girls – multiple pubertal markers evaluated							
Cheng et al. (2010)[64]	Prospective study; 222 German children (119 girls and 103 boys) DONALD Study	Nutrient-density-based NQI, and food group and nutrient-based RC-DQI at 2 and 3 years before the onset of pubertal growth spurt	ATO	3-day weighed dietary records	Birth weight, full breastfeeding for at least 4 months, rapid weight gain between birth and 24 months, physical activity (for NQI), maternal overweight, maternal education, smoking status of household, and prepubertal body composition	Children with lower dietary quality indicated by lower NQI scores entered puberty approximately 0.4 years earlier than children with higher NQI scores (ATO in lower and higher NQI categories were 9.2 years [95%CI 9.0–9.4] and 9.6 years [95%CI 9.4–9.9], $P = 0.02$), independently of prepubertal body composition.A similar association of the RC-DQI with ATO was largely explained by differences in baseline energy intakes	Children with lower dietary quality appear to enter puberty at an earlier age, independently of prepubertal body composition
Cheng et al. (2010)[65]	Prospective study; 227 German children (119 girls and 108 boys) DONALD Study	Dietary isoflavones, urinary isoflavones, and dietary fiber at 1 and 2 years before ATO	ATO, APHV, age at menarche/ voice break, pubertal stage for breast (B2) and gonadal (G2) development	3-day weighed dietary records. Urinary measurement: 24-h urine collection	Birth weight, maternal overweight, maternal education, smoking in the household, body composition and z-score of energy intake in childhood	Girls whose isoflavone intake was in the highest tertile experienced their Tanner stage 2 for breast development approximately 0.7 years later and reached PHV approximately 0.6 years later than girls whose intake was in the lowest tertile (age at B2 was 10.7 (10.4–10.9) versus 10.0 (9.7–10.3) years ($P = 0.04$), and age at PHV was 11.9 (11.6–12.2) versus 11.3 (11.0–11.6) years ($P = 0.04$). In boys, no association between dietary isoflavones and pubertal markers was found. In both girls and boys, urinary isoflavones and dietary fiber intakes were not associated with pubertal markers	Girls, but not boys, with higher prepubertal isoflavone intakes appear to enter puberty at a later age. Fiber intake was not relevant for pubertal timing in girls or boys

Günther et al. (2010)[66]	Prospective study; 112 German children (57 girls and 55 boys) DONALD Study	Protein intake, animal protein intake, and vegetable protein intake at ages 1, 1.5–2, 3–4, and 5–6 years; protein intake estimated from 24-h urinary nitrogen excretion at ages 3–4 and 5–6 years	ATO, APHV, age at menarche/ voice break	3-day weighed dietary records. Urinary measurement: 24-h urine collection	Sex, birth weight, breastfeeding, rapid weight gain between birth and age 2 years, maternal overweight, parental education, total energy intake, fat intake, fiber intake, prepubertal FMI SDS	According to the life-course plots, total or animal protein intake at age 5–6 years and vegetable protein intake at age 3–4 years were of particular importance for pubertal timing ($P \leq 0.06$). A higher total or animal protein intake at age 5–6 years was related to an earlier ATO. In the highest tertile (T) of animal protein intake, ATO occurred 0.6 years earlier than in the lowest tertile (T_1: 9.6 [95%CI 9.4–9.9] vs. T_3: 9.0 [95%CI 8.7–9.3] years; $P = 0.003$). Similar findings were seen for APHV ($P = 0.001$) and the age at menarche/ voice break ($P = 0.02$). Children whose dietary intake of vegetable protein was in the highest tertile at age 3–4 years reached their ATO, APHV, and menarche/voice break approximately 0.5 years later than children whose intake was in the lowest tertile ($P = 0.02$–0.04)	Animal and vegetable protein intake in midchildhood might be differentially related to the timing of puberty
Remer et al. (2010)[67]	Prospective study; 109 German children (55 girls and 54 boys) DONALD Study	Animal protein intake and AA 1 and 2 years before ATO	ATO, APHV, age at menarche and age at voice break, age at Tanner stage 2 for breast and genital development (B2/G2), and pubic hair	3-day weighed dietary records. Urinary measurement: 24-h urine collection	Sex, FMI at baseline, total energy intake SDS, urinary volume related to body surface area, gestational age, birth weight, breastfeeding $\geq$ 2 weeks, and maternal overweight	Animal protein intake prior to puberty was negatively associated with ATO and APHV ($P < 0.05$) and tended to be negatively associated with age at menarche/voice break ($P = 0.07$); these associations were independent of AA. Higher AA secretion predicted earlier ages at pubic hair development ($P < 0.0001$) and B2/G2 ($P = 0.009$), as well as a shorter pubertal growth acceleration period ($P = 0.001$), independently of animal protein intake	A higher animal protein intake may be involved independently of AA in an earlier attainment of pubertal growth development

Table 2 **Continued**

Reference	Study type; no. of participants	Predictors	Outcomes	Assessment method	Covariables	Results	Conclusion
Studies including girls only – multiple pubertal markers evaluated							
Berkey et al. [a] (2000)[68]	Prospective study; 67 US girls	Energy intake and intakes of animal protein, vegetable protein, and total fat at ages 1, 2, 3, 4, 5, 6, 7, 8, and 9 years	Age at menarche, APHV, peak height growth velocity	Dietary history interview	Age, energy intake	Girls aged 3–5 years with 1 SD higher vegetable protein (approximately 3 g/day) experienced menarche 0.87 years later ($P < 0.05$). Girls aged 3–5 years with 1 SD higher animal protein (approximately 8 g/day) experienced menarche 0.63 years earlier ($P < 0.05$). Girls aged 1–2 years with 1 SD higher dietary fat intake (approximately 8 g/day) had their APHV 0.63 years earlier ($P < 0.05$)	Intakes of protein and fat in childhood are associated with pubertal timing
de Ridder et al.[a] (1991)[69]	Prospective study; 63 Dutch girls	Energy intake, fiber intake (grain fiber intake, vegetable fiber intake, fruit fiber intake), total protein intake, animal protein intake, vegetable protein intake, carbohydrate intake, and fat intake at ages 10 and 12 years	Breast development stage, plasma concentrations of gonadotropins, and plasma concentrations of estradiol at age 9–13 years (measured twice a year from 1986 to 1987)	7-day food record	Energy intake, polysaccharides, height, and time of 7-day food record	Girls with a lower grain fiber intake at age 10 years had a lower stage of breast development at age 11–12 years ($P < 0.05$). Girls with a lower intake of dietary grain fiber at age 10 years had significantly higher plasma concentrations of gonadotropins and estradiol at age 12–13 years compared with girls with a higher intake of fiber ($P < 0.05$). No association was found between intake of vegetable and fruit fiber and stage of breast development. Girls with a higher vegetable protein intake at age 10 years had a lower stage of breast development at age 11.5 years ($P < 0.05$). Energy intake, total protein intake, dietary fat, or carbohydrate intake were not significantly associated with breast development	Diet rich in vegetable products, especially fiber, may be associated with physical and hormonal sexual maturation

Studies including girls only – age at menarche used as pubertal marker							
Maclure et al.[a] (1991)[72]	Prospective study; 213 US girls	Intakes of total fat, specific fatty acids, cholesterol, protein, sucrose, carbohydrates, fiber, and vitamins at age 10 years	Relative risk of menarche before age 12.5 years	Semiquantitative food frequency questionnaire (parents reported)	Linear regression of the log of nutrient intake on the log of energy intake, and height, weight, and BMI	Age at menarche was not associated with intake of energy or energy-adjusted intake of protein or carbohydrate. Higher intake of saturated fatty acids was associated with later menarche (RR 0.7 [95%CI 0.4–1.2] for highest vs. lowest category, $P = 0.02$). Higher vitamin A intake was associated with earlier age at menarche (RR 1.3 [95%CI 0.7–2.3] for highest vs. lowest category, $P = 0.002$). Higher intake of ω-3 fatty acids was associated with earlier age at menarche (RR 2.7 [95%CI 1.6–4.6] for highest vs. lowest category, $P = 0.008$)	Nutritional factors in childhood are associated with age at menarche
Merzenich et al.[a] (1993)[73]	Prospective study; 261 German girls	Fat intake, protein intake, carbohydrate intake at age 8–15 years	Relative risk of menarche	7-day food record	Energy intake	Increased energy-adjusted fat intake was associated with higher risk of menarche (RR 2.1 [95%CI 1.1–4.0], highest vs. lowest quartile). Energy intake and intakes of carbohydrate and protein were not associated with age at menarche	Fat intake in childhood is associated with age at menarche
Meyer et al.[a] (1990)[74]	Prospective study; 109 Canadian girls	Energy intake, intakes of protein, lipid, and carbohydrate at age 9–12 years	Age at menarche	3-day dietary record (including 1 weekend day)	Age	Dietary energy intake at age 9–12 years was not associated with age at menarche. Intakes of carbohydrate, fat, and protein at age 9–12 years were not associated with age at menarche	Apart from extreme situations, prepubertal diet does not appear to be an important determinant of age at menarche
Moisan et al.[a] (1990a)[75]	Prospective study; 2,299 Canadian girls (911 girls had reached menarche and 1,388 were still premenarcheal at the end of follow-up)	Energy intake, proteins, carbohydrates, lipids, SFA, MUFA, PUFA, cholesterol, calcium, iron, phosphorus, crude fiber, and vitamins A, B6, B12, C, D, E, folacin, niacin, riboflavin, and thiamine at age 10–13 years	Age at menarche	3-day dietary record	Girl's age and the mother's age at the beginning of the study	A higher vitamin C intake at age 10–13 years was related to earlier age at menarche. Dietary fiber and protein intakes were not associated with age at menarche	Diet was not associated with age at menarche

Table 2 **Continued**

Reference	Study type; no. of participants	Predictors	Outcomes	Assessment method	Covariables	Results	Conclusion
Moisan et al.[a] (1990b)[76]	Prospective study; 666 Canadian girls (333 menarcheal girls, 333 premenarcheal girls)	Energy intake, protein, carbohydrates, lipids, SFA, MUFA, PUFA, cholesterol, calcium, iron, phosphorus, crude fiber, and vitamins A, B6, B12, C, D, E, folacin, niacin, riboflavin, and thiamine at age 9.5–12.5 years	Ratio of the odds of having reached menarche in a given quartile of one nutrient to the odds among those in the lowest quartile	3-day dietary record	Age, energy intake	Girls with higher energy intake were likely to experience menarche earlier than those with lower energy intake (OR 1.5 [95% CI 0.9–2.3] for highest vs. lowest quartile). Fiber intake was not associated with age at menarche. Girls with higher MUFA intake were likely to experience menarche later (OR 0.6 [95%CI 0.4–0.9] for highest vs. lowest quartile). Girls with higher dietary vitamin A experienced menarche later (OR 0.5 [95%CI 0.3–0.8] for highest vs. lowest quartile)	Diet in childhood was associated with age at menarche
Petridou et al.[a] (1996)[77]	Prospective study; 345 Greek girls	Total energy intake, intakes of SFA, MUFA, PUFA, protein, and carbohydrates at age 9–16 years	Risk of menarche	Interviewer-administered FFQ	Total energy intake	Girls with higher total energy intake experienced menarche later than girls with lower total energy intake (an increase of 1 SD energy intake (~677 kcal) is the rate ratio 0.87 [95%CI 0.74–1.02]). Energy-adjusted macronutrients were not associated with age at menarche	An alteration of energy balance in childhood could delay age at menarche
Rogers et al. (2010)[78]	Prospective study; 3,298 British girls	Nutrients at ages 3, 7, and 10 years: energy, total fat, SFA, MUFA, PUFA, starch, sugar, total protein, animal protein, vegetable protein, NSP (a measure of fiber intake), iron, calcium, zinc, magnesium, and carotene. Foods at ages 3, 7, and 10 years: intakes of fruit, vegetables, total fish, oily fish, meat, dairy products, soy meat/textured vegetable protein, and legumes, and whether the child ate a vegetarian diet	Age at menarche yes/no at age 12 years 8 months (median age in this cohort)	FFQ at ages 3 and 7 years, and 3-day dietary record at age 10 years	Height and BMI at 7–10 years	After adjustment for body size, the association of higher energy intakes with the early occurrence of menarche was removed. Total and animal protein intakes were positively associated with age at menarche ≤12 years 8 months (OR for 1 SD increase in protein 1.17 [95%CI 1.07–1.28]). Higher PUFA intakes were positively associated with early occurrence of menarche (OR for 1 SD increase in PUFA 1.11 [95%CI 1.02–1.21]). Intakes of magnesium and zinc were associated with the early occurrence of menarche (OR for 1 SD increase in magnesium 1.09 [95%CI 1.00–1.19], for 1 SD increase in Zn 1.10 [95%CI 1.01–1.21]). Meat intake at age 7 years was strongly positively associated with reaching menarche by 12 years 8 months (OR 1.57 [95%CI 1.03–2.37] in the highest vs. the lowest category of meat consumption)	Higher intakes of protein and meat in early to midchildhood may lead to earlier menarche

Kissinger and Sanchez[a] (1987)[70]	Prospective study; 230 white US girls	Nutrients at age 9–15 years: energy intake, carbohydrate, protein, fat, vitamin A, thiamine, riboflavin, niacin, vitamin C, calcium, phosphorus, potassium, iron, and vitamin B12. Food groups at age 9–15 years: 1) meat, poultry, fish, and seafood 2) dairy products 3) meat analogues 4) fresh and canned fruits 5) nuts 6) grains 7) vegetables 8) beans and other legumes 9) candy and popcorn 10) snacks 11) soups and stews 12) salads 13) miscellaneous	Age at menarche	Multiple 24-h recalls	None	A significant association was found between meat intake and age at menarche, resulting in a 6-month earlier age of menarche among meat users compared with vegetarians ($P < 0.025$). Girls whose intake of carbohydrate, thiamine, and iron was in the upper quartile experienced menarche 7–8 months later than those whose intake of these nutrients was in the lowest quartile ($P < 0.05$). Total intake of protein or fat was not associated with age at menarche	A vegetarian dietary lifestyle is an important factor in retarding the onset of menarche
Koo et al.[a] (2002)[71]	Prospective study; 637 Canadian girls	Fiber intake, fat intake, and fatty acids intake at age 6–14 years	Risk of menarche	162-item FFQ	Age at entry, time-dependent age at entry, body weight, birth weight, log of energy intake, maternal age at menarche, and paternal occupational prestige rating	A higher energy-adjusted intake of dietary fiber was associated with a lower risk of (i.e., a later age at) menarche (relative hazard ratio 0.54 [95%CI 0.31–0.94] for highest vs. lowest quartile, $P = 0.027$). A higher energy-adjusted intake of cellulose was associated with a later age at menarche (relative hazard ratio 0.45 [95%CI 0.26–0.76] for highest vs. lowest quartile, $P = 0.009$). Increased intake of energy-adjusted animal fat was inversely associated with menarche (relative hazard ratio 0.52 [95%CI 0.32–0.85] for highest vs. lowest quartile, $P = 0.03$)	Premenarcheal dietary intake can influence age at menarche

Abbreviations: AA, adrenal androgen; APHV, age at peak height velocity; ATO, age at take-off; BMI, body mass index; FFQ, food frequency questionnaire; FMI, fat mass index; MUFA, monounsaturated fatty acids; NQI, nutritional quality index; NSP, a measure of fiber intake; PHV, peak height velocity; PUFA, polyunsaturated fatty acids; RC-DQI, revised children's diet quality index; RR, relative risk; SD, standard deviation; SDS, standard deviation score; SFA, saturated fatty acids.

[a] The time window of diet assessment potentially encompasses the onset of early pubertal signs (e.g., Tanner stage 2).

energy intake has been analyzed in numerous prospective observational studies in girls.[68,69,72–74,76–78]

No association between energy intake in childhood and timing of menarche[68,72–74,78] or stage of breast development[69] was observed in six studies of US and European girls. Furthermore, Moisan et al.[76] reported an association between higher energy intake at age 9.5–12.5 years and earlier age at menarche in 666 Canadian girls, while Petridou et al.[77] found higher energy intake to be related to later menarcheal age in 345 Greece girls aged 9–16 years.

In summary, the available evidence does not suggest a consistent association between energy intake levels in prepuberty and menarcheal age. In addition, due to general methodological problems in assessing energy intake, as well as the inconsistent adjustment for underreporting and body composition, it is difficult to compare these studies.

Fat intake (girls only). Various prospective observational studies in girls have examined whether fat intake, due to its potential influence on estrogen metabolism,[79] is related to age at menarche. Several of these studies[69,70,74,77] found no association, while others[68,71–73,76,78] reported associations between dietary fat intake and age at menarche.

Four studies[68,72,73,78] found higher intakes of total fat or polyunsaturated fatty acids (PUFA) were related to earlier menarcheal age. Using data from 63 girls in the United States, Berkey et al.[68] suggested that total fat intake at age 1–2 years was related to an earlier APHV. Similarly, Merzenich et al.[73] reported that higher levels of total fat intake at age 7–14 years were associated with earlier age at menarche. In addition, Maclure et al.[72] suggested that a higher intake of omega-3 fatty acids at age 10 years was related to earlier menarche in 213 US girls. Similarly, Rogers et al.[78] observed an increased risk of early occurrence of menarche in 3,298 British girls with higher PUFA intakes at ages 3 and 7 years.

By contrast, higher intakes of saturated fatty acids, monounsaturated fatty acids (MUFA), or animal fat were linked to a later age at menarche. Maclure et al.[72] reported that higher intakes of saturated fatty acids in 213 US girls aged 10 years were associated with a decreased risk of early menarche. Similar associations with higher MUFA intake at age 9.5–12.5 years were reported by Moisan et al.[76] in 666 Canadian girls. Furthermore, Koo et al.[71] analyzed data from 637 Canadian girls aged 6–14 years and suggested that higher animal fat intakes were related to a later age at menarche.

Taken together, these findings suggest that dietary fat intake may be implicated in the timing of menarcheal age. However, the pattern with which different fatty acids contribute to pubertal timing is difficult to interpret, and mechanistic explanations are lacking. This may reflect the fact that, in the 1990s, numerous studies analyzed the relevance of dietary fat intakes for various health-relevant outcomes. Emerging evidence on the relevance of prepubertal body composition for pubertal timing thus may have stimulated analyses on the relevance of dietary fat intake for pubertal development despite the absence of specific mechanistic considerations.

Fiber intake (girls and boys). A recent longitudinal study suggests that higher prepubertal estrogen levels predict shorter pubertal growth spurt in both boys and girls.[80] Age at menarche occurred earlier in girls with higher prepubertal estrogen levels.[80] Dietary fiber intake has been proposed to influence pubertal development by reducing the availability of circulating estrogen levels via a number of potential mechanisms. These include the following: 1) a reduced deconjugation of estrogen conjugates,[81] resulting in a reduced uptake of free estrogens via the enterohepatic circulation; 2) increased fecal estrogen excretion by binding of (deconjugated) estrogens[82]; 3) reduced bioavailability of estradiol due to increased hepatic expression of sex hormone-binding globulin[83]; and 4) direct action on the maturation or secretion of the hypothalamus-pituitary-gonad system.[69]

To date, two prospective observational studies in girls[69,71] have reported a delayed menarcheal age in relation to higher fiber intakes in childhood. Koo et al.[71] reported a clear risk reduction of 0.54-fold for early menarche among 637 Canadian girls whose fiber intake at age 6–14 years was in the highest quartile (>25.5 g/day) in comparison to girls with fiber intakes in the lowest quartile (≤18.2 g/day). The major contributors to this association were cellulose and insoluble fiber. Similarly, using data from 63 Dutch girls, de Ridder et al.[69] reported a later age at menarche and later breast development in those with higher intakes of grain fiber at age 10 years. In addition, girls with lower intakes of grain fiber (<5.5 g/day) had higher plasma concentrations of gonadotropins and estradiol compared to girls with higher intakes of grain fiber (<7.7 g/day).

However, three further studies did not confirm these associations. Moisan et al.[75] did not find an association between fiber intakes at age 10–13 years and age at menarche in 2,299 Canadian girls, which was confirmed by a later report from the same group of investigators in a case-control analysis of 666 girls.[76] Using data from the DONALD Study, Cheng et al.[65] analyzed the potential influence of fiber intake on the timing of puberty in 227 German girls and boys using various pubertal markers indicative of both earlier and later stages of pubertal development. These included markers of sexual maturation (Tanner stage 2 for breast development/testicular volume, and age at menarche/voice break) and growth

development (ATO and APHV). Neither total fiber intake nor fiber intake from different sources was related to any pubertal markers in either girls or boys.

These contrasting findings may be related, in part, to the fiber intake levels, which were particularly high in the two studies reporting an association of fiber intake with menarcheal age. On the other hand, since grain fiber is the major source of dietary isoflavones in Western diets,[84] the association of fiber intake – mainly stemming from grains – with the timing of puberty may, to some extent, reflect an effect of dietary isoflavones.

Dietary isoflavone intake (girls and boys). Isoflavones, which are structurally and functionally similar to endogenous estrogens,[85] have been proposed to be relevant for pubertal development thanks to two factors: 1) their inhibitory actions on the activity of aromatase[86] (the rate-limiting enzyme that converts androstenedione and testosterone to estrone and estradiol, respectively[87]) and 17β-hydroxysteroid dehydrogenase[88] (which catalyzes the interconversion of the relatively inactive 17β-keto steroids to active 17β-hydroxyl sex steroids[88]); and 2) their direct interaction with estrogen receptors[89] due to a structure similar to that of estradiol.[85]

To date, evidence for a potential influence of dietary isoflavones on the timing of puberty stems only from a recent analysis of the DONALD Study. Examining data from 227 German girls and boys, Cheng et al.[65] reported that girls ($n = 119$) whose dietary intake of isoflavones was in the highest tertile (≥423 μg/day) experienced their Tanner stage 2 for breast development approximately 0.7 years (~8 months) later and reached their peak height velocity approximately 0.6 years (~7 months) later than girls whose intake was in the lowest tertile (≤22 μg/day), controlling for prepubertal BMI and fiber intake. However, dietary isoflavone intakes were not found to be implicated in the timing of puberty in boys.

While this study has shown a strong association, further studies are needed before firm conclusions on the relevance of dietary isoflavones for the timing of puberty can be drawn. In particular, prospective data that investigate the complex interplay of "nutritional estrogens" and endogenous estrogen levels are warranted.

Protein intake (girls and boys). Due to its stimulatory effect on IGF-1 secretion[90] (Figure 3), animal protein intake during prepuberty may be of relevance. Günther et al.[66] observed that boys and girls aged 5–6 years whose animal protein intake was in the highest tertile experienced their ATO, APHV, and menarche/voice break approximately 0.6 years (~7 months) earlier than boys and girls whose intake was in the lowest tertile. Similarly, Berkey et al.[68] found that 3–5-year-old girls with a 1 standard deviation (SD) higher animal protein intake (approximately 8 g/day) experienced menarche 0.63 years (~7 months) earlier. Furthermore, in 3,298 British girls, the risk of early occurrence of menarche increased by 1.17-fold per 1 SD increase in animal protein intake (approximately 1.1 g/day).[78] Although dietary animal protein intake may increase adrenarchal androgen secretion in children,[91] Remer et al.[67] demonstrated that the association between animal protein intake and ATO, APHV, and menarche/voice break was independent of the effects of adrenal androgens. However, animal protein intake was not associated with age at onset of breast, genital, and pubic hair development,[67] which may be relevantly modulated by the maturation of the hypothalamic-pituitary-adrenal (HPA) axis.[60]

Three studies[66,70,78] have addressed the relevance of animal-protein-contributing food groups. Protein intake from cow milk and dairy products is suggested to stimulate the secretion of IGF-1. [92] Günther et al.[66] found that 5–6-year-old children whose protein intake from cow milk and dairy products was within the highest tertile experienced ATO approximately 0.4 years (~5 months) earlier than children in the lowest tertile. Conversely, Rogers et al. [78] reported that a higher meat intake in childhood was strongly associated with earlier age at menarche, i.e., the risk of early occurrence of menarche was 1.57-fold higher for girls in the category with the highest meat intake (>8 portions/week) than for girls in the lowest category (<4 portions/week). This finding is in line with a previous analysis by Kissinger and Sanchez,[70] who used data from 230 US girls and showed that those in the highest quartile of meat intake reached menarche 6 months earlier than girls in the lowest quartile.

To date, three observational studies have focused on the association of vegetable protein intake in childhood with the timing of puberty in girls[68,69] and in both genders.[66] de Ridder et al.[69] reported an association of higher vegetable protein intake with later breast development in 63 Dutch girls. Berkey et al.[68] suggested that girls aged 3–5 years with a 1-SD higher vegetable protein intake (approximately 3 g/day) experienced menarche 0.87 years (~10 months) later. Similarly, in a recent analysis of the DONALD Study, Günther et al.[66] reported that 3–4-year-old children whose dietary intake of vegetable protein was in the highest tertile reached their ATO, APHV, and menarche/voice break approximately 0.5 years (~6 months) later than children whose intake was in the lowest tertile. Due to the high content of dietary isoflavone or fiber intake in a number of plant foods and the negative association of vegetable protein intake with animal protein intake, studies that analyzed the association of vegetable protein intake in childhood with the timing of puberty may indirectly have addressed the effect of prepubertal dietary isoflavone/fiber/animal protein intake on the timing of puberty.

In summary, current evidence consistently suggests dietary protein intake is relevant for the timing of puberty; i.e., children with a higher vegetable protein intake may experience both earlier and later stages of pubertal development, up to 0.6 years (~7 months) later, while a prepubertal diet rich in animal protein, i.e., milk, dairy products, and/or meat, appears to be related to an earlier pubertal development of up to 0.6 years (~7 months).

Dietary micronutrients (girls only). It has been hypothesized that carotenoids may exert a peripheral antiestrogenic effect, such that they could perhaps interfere with the release of low concentrations of gonadotropins and prolactin.[72] Moreover, lower intakes of vitamin C and β-carotene have been shown to be associated with higher leptin concentrations in children aged 6–14 years,[93] and leptin has been proposed to be a signal for puberty onset (Figure 3).

Using data from 213 girls in the United States, Maclure et al.[72] reported that higher vitamin A intake in girls was related to earlier age at menarche. In contrast, a prospective study of 666 Canadian girls[76] found that higher vitamin A intake was associated with a later age at menarche. In contrast to the finding that lower vitamin C intake is associated with higher leptin concentrations,[93] which may, in turn, predispose to an earlier timing of puberty,[94] Moisan et al.[75] found that lower vitamin C intakes at age 10–13 years were related to a later menarcheal age in 2,299 Canadian girls.

In addition, in 3,298 British girls, higher intakes of magnesium at age 10 years, or of zinc at age 7 years, were related to an earlier menarcheal age.[78] These associations may partly reflect the fact that meat is a good source of bioavailable zinc and, to some degree, of magnesium as well. Finally, Kissinger and Sanchez[70] reported that 230 US girls with higher intakes of thiamine or iron at age 9–15 years had a later menarcheal age.

Taken together, the currently available findings regarding the influence of micronutrients on the timing of puberty are controversial. In particular, possible mechanisms mediating potential associations of micronutrients with the timing of puberty should be unraveled.

Dietary quality (girls and boys). It is conceivable that macronutrients, micronutrients, and/or food groups may influence puberty onset through their combined effects.

To date, the association of overall dietary quality in childhood with the timing of puberty has only been investigated in the DONALD Study,[64] which found higher dietary quality in prepuberty to be associated with later ATO in both boys and girls. In this study, higher dietary quality was defined as adherence to nutrient-specific recommendations; i.e., a higher dietary quality was characterized by a lower intake of total fat and higher intakes of carbohydrates, fiber, and micronutrients. Children with higher dietary quality experienced their pubertal growth spurt approximately 0.4 years (~5 months) later than children with lower dietary quality. This association was observed independently of prepubertal body composition.

In this analysis, overall dietary quality was defined by a dietary quality index, which is an *a priori* dietary pattern created on the basis of previous knowledge.[95] Dietary quality indices do not consider the correlation structure of foods and nutrient intakes. In this context, the statistical method known as reduced rank regression[96] may be worth considering in future analyses, since it would allow the extraction of a food pattern that maximally explains the variation of hormones. Such a pattern can then be evaluated in its ability to predict the timing of pubertal markers. In conclusion, initial prospective observational data from the DONALD Study suggests that dietary quality in childhood is relevant for the timing of puberty.

Nutrition in early life

Breastfeeding – direct evidence. 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,[73,76,97,98] ATO, or APHV.[97] 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.[66]

Birth weight – indirect evidence. Nutritional imbalances during pregnancy may be implicated in the programming of the fetal metabolism, including the setting of the hypothalamic-pituitary axis[45] 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[99] (Figure 3). 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[100] to deficiencies in micronutrients vitamin B_{12}, or docosahexaenoic acid intake.[101] A recent study has suggested maternal vitamin D status in early pregnancy may play a role in both birth weight and subsequent growth velocity.[102] With respect to the timing of puberty, a lower birth weight has been related to an earlier menarche.[45,103–105] The DONALD Study confirmed

this association for other pubertal markers (ATO and APHV) in both boys and girls.[97]

Interactions of pre- and postnatal influences. 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).[100] 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).[106] Rapid weight gain during infancy and early childhood has, in turn, repeatedly been linked to a notably earlier onset of menarche[46,103,105] and other early and late pubertal markers.[48,97,107] In line with the mismatch theory outlined above, 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.[45,97,103,108–110]

Environmental stressors in relation to nutrition

Apart from nutrition (both in midchildhood and in early life), a variety of stressors, including psychosocial[111] and physical (e.g., nutritional deprivation and excessive physical exercise) stress forms, may influence pubertal maturation. Delayed pubertal development has been demonstrated in highly trained runners[112,113] and elite gymnasts,[114] who usually have increased glucocorticoid levels induced by chronic activation of the HPA axis.[115,116] When in excess, glucocorticoids can inhibit growth hormone secretion,[117] linear growth, and skeletal maturation in children[118,119]; they may also suppress the functioning of the hypothalamic-pituitary-gonadal axis (140,141,142). However, few studies investigating the influence of nutrition on the timing of puberty have taken physical activity into account, and most of them used semiquantitative data. Thus, the extent to which physical activity may relevantly modify nutritional influence on pubertal timing remains to be determined.

CONCLUSION

The contribution of childhood overweight to an earlier timing of puberty, although obviously existing, may have been overemphasized, since secular trends toward an earlier age at menarche have not been a universal finding during the recent obesity epidemic. Nonetheless, evidence is convincing that girls with higher prepubertal body mass commonly experience an earlier menarche. Whether the importance of prepubertal body composition extends to other pubertal markers is uncertain, because menarche (as the endpoint of a complex sequence of maturational events) is primarily controlled by hypothalamic-pituitary-ovarian maturation, whereas initiation of breast and pubic hair development may be relevantly modulated by the maturation of the HPA axis. Therefore, different pubertal events might respond differently to the influence of environmental or peripheral signals, and in this regard, boys and girls also appear to respond differently, at least in part.

The recent focus on the relevance of overweight has shifted from nutritional factors that affect the timing of puberty to those related to energy imbalance. Current observational studies show magnitudes of associations between dietary factors and the timing of puberty that are in the order of effect sizes observed for endocrine factors; for example, children with a more intensive adrenarchal process (i.e., in the highest group of adrenal androgen excretion) experience onset of breast and genital development 9 months earlier. Similarly, children with the highest intakes of vegetable proteins or animal protein experience at least their growth-related puberty onset up to 7 months later or 7 months earlier, respectively, than children in the lowest groups. Moreover, girls with the highest levels of dietary isoflavone intake may experience their onset of breast development and reach their peak height velocity approximately 7–8 months later than girls with the lowest levels of intake. Delays in pubertal timing in response to beneficial dietary habits (higher intakes of vegetable protein and isoflavones, and lower intakes of animal protein) may be of substantial public health relevance: A later age at both peak height velocity and menarche is related to a reduced risk of breast cancer, and a later menarcheal age is also associated with a lower total mortality. Hence, a delay in the timing of puberty by approximately 7–8 months that is achievable with dietary modifications may translate into a 6% reduction in breast cancer risk and an up to 3.4% decrease in total mortality.

Acknowledgment

Funding. This review was funded by a grant from the Long-range Research Initiative (LRI) of the European Chemical Industry Council (Cefic).

Declaration of interest. The authors have no relevant interests to declare.

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