

## **Secular Trends in Puberty**

Premature sexual maturation is a common reason for referral to a pediatric endocrine unit. There is a significant overlap between precocious puberty and normal variations. The timing of onset of puberty seems to be decreasing all over the world especially in girls and newer age limits for the diagnosis of precocity are being suggested(1). It is therefore important to clearly differentiate between the normal and the abnormal and longer periods of observation are often needed before a precise diagnosis is made. Parental concerns about sexual precocity appear to be greater in girls than in boys but as pediatricians we need to address these issues in both sexes(2).

### **Variations in the timing of normal puberty**

Puberty results from the awakening of a complex neuroendocrine mechanism. Menarche is a major landmark event in girls but no such event occurs in boys, making it difficult to interpret historic data in boys.

The generally accepted starting point of puberty in boys is enlargement of the testes beyond 3 ml and the equivalent change in girls is breast budding (Tanner breast stage 2)(3). Appearance of axillary and /or pubic hair is not necessarily a sign of onset of puberty in either sex because adrenarche occurs independently of pituitary-gonadal maturation (gonadarche)(4). Similarly menarche in girls and appearance of facial hair in boys are late signs and mark almost the end of the pubertal process. The timing of onset and tempo of puberty are not inter-linked and early onset does not necessarily mean a rapid progression of the pubertal process.

The mean age of attainment of testicular volume of 4 mL has not shown much change and is largely constant at around 11.4 years but the mean age at which girls attain breast stage two (B2) seems to be declining around the world(5). It has also been noted that although the onset of breast development is seen earlier in girls, the duration between breast budding and menarche is increasing, suggesting that unidentified external factors may cause breast development earlier without affecting menarcheal age(1).

Food and energy availability influence sexual maturation and these are unequally distributed around the world. Even within countries the age of beginning of puberty needs to be assessed separately in urban and rural areas and in well-off and under-privileged conditions, especially in the developing parts of the world such as India(6).

In Western Europe where data for nearly last 200 years is available, the age of menarche can be observed to have decreased from 17 years to 12.8 years(7,8). In urban India the age of menarche was shown to be 12.6 years as per Agarwal's data, which is similar to the age of menarche in the developed world(9).

Although large-scale data on the recent age of menarche in rural India is lacking, there is a general observation that age of menarche is late, around 15-16 years in rural girls who are relatively thinner and undernourished.

In countries such as China and Senegal from where large data is available, the mean age of menarche in rural areas is still as high as 16.1 years(10). Taken together these data highlight the crucial role of socio-economic and nutritional conditions on the timing of puberty.

There also seems to be a negative impact of early involvement in intense physical activity and energy expenditure on the timing of puberty.

*Secular trends:* As stated earlier the age of menarche has been shown to have reduced from the 19th to 21st century. A decline of about 0.3 year per decade could be calculated from Norwegian and Finnish data(8). This secular trend of progressive reduction in the age of menarche was very pronounced in US and Western Europe from 1960 to the 1990s. Recently however, the secular trend towards earlier menarche in US and Western Europe seems to have halted(1,11). Agarwal, et al. have mentioned the age of menarche to be 12.6 years in their paper in 1992 and in author's own studies done in 2005 the age of menarche is 12.5 suggesting that even in urban India the drop in age of menarche could be slowing down (unpublished observations). There is a north to south gradient in the age of menarche with girls in the southern parts achieving an earlier menarche suggesting the influence of climatic conditions. It has also been shown that more girls attain menarche in winter than summer suggesting inhibitory effect of photo stimulation on puberty(12).

*Mechanisms and hypotheses for the secular trend and variation in the timing of puberty:* Inquisitive researchers and clinicians have tried to find the reasons for the phenomenon of decreasing menarcheal age and certain conclusions have been reached. Improved nutrition and body mass seem to be the most important contributors to early sexual maturity. Frisch, *et al.*(13) have shown that a critical amount of fat mass is needed for the onset of puberty and this has been confirmed by many others(13,14).

With urbanizations, sedentary life style and improving nutrition, there is a sharp rise in

urban obesity in India as shown by many recent reports(15-17). Leptin, IGF-1, ghrelin and most importantly insulin are related to energy availability and body size and they have a permissive role in the initiation of puberty(18). In fertile races like Indians and Africans the onset of puberty is probably programmed to be early and with improved nutrition, circulating levels of energy availability markers such as leptin and insulin are high, allowing the puberty to start early.

Various genes, such as CYP17, and androgen receptor genes have been shown to be involved in the determination of timing of puberty and it is suggested that a cascade of genes may determine the variations in the timing of pubertal onset. Estrogens metabolizing gene polymorphism, but not estrogens receptor gene polymorphisms, have been shown to be associated with the early onset of menarche(19).

Protein source of food in early life could also influence the timing of puberty because high animal vs. vegetable protein ratio at ages 3-5 yr is associated with early puberty even after controlling for body size. The sum effect of phytoestrogens in the diet is clearly anti-estrogenic. A phyto-estrogens rich diet may delay puberty and the converse may initiate the puberty early(20).

Intense psychological stress such as at the time of war is known to delay the onset of menarche significantly as suggested by data from Bosnia and Croatia(21,22). Finally, many endocrine disrupting chemicals such as Dichloro-Diphenyl-Trichloro-Ethane (DDT) have been shown to be in a higher quantity in children who enter puberty early. The timing of exposure to these chemicals probably influences the timing of puberty and may explain the phenomenon of early puberty in adopted children from the developing

countries(23).

*Age thresholds for the definition of sexual precocity:* Establishing appropriate age limits for the distinction between precocious and early (premature) puberty is crucial to restrict diagnostic evaluation and therapeutic intervention(5).

The standard accepted age limit of precocious puberty until late 1990 was onset of puberty before the age of 9 years in boys and 8 years in girls. In the United States of America, due to the general trend of early sexual maturation in the population of children, particularly colored races, there is a suggestion for changing the age limits for defining precocious puberty. The Lawson Wilkins Pediatric Endocrine Society has recommended that these limits may be lowered further to 7 years in Caucasian and 6 years in African-Americans girls whereas there is no change suggested for boys(24), this phenomenon appears to be global and the situation may be similar in India in urban well-nourished areas(6).

The disadvantage of lowering the age limits is that we could miss major medical problems such as intracranial pathology in girls between the ages of 6 and 8 who present with premature sexual maturation. In a recent review of 223 patients referred for sexual precocity occurring between 7 and 8 years in white girls and 6 and 7 years in black girls, Midyett et al found that the occurrence of sex characteristics between 6 and 8 years is not necessarily benign and needs diagnostic and therapeutic intervention(25). Thus, the question of age thresholds for definition of sexual precocity does not have an unequivocal answer, at least at the present time

To conclude, the individual variability in the timing of onset of puberty seems to be determined by genetic control of a complex cascade of signals in the hypothalamus. This

process is partially influenced by peripheral and environmental signals, which essentially play a permissive role. Explanation of the phenomenon of early and precocious puberty thus remains a continuing challenge to clinicians and researchers alike. Newer age limits for the diagnosis of precocious puberty should be used with caution at least at the present time.

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