Study of pubertal development in Abruzzo (Italy) and analysis of factors implicated in puberty variability

G. Mascaretti, C. Di Berardino

Department of Ostetrics and Gynecology, University of L'Aquila (Italy)

Summary

The aim of the study was to confirm whether there is a secular trend towards the early onset of puberty without an early onset of menarche. The study included a total of 1,266 subjects, 771 females and 495 males, with an age range between 5.9 and 18.2 years. In all subjects height, percentile of height, weight, percentage of overweight, bone age and pubertal stages were evaluated. On the basis of pubertal stage the population was subdivided into Tanner's corresponding classes. The obtained data for the female population showed a stabilized onset of puberty compared to the last decades and prolonged length of the pubertal period. Pubertal development in males, instead, did not appear to have changed over the last decades. The study is in line with American studies; the earlier onset of puberty verified in the last decades has slowed prolonging the length of the pubertal period. The specific mechanisms implicated in sexual maturation are not yet well known and need further studies.

Key words: Puberty; Menarche age; Tanner scale; Thelarche; Sexual maturation.

Introduction

Puberty is a transition period from childhood to adulthood characterized by important changes in hormones, secondary sex characteristies and behavior. During this period anatomic-functional maturation of the gonads occurs and individuals are able to procreate, while at the same time growth and somatic structure, intelligence and psychological and social attitudes are being modified [1]. The beginning of puberty is in relation to the total level of maturation of all somatic and visceral structures of individuals, but in spite of numerous studies and knowledge up to now, the mechanism that unhooks the onset of puberty still remains unclear.

A peculiarity of sexual maturation in the human species is the four to five years of physiological variations in age at onset of puberty observed among normal individuals despite relatively similar life conditions [2]. Furthermore, whereas reference data seemed to have stabilized in most industrialized countries during the last century, two fairly recent American studies [3, 4] highlighted an unexpected and unexplained advance in physiological age at the onset of breast development. Results obtained in these studies are very close to the data obtained in most European countries.

The survey of those data raises the issue of whether or not the onset of puberty has shifted toward earlier ages. The mean age of menarche found in the PROS study [3] did not show the same shift as age at the onset of breast development because age at menarche (12.9 years) was unchanged when compared with data reported earlier. Moreover in the NHANES III study [4] menarche occurred at 12.5 years, similar to that reported in the PROS study. It appears that mean menarche age is almost stable, whereas age at beginning of breast development has a trend to be earlier.

On the basis of data obtained by American studies the need arises to demonstrate that the age of pubertal development has changed in Italy and, in particular, to confirm whether or not there is a secular trend towards early onset of puberty without an early age of menarche. In addition to purely scientific reasons, clinical postulates also exist and therefore it is important to confirm these data. What is simply the onset of puberty should not be considered precocious puberty and, in particular, therapeutic treatment with the aim of stopping early onset puberty should be avoided.

Materials and Methods

The study was carried out on a healthy population at the Auxologic Center and Gynecology Adolescent Ward of "San Salvatore" Hospital, L'Aquila to monitor growth in the period between January 1999 and September 2005.

A total of 1,266 subjects (771 females and 495 males) ranging in age from 5.9 to 18.2 years for females and from 7.3 to 17.9 years for males were included.

All subjects were evaluated for height, percentile of height, weight, percentage of overweight, bone age and pubertal stages. Height was measured with a Holtain stadiometer with Tanner's standards as the reference [5, 6]. Weight was precisely measured and the percentage of overweight was determined on the basis of Tanner's standards. Bone age was determined by a radiograph of the left hand, also according to Tanner's methods.

Determination of pubertal stages was carried out by expert staff based on the Tanner and Marshall criteria [5, 6]. In particular testicular and breast development, and the onset of pubic hair were evaluated. For testicular development an increase of testicular size of more than 4 ml, corresponding to Tanner's

Revised manuscript accepted for publication May 10, 2007

stage G_2, was the only significant event that was connected to the beginning of male sexual development.

The pubertal female stage was assessed primarily through evaluation of breast development, because menarche, another marker generally used for determining pubertal development, represents the endpoint of a complex sequence of maturation events, while breast development results more simply from the onset of estrogenic action.

On basis of pubertal stage (pubic hair - P, testicular development - G, and breast development - B), males and females were subdivided into Tanner's corresponding classes (Tables 1 and 2). For each pubertal stage the mean and standard deviation of chronological age were calculated. Statistical analysis was performed using STATA 8.2 (StataCorp, College Station, Texas, USA).

Table 1. — *Number of male subjects examined.*

G	No.	Pubic hair	No.
G_2	148	P_2	138
G_3	164	P_3	172
G_4	100	P_4	100
G_5	83	P_5	83

Table 2. — *Number of female subjects examined.*

Breasts	No.	Pubic hair	No.
B_2	250	P_2	238
B_3	297	P_3	301
B_4	138	P_4	140
B_5	86	P_5	92

Results

Results of the data with means and standard deviations of age for males are reported in Tables 3 and 4 and for females in Tables 5 and 6.

Table 3. — *Genitals: mean age and SD on basis of puberty stage in males (Tanner and Marshall criteria).*

Genitals	Observed	Mean	SD	95% CI
G_2	148	11.39	1.35	11.17-11.60
G_3	164	12.43	1.15	12.25-12.60
G_4	100	13.70	1.66	13.37-14.02
G_5	83	15.90	1.40	15.59-16.20

SD = standard deviation; CI = confidence interval.

Table 4. — *Pubic hair: mean age and SD on basis of puberty stage in males (Tanner and Marshall criteria).*

Pubic Hair	Observed	Mean	SD	95% CI
P_2	138	11.74	1.76	11.44-12.03
P_3	172	12.21	1.42	11.99-12.42
P_4	100	13.65	1.57	13.33-13.96
P_5	83	15.90	1.48	15.57-16.22

SD = standard deviation; CI = confidence interval.

Table 5. — *Breast: mean age and SD on basis of puberty stage in females (Tanner and Marshall criteria).*

Breasts	Observed	Mean	SD	95% CI
B_2	250	9.20	1.79	8.97-9.42
B_3	297	10.20	1.63	10.01-10.38
B_4	138	13.25	1.38	13.01-13.48
B_5	86	14.25	1.79	13.86-14.63

SD = standard deviation; CI = confidence interval.

Table 6. — *Pubic hair: mean age and SD on basis of puberty stage in females (Tanner and Marshall criteria).*

Pubic hair	Observed	Mean	SD	95% CI
P_2	238	9.10	1.66	8.88-9.31
P_3	301	10.10	1.49	9.93-10.26
P_4	140	12.95	1.50	12.69-13.20
P_5	92	14.25	1.72	13.89-14.60

SD = standard deviation; CI = confidence interval.

The data showed stabilized onset of puberty for females compared to previous decades with a prolonged length of the puberty period based on findings of earlier thelarche.

Pubertal development in males, instead, does not appear to have changed in the last decades. Our study showed that boys reach stage G2 at a mean age of 11.39 years which is in line with results obtained by other studies: in the USA (11.5 years) [7], in Sweden (11.6 years) [8], in the Netherlands (11.5 years) [9], and in Switzerland (11.2 years) [10].

Discussion

In 1997 a study of the American Academy of Pediatrics (PROS) [3] on more than 1,700 girls demonstrated a mean age of stage B2 to be ten years in white American girls and 8.9 years in African-American girls with lower limits of 6.3 and 5 years, respectively. In another large cross-sectional American study, the National Health and Nutrition Examination Survey (NHANES III) [4] found a similar early median age of 9.7 years for B2. These data are similar to data obtained in our study where stage B2 was attained at a median age of 9.2 years.

In 1970 Tanner obtained a mean age at stage B2 of 11.9 years [5]; if we compare this result with the reference value of 9.2 years in our study, we can see that in the last decades earlier onset of breast development has been occurring. This early onset, however, does not correspond to early menarche since stage B4 corresponds to 13.25 years and stage B5 corresponds to 14.15 years, values that have not changed when compared with Tanner's values of 1970 (B4 at 13.11 years and B5 at 15.23 years). Therefore, our results are in line with American studies. It thus appears that the average menarche age has almost stabilized, whereas age at onset of breast development is much earlier. The increasing difference between trends in

age at B2 and menarche involves an inverse correlation between age at onset of puberty and duration of puberty. Therefore, we can affirm that a secular trend towards early onset of puberty has stopped due to the early beginning of thelarche. The question arises as to the possible mechanisms involved in determining variability of the pubertal period and the early onset of puberty found in females. Numerous hypotheses have been proposed, some of which are still under study.

Factors related to the environment such as nutrition, light, stressors, and endocrine disrupters might impinge on the hypothalamic signalling network directly or through peripheral signals. Each variable – hypothalamic, peripheral and environmental – makes a possible contribution to the differences in timing of puberty and to the early activation of the hypothalamic-pituitary-gonadal system. Thus, intrauterine alterations are possibly associated with disorders of puberty and reproduction, but their role in the physiological variations in puberty remain uncertain.

A direct relationship between body weight and age at onset of puberty was suggested by Frisch and Revelle [11], with a study in which a critical amount of body fat was needed for the onset of puberty. The Frisch and Revelle hypothesis has triggered a number of studies that have either confirmed [7, 12, 13] or not [14, 15] a significant relationship between menarcheal age and fat mass estimated through the body mass index (BMI) or the sum of skinfold thickness.

The question is really complex because, even if a significant correlation between body fat and menarcheal age has been assessed, we have to understand whether this relationship is causal or consequential. The link between the two parameters can only be indirect because they share similar genetic determinants. With this aim, numerous studies found that a link between nutritional status and physiological variations in timing of puberty could be significant but not particularly strong, suggesting that the relationship is indirect or partial and superseded by other factors [16-19].

Nutritional factors take on an important role in the quality of foods assumed in the diet because a high animal versus vegetable protein ratio at the ages of three to five years has been associated with early menarche [20]. Phytoestrogens in the diet might play a role in the regulation of puberty both directly and indirectly, because they interact with estrogen receptors, having either agonistic or antagonistic effects depending on the endogenous hormonal balance [21]. This could also explain why children from developing countries (where there is a high consumption of soybean or cassava), after migration to European countries and undergoing nutritional changes, can have early puberty.

Endocrine disrupting chemicals (EDCs) are widespread environmental substances that have been introduced by man and may influence the endocrine system in a harmful manner [22]. EDCs account for several disturbances in wildlife and may also play a role in human disorders of sex differentiation and the reproductive organs and functions [22, 23]. The possible relationship between sexual precocity and fetal or perinatal exposure to EDCs is raising the issue of length of exposure during development. Although the mechanism underlying such an association is unclear, it indicates the importance of long-term studies. This is a complex question because the number of potential EDCs in the environment has drastically increased and isolation of responsible agents is not usually possible.

Conclusion

The main intent of our study was to attempt to understand if pubertal development has changed in Abruzzo (Italy), confirming whether or not the results of American works that hypothesized a longer pubertal period due to early onset of breast development but with menarcheal age remaining more or less constant. This conclusion shows a secular trend towards early puberty which in the last decades has really been due to better quality of life, but which now seems to have stabilized.

From American studies [3, 4] it emerged that the age of telarche is in line with our results since the mean age of stage B_2 for girls in our region is 9.2 years. If we compare this current value of 9.2 years with Tanner's values obtained in 1970, in which stage B_2 corresponded to 11.69 years, we can understand that earlier breast development has occurred in the last decades. However, this early development does not correspond to early menarcheal age since stage B_4 corresponds to age 13.25 years and stage B_5 corresponds to age 14.25 years, values which are not different if compared with Tanner's values of 1970 (B_4 at 13.11 years and B_5 at 15.33 years).

Results obtained from our study are in line with American studies; thus we can assert that the early onset of puberty verified in the last 30 years has really been arrested due to a longer pubertal period based on early thelarche. Instead for males pubertal development has not changed significantly over the years.

The possible mechanisms that cause variability in the pubertal period and early onset puberty in girls are still under study. Certainly genetic factors play a role but also others can significantly influence the maturation process, including nutrition, intrauterine conditions, the light-darkness cycle, climate conditions and exposure to different chemical substances.

In conclusion mechanisms that bring about early onset puberty and the different factors implicated in sexual maturation are still not clear and need further study.

References

[1] Durand C.: "La pubertà". *Min. Ginecol.,* 1974, *26,* 82.
[2] Tanner J.: "Growth at adolescence". 2nd ed., Oxford, UK, Blackwell, 1962.
[3] Herman-Giddens M., Slora E., Wasserman R., Bourdony C., Bhapkar M., Koch G., Hasemeier C.: "Secondary sexual characteristics and menses in young girls seen in office practice: a study from the Pediatric Research in Office Settings network". *Pediatrics*, 1997, *99*, 505.

[4] NHANES III: "Reference manuals and reports. Analytic and reporting guidelines: the third National Health and Nutrition Examination Survey (1988-94)". Hyattsville, M.D. National Center for Health Statistics, Centers for Disease Control and Prevention, 1997.
[5] Marshall W.A., Tanner J.M.: "Variations in pattern of pubertal changes in girls". *Arch. Dis. Child.,* 1969, *44*, 291.
[6] Marshall W.A., Tanner J.M.: "Variation in the pattern of pubertal changes in boys". *Arch. Dis. Child.*, 1970, *46*, 13.
[7] De Ridder C.M., Thijssen J.H., Bruning P.F., Van den Brande J.L., Zonderland M.L., Erich W.: "Body fat mass, body fat distribution, and pubertal development: a longitudinal study of physical and hormonal sexual maturation of girls". *J. Clin. Endocrinol. Metab.*, 1992, *75*, 442.
[8] Lindgren G.: "Pubertal stages 1980 of Stockholm school children". *Acta Paediatric.*, 1996, *85*, 1365.
[9] Mul D., Fredriks M., Van Buuren S., Oosdijk W., Verloove-Vanhorick S., Wit J.: "Pubertal development in the Netherlands 1965-1997". *Pediatr. Res.*, 2001, *50*, 479.
[10] Largo R., Prader A.: "Pubertal development in Swiss boys". *Helv. Paediat. Acta*, 1983, *38*, 211.
[11] Frisch R.E., Revelle R.: "Height and weight at menarche and a hypothesis of critical body weight and adolescent events". *Science*, 1970, *169*, 397.
[12] Wattigney W.A., Srinivasan S.R., Chen W., Greenlund K.J., Berenson G.S.: "Secular trend of earlier onset of menarche with increasing obesity in black and white girls, the Bogalusa heart study". *Ethn. Dis.*, 1999, *9*, 181.
[13] Stark O., Peckham C.S., Moynihan C.: "Weight and age at menarche". *Arch. Dis. Child.*, 1989, *64*, 383.
[14] Adair L.S., Gordon-Larsen P.: "Maturational timing and overweight prevalence in US adolescent girls". *Am. J. Public. Health.,* 2001, *91*, 642.
[15] Legro R.S., Lin H.M., Demers L.M., Loyd T.: "Rapid maturation of the reproductive axis during perimenarche independent of body composition". *J. Clin. Endocrinol. Metab.,* 2000, *85*, 1021.
[16] Cooper C., Kuh D., Egger P., Wadsworth M., Barker D.: "Childhood growth and age at menarche". *Br. J. Obstet. Gynaecol.*, 1996, *103*, 814.
[17] Kaprio J., Rimpela A., Winter T., Viken R., Rimpela M., Rose R.: "Common genetic influence on BMI and age at menarche". *Hum. Biol.*, 1995, *67*, 739.
[18] Quing H., Karlberg J.: "BMI in childhood and its association with height gain, timing of puberty, and final height". *Pediatr. Res.*, 2001, *49*, 244.
[19] Karlberg J.: "Secular trends in pubertal development". *Horm. Res.,* 2002, *57* (suppl. 2), 19.
[20] Berkey C.S., Gardner J.D., Frazier A.L., Colditz G.A.: "Relation of childhood diet and body size menarche and adolescent growth in girls". *Am. J. Epidemiol*., 2000, *153*, 446.
[21] Kuiper G.G., Lemmen J.G., Carlsson B., Corton J.C., Safe S.H., Van der Saag P.T. *et al.*: "Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor b". *Endocrinology*, 1998, *139*, 4252.
[22] Marshall E.: "Search for a killer: focus shifts from fat to hormones". *Science*, 1993, *259*, 618.
[23] Skakkebaek N.E., Rajpert-De Meyts E., Main K.M.: "Testicular dysgenesis syndrome: an increasingly common developmental disorder with enviromental aspects". *Hum. Reprod.,* 2001, *16*, 972.

Address reprint requests to:
G. MASCARETTI, M.D.
Dipartimento di Scienze Chirurgiche
Facoltà di Medicina e Chirurgia
Università degli Studi di L'Aquila
Piazzale S. Tommasi, 1
67010 Coppito (AQ) Italy
e-mail: giulio.mascaretti@cc.univaq.it