Pubertal maturation in girls and the relationship to anthropometric changes: Pathways through puberty

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As females began puberty, a substantial minority experience a disparity between breast and pubic hair maturation.1-5 We hypothesized that there are baseline differences in anthropometric measures between those females who had pubic hair development as the initial manifestation of secondary sexual characteristics ("adrenarche" pathway) and those who had areolar/breast development ("thelarche" pathway).

**METHODS**

**Subject Selection**

The participants were from 3 clinical sites of the National Heart, Lung, and Blood Institute Growth and Health Study (NGHS). Briefly, the NGHS is a longitudinal study that examined the impact of growth and development on cardiovascular risk factors among black and white adolescent females. Participants were a socioeconomically diverse group of females who were 9 and 10 years of age at entry. They were recruited from public and parochial schools in metropolitan Cincinnati, Ohio; the Richmond, California Unified School District; and a random sample of participants from a health maintenance organization in Washington, DC. The NGHS and subject recruitment have been described in detail.6 Race was defined at study entry (1986-1987) by self declaration of subject and parents (white or black) living in a racially concordant household; Hispanics and other ethnic groups were not included.

**Objective** Patterns of pubertal maturation may have an impact on several risk factors associated with adult morbidity and mortality, such as obesity. We examined the relationship of the initial manifestation of puberty in girls with anthropometric measures, as well as age at menarche.

**Methods** White females (n = 1166, ages 9 and 10 at intake) were followed with annual visits for 10 years. Physical examinations included height, weight, skinfold thicknesses, and pubertal maturation assessment.

**Results** During the course of the study, 443 of 859 eligible females (51.6%) were observed to have asynchronous maturation in the development of puberty, that is, initial areolar/breast (thelarche pathway) or pubic hair (adrenarche pathway) development, without development of the other characteristic. Using a longitudinal regression model, significant interactions were noted between initial pubertal manifestation and years since onset of puberty on the following outcomes: sum of skinfolds thickness, percent body fat, waist-to-hip ratio, and body mass index (BMI). However, age of onset of pubertal maturation was the same in the 2 groups (10.7 years). Females in the thelarche pathway had earlier menarche (12.6 vs 13.1 years) as well as greater skinfolds, body fat, and BMI at the time of menarche. Females in the thelarche pathway also had greater body fat and BMI 1 year before puberty and throughout puberty compared with those in the adrenarche pathway.

**Conclusions** Females who enter puberty through the thelarche pathway, as compared with the adrenarche pathway, had greater sum of skinfold thicknesses, BMI, and percent body fat 1 year before the onset, as well as throughout, puberty. Because larger body composition and earlier age of menarche of females in the thelarche pathway parallel the epidemiologic profiles of women who are obese or at risk for obesity, these females may be at greater risk for adult obesity. (J Pediatr 2003;142:643-6)

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BMI Body mass index
NGHS National Heart, Lung, and Blood Institute Growth and Health Study

See related article, p 637.
Methodology
Subjects were seen at annual visits for 10 years. During the annual visits, physical examinations were performed, which included height, weight, sum of skinfold thicknesses (at triceps, subscapular, and suprailliac sites), pubertal maturation assessment, and after the first year, waist and hip circumferences. The methods for anthropometric measurements have been described. Briefly, examiners were centrally trained and certified by designated master trainers; they were retrained and recertified annually. Two measurements were taken of each variable with a third measurement if the two differed by a preset amount. The mean of the two closest measurements were used. Body mass index (BMI) was calculated as kg/m². Percent of body fat was calculated from the triceps and subscapular skinfolds by using the formulae of Slaughter et al. Height velocity was determined by change in height over a 1-year period, comparing results of any two consecutive annual visits, and adjusting for a 12-month interval. Pubertal maturation assessment was performed according to Tanner for pubic hair stages and by the system of Garn and Falkner, as cited by Biro et al for areolar stages. Age at onset of puberty was defined by age at the first annual visit at which an examiner noted pubic hair and/or areolar development. Anthropometric measures at menarche were obtained from examinations within 6 months of the stated time of menarche. All physical examination procedures were performed by female examiners.

Females who had areolar maturation as the initial manifestation of puberty were designated in the thelarche pathway, and those who had pubic hair as the initial manifestation of puberty were designated in the adrenarche pathway. Females in whom the order of pubic hair and areolar maturation could not be determined, or those who entered puberty after age 12, were excluded from further analysis.

The study was approved by the Institutional Review Boards of University of Cincinnati and Children’s Hospital Medical Center, Cincinnati, Ohio; University of California at Berkeley; and Westat/Group Health Association in Rockville, Maryland. All participants and their parents/legal guardians gave informed consent.

Statistical Analysis
Analyses were performed using SAS version 6.12. An analysis of variance was used to test the effect of pubertal pathway, at the time of menarche, on height, BMI, sum of skinfolds, height velocity, percent body fat, and waist-to-hip ratio. Females who did not declare their menarcheal status were excluded from analyses regarding age or anthropometry at the time of menarche.

To examine longitudinally the effect of time since onset of puberty and pathway on anthropometric variables (height velocity, sum of skinfolds, BMI, waist-to-hip ratio, and percent body fat), regression models were fitted using the generalized estimating method of Liang and Zeger. Least squares estimates of model coefficients were obtained and residuals from the fitted model were used to adjust the standard errors of model coefficients to take account of within-individual correlations in repeated measurements of the dependent variable.

Differences in anthropometric variables, by pathway in the trends with time since puberty, were tested using pathway by time since puberty interaction terms.

RESULTS
There were 358 black participants who had asynchronous maturation. Many black participants recruited at age 10 (as well as 9-year-old recruits) were beyond early pubertal maturation at intake, eliminating all early and many on-time matures from analysis. To evaluate a potential bias of analyzing only 10-year-old black participants at entry with a specified pubertal pathway, females who were <10 years of age were compared with those who were 10 years at intake. The 3-way interaction between race, pathway, and age of onset of puberty was not significant, using the outcome variables BMI, sum of skinfolds, and calculated percent body fat. More than half (198 of 358, 55%) of black participants had thelarche as the initial manifestation of puberty. However, when examining age at entry to the study by pathway, significantly more 9-year-old black females entered through adrenarche (52%) when compared with black females aged 10 at entry (37% of whom entered through adrenarche) (P < .005). Because of these disparities in the preliminary analyses and the potential bias of including black participants, many of whom were mid-pubertal at time of intake, only data on white participants have been presented in this work.

Of 1166 white participants, 1092 had complete information on menarche. There were 143 excluded because they had begun puberty before entry into the study. An additional 338 began puberty after entry into the study but demonstrated both areolar and pubic hair maturation at that visit. There were 78 excluded because they had an apparent “regression” of areolar or pubic hair maturation and because the pathway could not be defined. Finally, 164 subjects had missing data. Analyses were performed on the 443 (of 859 eligible, 51.6%) white participants who were noted to have had the onset of puberty through adrenarche or thelarche alone.

The females with asynchronous maturation were more likely to have had thelarche (291 of 443, 65.7%) rather than adrenarche as the initial manifestation of puberty. The mean ages (± SD) for onset of puberty among participants were 10.7 ± 0.7 years in the thelarche pathway and 10.7 ± 0.9 in the adrenarche pathway. Because there was no difference in age of pubertal onset between pathways (P = .31), subsequent longitudinal analyses did not include age of onset of puberty. When followed 1 year after the onset of puberty, among females in the thelarche pathway, 29% advanced in areolar maturation and 80% advanced in pubic hair maturation (P < .001). In the year after the onset of puberty, 78% of the females in the adrenarche pathway advanced in areolar maturation and 37% advanced in pubic hair maturation (P < .001). Females in the thelarche pathway had a younger age of menarche when compared with females in the adrenarche pathway (12.6 ± 1.0 years vs 13.1 ± 1.2 years, P < .001). At the time of menarche, females in the thelarche pathway had significantly greater sum of skinfolds (P < .01), percent body fat from skinfolds (P < .01), waist-to-hip ratio (P < .001), and BMI (P < .001) (Table).
Anthropometric Changes: Pathways Through Puberty

In a longitudinal regression model of the anthropometric variables (BMI, sum of skinfolds, percent body fat, and waist-to-hip ratio, each analyzed separately), the effect of the number of years before/after onset of puberty, as well as pathway, were all significant at \( P < .001 \). BMI, sum of skinfolds, and percent body fat all increased with years since onset of puberty and were greater among females in the thelarche pathway. For BMI, there were significant interactions between time and pathway, with an additional increase in BMI for subjects in the thelarche pathway. For BMI, there were significant interactions between time and pathway, with an additional increase in BMI for subjects in the thelarche pathway. Similarly, there was a significant interaction between time and pathway on sum of skinfolds, with additional increase in sum of skinfolds for the thelarche pathway \((P = .013)\) (Fig 1, available at The Journal of Pediatrics online, www.us.elsevier-health.com/jpeds). Similarly, there was a significant interaction between time and pathway on sum of skinfolds, with additional increase in sum of skinfolds for the thelarche pathway \((P = .013)\) (Fig 1, available at The Journal of Pediatrics online, www.us.elsevier-health.com/jpeds). When examining waist-to-hip ratio, both pathway and time since onset of puberty were significant explanatory variables \((P < .001)\); the waist-to-hip ratio was greater for females in the thelarche pathway and although still significantly different, differences decreased after onset of puberty. Although time since onset of puberty was significant for height \((P < .001)\), pathway was not. The peak height velocity, based on 12-month height measurements, occurred in the first 2 years after the onset of puberty, regardless of pathway (data not shown).

DISCUSSION

This study analyzed longitudinal data from 443 of 1166 white females in a 10-year study in whom we observed asynchronous maturation in the initial manifestation of puberty, exhibiting either areolar and/or breast development (thelarche pathway) or pubic hair development (adrenarche pathway). We found that 67% of white participants entered pubertal maturation through the thelarche rather than the adrenarche pathway. These data are in agreement with those of Reynolds and Wines, who reported that 72% of females demonstrated breast development prior to pubic hair development,\(^2\) and similar to Taranger et al, who noted 85% of those with asynchronous maturation had breast development before pubic hair development; however, the latter authors reported synchronous breast and pubic hair in 47% overall.\(^4\) These results differ from those of Largo and Prader,\(^5\) who reported a higher rate of pubic hair development as the initial sign of puberty (75%) in a longitudinal study of Swiss females. The cited studies used the pubertal staging schema of Reynolds and Wines\(^2\) and of Tanner,\(^9\) although Reynolds and Wines compared consecutive photographs of their subjects to establish their pubertal status. Our protocol used the areolar staging system of Garn and Falkner.\(^9\) We have previously reported on the high correlation between areolar and breast staging, comparing the areolar staging of Garn and Falkner to the breast staging system of Tanner (Spearman correlation coefficient, 0.94) and noted that in any discrepancies between the two systems, the latter (Tanner’s system) tended to overestimate early puberty, particularly in obese females.\(^9\) Because the observations in the NGHS were based on annual visits (rather than more frequent visits), the order of progression from a prepubertal to pubertal status in the majority of the females was simultaneous for both pubic hair and areolar and/or breast maturation.

In the participants for whom a disparity in early puberty was observed (ie, either initial areolar or pubic hair maturation), there were several important similarities as well as differences. Age of onset of puberty was the same for both groups, as was height, throughout puberty. One year after the onset of puberty, females were more likely to have progressed to a greater degree of maturation in the other secondary characteristic of puberty (for example, the females in the thelarche pathway were more likely to have progression of pubic hair, rather than further areolar maturation, one year after initiation of puberty). Throughout puberty, as well as the year prior to the onset of puberty, the females who entered puberty through the thelarche pathway had a significantly higher BMI and proportion of body fat, as determined by sum of skinfolds and calculated percent body fat, than females in the adrenarche pathway. Similar findings were seen at the time of menarche; females in the thelarche pathway were noted to have earlier menarche and greater body fat and BMI at menarche than females in the adrenarche pathway, who attained menarche at lower body fat and BMI.

The association between the thelarche pathway and higher body mass and proportion of body fat raises an issue regarding the impact of body morphology and proportion of body fat on pubertal maturation. Previous observations have noted a positive association between greater weight and body mass with earlier maturation.\(^12\-\!16\) Researchers have proposed that additional factors exist that influence the association between anthropometric measures and menarche.\(^14\) Females who enter puberty through the thelarche pathway have greater prepubertal weight and body mass and thus may be the subjects who contribute to the earlier maturation noted in heavier females. However, greater BMI, which this study noted in the year before the onset of puberty, may influence both the type

Table. Anthropometric measures at age of menarche, by pathway, in white females who had asynchronous development to begin pubertal maturation

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Number</th>
<th>Age at menarche (y)</th>
<th>BMI (kg/m²)</th>
<th>Waist-to-hip ratio</th>
<th>Sum of skinfolds (mm)</th>
<th>% Body fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thelarche</td>
<td>291</td>
<td>12.6 ± 0.9</td>
<td>21.2 ± 3.9</td>
<td>77.9 ± 4.6</td>
<td>41.9 ± 20.6</td>
<td>23.9 ± 8.6</td>
</tr>
<tr>
<td>Adrenarche</td>
<td>152</td>
<td>13.1 ± 1.1</td>
<td>19.3 ± 2.9</td>
<td>75.9 ± 4.0</td>
<td>35.7 ± 17.3</td>
<td>21.4 ± 7.3</td>
</tr>
</tbody>
</table>

P < .001  P < .001  P < .001  P < .01  P < .01
of pubertal development and the age of menarche or be associated with an underlying factor, such as leptin.\textsuperscript{17}

We postulate that the pathway through which a girl enters puberty may have important consequences regarding adult morbidity and mortality, especially obesity and breast cancer. The Tecumseh Community Health Survey, which examined nearly 2500 women born between 1890 and 1940, noted that women with higher degrees of body fat as adults had earlier ages of menarche.\textsuperscript{18} Additionally, women who reported earlier pubertal maturation and menarche were more obese than late matures (risk ratio, 1.8).\textsuperscript{19} Thus, those females who entered puberty via the thelarche pathway, who have an earlier age of menarche, may have a tendency toward adult obesity.

Epidemiologic studies have noted a greater risk of breast cancer in those women who reported an earlier age of menarche.\textsuperscript{20-26} There is also an association among breast cancer, an earlier age of menarche, and greater BMI and body fat.\textsuperscript{23,25,27} Thus, thelarche pathway may serve as a risk marker for breast cancer because females who enter puberty through thelarche have an earlier age of menarche and greater BMI and body fat. This association may reflect the increased extragonadal aromatization of androgens to estrogens,\textsuperscript{23} which appears related both to onset of menarche and breast cancer. The initial pathway of the onset of puberty may be an additional manifestation of these same factors, through increased sensitivity or greater amount of adipocyte-specific aromatase, or mediated through another biochemical factor, such as leptin.\textsuperscript{17}

This study had several limitations. If there had been more frequent observations, we might have seen a greater number of females enter pubertal maturation through either the thelarche or adrenarche pathway, although we would expect a similar proportion between the pathways overall. Because participants were more likely to mature in the other external manifestation of puberty, and a relatively robust proportion of participants were in 1 of the pathways, we do not believe we analyzed data on females with premature adrenarche and thelarche. Because of lack of comparable data in black participants, it is unclear whether the impact of asynchronous maturation is the same in black females as it is in white females.

In summary, we have found in a longitudinal analysis of normal female puberty that white females who had asynchronous maturation in the initial manifestation of puberty, (that is areolar/breast or pubic hair maturation without development of the other) were more likely to enter through the thelarche pathway (65.7% vs 34.3%). Females who entered via the thelarche pathway had greater body mass and body fat and earlier menarche. This profile is the same as that noted in epidemiologic studies investigating risk factors for adult obesity.

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REFERENCES

**Fig 1.** Body mass index by years since puberty and pathway.

**Fig 2.** Sum of skinfolds by years since puberty and pathway.