Secondary Sexual Characteristics in Boys: Data From the Pediatric Research in Office Settings Network

WHAT’S KNOWN ON THIS SUBJECT: Recent investigations of pubertal onset in US girls suggest earlier maturation. The situation for US boys is unknown, and existing investigations are outdated and lack information on a key physical marker of male puberty: testicular enlargement.

WHAT THIS STUDY ADDS: US boys appear to be developing secondary sexual characteristics and achieving testicular enlargement 6 months to 2 years earlier than commonly used norms, with African American boys entering Tanner stages 2 to 4 earlier than white or Hispanic boys.

abstract

BACKGROUND: Data from racially and ethnically diverse US boys are needed to determine ages of onset of secondary sexual characteristics and examine secular trends. Current international studies suggest earlier puberty in boys than previous studies, following recent trend in girls.

METHODS: Two hundred and twelve practitioners collected Tanner stage and testicular volume data on 4131 boys seen for well-child care in 144 pediatric offices across the United States. Data were analyzed for prevalence and mean ages of onset of sexual maturity markers.

RESULTS: Mean ages for onset of Tanner 2 genital development for non-Hispanic white, African American, and Hispanic boys were 10.14, 9.14, and 9.63 years respectively. Mean years for achieving testicular volumes of $\geq 3$ mL were 9.95 for white, 9.71 for African American, and 9.63 for Hispanic boys; and for $\geq 4$ mL were 11.46, 11.75, and 11.29 respectively. African American boys showed earlier ($P < .0001$) mean ages for stage 2 to 4 genital development and stage 2 to 4 pubic hair than white and Hispanic boys. No statistical differences were observed between white and Hispanic boys.

CONCLUSIONS: Observed mean ages of beginning genital and pubic hair growth and early testicular volumes were 6 months to 2 years earlier than in past studies, depending on the characteristic and race/ethnicity. The causes and public health implications of this apparent shift in US boys to a lower age of onset for the development of secondary sexual characteristics in US boys needs further exploration.

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AUTHORS: Marcia E. Herman-Giddens, PA, MPH, DrPH,* Jennifer Steffes, MSW, Donna Harris, MA, Eric Slora, PhD, Michael Hussey, MS, Steven A. Dowshen, MD, Richard Wasserman, MD, MPH,* Janet R. Serwint, MD, Lynn Smitherman, MD, F, and Edward O. Reiter, MD

Departments of *Maternal and Child Health, and *Biostatistics, Gillings School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; Pediatric Research in Office Settings, Department of Research, American Academy of Pediatrics, Elk Grove Village, Illinois; Department of Pediatrics, Alfred I. DuPont Hospital for Children, Wilmington, Delaware; Department of Pediatrics, University of Vermont, College of Medicine, Burlington, Vermont; Department of Pediatrics, Johns Hopkins University, School of Medicine, Baltimore, Maryland; Continuity Research Network, Academic Pediatric Association, McLean, Virginia; Children’s Hospital of Michigan, Wayne State University School of Medicine/Detroit Medical Center, Detroit, Michigan; NMA PedsNet, National Medical Association, Silver Spring, Maryland; and Baystate Children’s Hospital, Tufts University School of Medicine, Springfield, Massachusetts

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(Continued on last page)
The secular trend toward a younger age of onset of puberty in girls in many countries is now generally accepted.1–3 An expert panel convened in 2003 by Sero- Don Sox International, Inc., concluded that US girls were entering puberty at an earlier age than 40 years ago.1 One of the key studies leading to this conclusion, conducted by the American Academy of Pediatrics (AAP), found girls were typically developing about a year earlier than previously assumed.4 For boys, the panel concluded secular evidence was insufficient and further studies were needed. The most recent data on US boys comes from several analyses of the National Health and Nutrition Examination Survey (NHANES) III 1988–1994.15–7; however, the data are 20 years old, the accuracy of the genital staging has been questioned, and testicular volumes were not obtained.5,8,9 No recent studies representative of US boys or with large numbers in varied locales have been published. Data on male puberty are more difficult to obtain than female data because of the absence of an easily determined marker, such as menarche. Male pubertal stages are harder to assess visually than girls’ stages, and orchidometry, an intrusive procedure, is not part of well-child exams. Consequently, the AAP’s Pediatric Research in Office Settings (PROS) practice-based research network undertook this cross-sectional study to determine the current ages of onset of sexual maturity stages 2 to 5 and early testicular volumes in US boys seen for well-child care and to assess whether there has been a shift in what is seen in office practice as compared with older studies. Puberty is complex, including many dynamic components. This study was designed to report only physical changes, and not hormonal or other changes.

METHODS
Characteristics of Practice Participants
Clinicians were recruited from PROS practices, the National Medical Association Pediatric Research Network, and the Academic Pediatric Association’s Continuity Research Network. Participating clinicians comprised 196 (93%) pediatricians, 1 family medicine physician, and 15 (7%) nurse practitioners. Practices from 41 states and 1 Canadian province enrolled subjects between July 2005 and February 2010. Seventeen percent of practices were located in the Midwest, 24% in the Northeast, 31% in the South, and 28% in the West. Approval was obtained from the AAP’s Institutional Review Board and 54 local institutional review boards affiliated with participating practices.

Data Collection Process
Before the main study, Secondary Sexual Characteristics in Boys (SSCIB), we established ‘trained clinicians’ inter-rater reliability for Tanner staging and orchidometry.10 Tanner staging is a 5-stage visual method for assessing development of secondary sexual characteristics (genital and pubic hair growth for males) from prepubertal (stage 1) to fully mature (stage 5).11 Using the study training manual,12 participating clinicians learned Tanner staging and how to use a Prader orchidometer modified to contain only the 1-mL to 4-mL beads. Clinicians demonstrated competency by passing a question-and-photograph qualifying examination. Intraclass correlations in the clinical setting, where 2 practitioners in 8 practices rated a total of 79 boys, ranged from 0.61 for left testis size to 0.94 for pubic hair stage (all significant at P < .001), which indicate moderate to substantial agreement depending on the variable being measured.10 For the main study, SSCIB, 212 qualifying clinicians screened boys through 16 years of age presenting for well-child care for eligibility; each enrolled up to 30 consecutive boys (15 from 6–12 years of age and 15 from 13–16) from English- or Spanish-speaking families. Informed consent was obtained from parents/guardians and assent from boys 7 and older before examination. Data for each subject were collected on a form with numbered drawings and verbal anchors to maximize accuracy. The physical examination included height and weight, using each clinician’s office equipment, Tanner staging, testicular volume measurement from 1 through 4 mL, and breast palpation for gynecomastia. Testicular volume was collected for each testis as a categorical variable: ≤1, 2, 3, or ≥4 mL. Examiners graded down the Tanner stage or testis volume if either appeared to fall between categories. Additional demographic data were ascertained by observation, questioning, and medical chart review.

Data Analysis
We defined continuous age (years) as the number of days between the month of birth, (assuming the subject was born on the first of the month), and the examination date divided by 365.25. When necessary, continuous age was categorized as age rounded to the nearest year. We classified subjects as African American if African American was indicated on the study form (regardless of any other race/ethnicity indication), Hispanic if Hispanic ethnicity was indicated (regardless of any other indication other than African American), and white if only white was indicated. We calculated descriptive statistics, with exact binomial 95% confidence intervals (CIs) for prevalence of Tanner stage 2 or greater pubic hair and genital development within each age category. We used stratified Mantel-Haenszel row mean score statistics to assess
homogeneity of prevalences by race/ethnicity adjusted for age group.
Median ages and SDs for transition into Tanner stages 2 to 5 were estimated by using probit regression, which links a linear combination of covariates to the cumulative normal probability of having achieved a stage. In probit analysis, the median age is assumed to equal the mean. For testicular volume analysis, we used the larger of the testes if there was a right-left difference. For each outcome, the probit model adjusted for continuous age, categorical race/ethnicity (reference group: whites), and their interaction. Model coefficients were used to jointly test \( \alpha = 0.05 \) for equality of the mean ages of transition across the 3 race/ethnicity groups. Pairwise comparisons of race/ethnicity groups were conducted with Bonferroni correction for multiple testing (ie, significance level \( \alpha = 0.05/3 = 0.017 \)). We calculated 95% CIs for the mean ages of transition using Fieller’s Theorem. All analyses used SAS 9.2 (SAS Institute, Inc, Cary, NC).

RESULTS
We enrolled 5355 participants from 144 sites between 2005 and 2010. After exclusion for chronic conditions or medications that could affect puberty, missing data, or “other racial” category, 4131 boys remained for analysis (Fig 1). Of these, 2070 (50%) were classified as white, 1062 (26%) African American, and 999 (24%) Hispanic. Demographic and clinical characteristics of the study population are presented in Table 1.

Fig 2 shows the proportion of boys (95% CIs) entering Tanner stage 2 or greater genital development and pubic hair growth by race/ethnicity and age. Adjusted for age, the proportion for both genital and pubic hair development was found to be statistically different among the 3 race/ethnicity groups \( (P < .001) \). African American boys had higher proportions at a given age for both genital and pubic hair development than white (both \( P < .001 \)) and Hispanic boys (both \( P < .001 \)), but white and Hispanic boys showed no difference \( (P = .54 \text{ and } P = .16, \text{ respectively}) \).

Table 2 presents estimates of the mean age of transition to stages 2 to 5 for genital development and pubic hair growth. Entry into stage 2 genital development occurred at 10.14 years for white boys, 9.14 for African American boys, and 10.04 for Hispanic boys.

### TABLE 1 Demographic and Clinical Characteristics of Study Subjects by Race/Ethnicity

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>White</th>
<th>African American</th>
<th>Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Payment status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>349 (17.5)</td>
<td>673 (65.9)</td>
<td>607 (63.0)</td>
</tr>
<tr>
<td>Insurance</td>
<td>1618 (80.9)</td>
<td>340 (33.3)</td>
<td>333 (34.6)</td>
</tr>
<tr>
<td>Self-pay</td>
<td>32 (1.6)</td>
<td>9 (0.8)</td>
<td>23 (2.4)</td>
</tr>
<tr>
<td>Total</td>
<td>1999</td>
<td>1022</td>
<td>963</td>
</tr>
<tr>
<td>Chronic disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1681 (81.8)</td>
<td>775 (73.3)</td>
<td>806 (80.7)</td>
</tr>
<tr>
<td>Asthma only</td>
<td>137 (6.6)</td>
<td>149 (14.1)</td>
<td>82 (8.2)</td>
</tr>
<tr>
<td>Other only</td>
<td>217 (10.5)</td>
<td>115 (10.9)</td>
<td>101 (10.1)</td>
</tr>
<tr>
<td>Asthma and other</td>
<td>22 (1.1)</td>
<td>18 (1.7)</td>
<td>10 (1.0)</td>
</tr>
<tr>
<td>Total</td>
<td>2067</td>
<td>1057</td>
<td>999</td>
</tr>
<tr>
<td>Chronic disease and medications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1647 (79.8)</td>
<td>756 (71.7)</td>
<td>796 (79.3)</td>
</tr>
<tr>
<td>Disease, no chronic medications</td>
<td>43 (2.1)</td>
<td>16 (1.5)</td>
<td>9 (0.9)</td>
</tr>
<tr>
<td>Medication, no chronic diseases</td>
<td>196 (9.5)</td>
<td>151 (14.2)</td>
<td>119 (11.9)</td>
</tr>
<tr>
<td>Chronic diseases and chronic medications</td>
<td>179 (8.6)</td>
<td>134 (12.6)</td>
<td>73 (7.3)</td>
</tr>
<tr>
<td>Total</td>
<td>2065</td>
<td>1060</td>
<td>997</td>
</tr>
<tr>
<td>History of genital abnormalities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1961 (95.9)</td>
<td>1011 (96.8)</td>
<td>957 (97.9)</td>
</tr>
<tr>
<td>Undescended testes</td>
<td>28 (1.4)</td>
<td>13 (1.3)</td>
<td>8 (0.8)</td>
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<tr>
<td>Hypospadias</td>
<td>12 (0.6)</td>
<td>3 (0.3)</td>
<td>2 (0.2)</td>
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<tr>
<td>Varicocele</td>
<td>16 (0.8)</td>
<td>3 (0.3)</td>
<td>4 (0.4)</td>
</tr>
<tr>
<td>Undescended testes+hypospadias</td>
<td>3 (0.2)</td>
<td>1 (0.1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other</td>
<td>26 (1.1)</td>
<td>12 (1.2)</td>
<td>7 (0.7)</td>
</tr>
<tr>
<td>Total</td>
<td>2046</td>
<td>1043</td>
<td>978</td>
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</table>

There were 147 missing values for payment status, 8 missing for chronic disease, and 64 missing for history of genital abnormalities.
Overall, these were statistically different ($P < .0001$). Pairwise differences were found between African American and white boys ($P < .0001$), African American and Hispanic boys ($P < .0001$), but not between white and Hispanic boys ($P = .48$). For pubic hair, mean ages of entry into stage 2 were 11.47, 10.25, and 11.43 years respectively; overall, these were statistically different ($P < .0001$). Pairwise differences were found between African American and white boys ($P < .0001$), and African American and Hispanic boys ($P < .0001$), but not between white and Hispanic boys ($P = .69$).

Because earlier pubertal studies assessing testicular volume have used volumes of 3 mL, ≥ 5 mL, ≥ 4 mL as indicative of central pubertal take-off, we present mean ages of transition for both ≥ 3 mL and ≥ 4 mL (Table 2). Data on Cincinnati boys$^{15}$ and Swedish boys$^{16}$ show that the transition from 2 to 3 mL indicates pubertal take-off. White boys in this study reached a mean age of transition to 3 mL at 9.95 years, African American boys at 9.71, and Hispanic boys at 9.63, with no significant difference ($P = .11$).

Mean ages for reaching volumes of ≥ 4 mL were 11.46, 11.75, and 11.29 years, respectively. Overall, these were found to be statistically different ($P = .008$), with pairwise significance only between African American and Hispanic boys ($P = .002$).

Data on progression to full sexual maturity present a slightly different pattern. For stages 3 and 4, statistical differences by race/ethnicity were observed, but not for stage 5. Pairwise differences between white and Hispanic boys were found for stages 3 and 4 pubic hair and stage 4 genital development. Estimated ages for entry into stage 5 (sexual maturity) for genital development were 15.57, 15.51, and 15.58 years, and 15.83, 15.72, and 15.89 for pubic hair for white, African American, and Hispanic boys, respectively.
we examined relationships between BMI and ages of onset of sexual maturity stages. Pooling race/ethnicity (because of small sample size) and controlling for age, boys with BMI <15th percentile had later mean ages of transition to stages 2 to 4 for genital and pubic hair growth than boys with BMI ≥85th percentile (data not shown). No other comparisons for stages or BMI categories were significant. The finding is unclear, as no existing studies inform differences in mean testicular size at given ages, by race/ethnicity, and sexual maturity stage; or in racial/ethnic differences in the rate of advancement through the Tanner stages over time.

Of consequence are the differences we found comparing our results with the 40-year-old data from Marshall and Tanner’s landmark study on 228 white institutionalized boys in London. White boys in our study entered stage 2 genital growth 1.5 years earlier than the British boys (10.14 vs 11.60 years of age). Comparing ages of onset of stage 2 pubic hair growth from the British study (estimated at 13.4 years of age) is not possible because, as the authors stated, the age “was not accurately determined,” because assessments were from photographs. Their observation for entry into stage 3 pubic hair, 13.9 years, is likely more reliable, as stage 3 hair would be visible in photographs. White SSCIB study subjects entered stage 3 pubic hair development at a mean of 12.89 years, a full year earlier. For stage 2 pubic hair, US studies from 1948 to 1995
<table>
<thead>
<tr>
<th>Study/Authors</th>
<th>Data Collected, Year Span</th>
<th>Type of Study</th>
<th>Country Subjects</th>
<th>Age Range, y</th>
<th>TV ≥ 3 mL</th>
<th>TV ≥ 4 mL</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
<th>G5</th>
<th>PH2</th>
<th>PH3</th>
<th>PH4</th>
<th>PH5</th>
<th>Mean Age, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fels Institute21</td>
<td>1960s–1990s</td>
<td>L</td>
<td>United States</td>
<td>59 White</td>
<td>9–21</td>
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<tr>
<td>NHES II/III22</td>
<td>1963–1970</td>
<td>C-S</td>
<td>United States</td>
<td>3047 White</td>
<td>12–17</td>
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<tr>
<td>Bogalusa Heart Study24</td>
<td>1973–1974</td>
<td>C-S</td>
<td>United States</td>
<td>1153 White; 676 African American</td>
<td>5–14</td>
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<tr>
<td>NHANES III26</td>
<td>1988–1994</td>
<td>—</td>
<td>United States</td>
<td>536 White; 781 African American; 797 Mexican American</td>
<td>8–19</td>
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<td></td>
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<tr>
<td>Biro Study27</td>
<td>1984–1987</td>
<td>L</td>
<td>United States</td>
<td>278 White; 237 African American</td>
<td>10–18</td>
<td>12.18</td>
<td></td>
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<tr>
<td>Susman Study28</td>
<td>2000–2006</td>
<td>L</td>
<td>United States</td>
<td>364 White; 82 African American</td>
<td>9.5–15.3</td>
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</table>

C-S, cross-sectional; G, genital; L, longitudinal; NHES, National Health Examination Survey; PH, pubic hair; TV, testicular volume.
found a mean age of onset from 12.0 to 12.8 years of age for white boys. Results from SSCIB boys demonstrate this is occurring 6 months to a year earlier than previously reported.

Although comparison of our results with those of earlier studies is limited because of lack of early data on minorities and differences in methodologies, socioeconomic status, age at enrollment, and small numbers of subjects in most studies,14,18 the 6-month to 2-year earlier development of secondary sexual characteristics or testicular enlargement as documented in our study is notable. Few older studies on African American or Hispanic boys exist. Results from the 40-year-old nationally representative US Health Examination Survey, Cycle III, on African American boys were stated to be “comparable to the mean ages in Marshall and Tanner’s data on white boys.”22 Foster et al,23 in a study 35 years ago, found African American boys in Louisiana began genital and pubic hair development at 11.2 and 11.7 years as compared with our ages of 9.14 and 10.25.

The only previous US studies on Hispanic boys involved Mexican American boys: the Hispanic Health and Examination Survey (HHANES), 1982 to 1984, and NHANES III, 1988 to 1992.5–7,24 Because we enrolled Hispanic boys without regard to country of origin, direct comparison may not be valid. HHANES and NHANES III found attainment of genital stage 2 declined from 12.4 to 10.4 years of age over a 10-year period, although the accuracy of the latter’s genital data has been questioned as discussed in the following paragraph.5–7,24 SSCIB Hispanic boys entered stage 2 genital development at 10.04 years.

Findings for genital data between the PROS study and NHANES III are similar; however, it should be noted that several authors have questioned the accuracy of the NHANES III results,5,8,9,18 which found very early onset of genital stage 2 for all groups and noted that the 2-year span between genital stage 2 and pubic hair stage 2 was longer than that found in any other puberty study. Thus, genital Tanner stage misclassification may have occurred and the genital data may be unreliable. Stage 2 pubic hair onset for Mexican American boys between HHANES and NHANES III declined from 12.8 to 12.3 years. SSCIB Hispanic boys reached stage 2 pubic hair at a mean of 11.43 years of age. Non-Hispanic white and African American boys in SSCIB reached stage 2 pubic hair 0.53 and 0.95 years earlier than the NHANES III boys. Comparisons of pubic hair stages should be more reliable, as assessment of pubic hair is not as subjective as that of genital development. Our findings are also similar to a recent longitudinal puberty study that included 364 white and 63 African American boys (Table 3).25 Very few European or US studies have included testicular volumes. Largo and Prader’s landmark 198314 longitudinal study on white Swiss boys proposed testicular volume of 3 mL as the most accurate sign of central pubertal takeoff based on their earlier work, later confirmed by the Cincinnati15 and Swedish studies.16 Boys in the Swiss study were a mean age of 11.2 at genital stage 2 and 11.8 at a testicular volume of 3 mL. The study by Biro et al15 is the only US puberty study that reported testicular volumes. Their subjects, studied from 1984 to 1987 (Frank M. Biro, MD, personal communication, 2010), had a mean age of 12.18 years when reaching a volume of 3 mL, with no differences between the white and African American boys. SSCIB white and African American boys were 2.23 and 2.47 years younger, respectively. Recent data from Denmark also report a decline in age for achieving a testicular volume >3 mL.8 Because our study is the first US study to measure testicular volumes on widely distributed boys, it can serve as a baseline for future studies.

We also note the pattern presented by our data on progression to stage 5 genital development and pubic hair growth indicating sexual maturity. Our subjects reached stage 5 at ages 15.7 to 15.8 for all racial/ethnic groups, similar to the NHANES III data; however, our stage 5 probit model estimates (including comparisons of race/ethnicity) should be interpreted with caution because they are artificially bounded by SSCIB’s maximum enrollment age of 16 years. It is interesting that the 2010 US longitudinal study found boys’ age for genital maturity to be 14.9 and 14.3 for white and African American boys, respectively.25

The strengths of the PROS study include its large sample size and broad geographical and minority patient representation. In addition, observations were made only on well boys in primary care sites by trained pediatricians and other clinicians. Testicular volumes were measured through 4 mL.

The study has several limitations. Our convenience sample of US boys seen in pediatric offices for well-child care is not a statistically representative sample of the US population. The study results could be questioned if the boys in our study were biologically different from boys in the US population; however, there is no plausible reason that would support this contention. Because these data are cross-sectional, statistical methods allow for only the estimation of mean ages of transition into the sexual maturity stages. Longitudinal data are required to assess duration, peak height velocity, and relationships between duration and timing of pubertal stages. Population-based longitudinal studies in the United States have not been conducted because of methodological challenges and expense. Our age calculations may
lack precision because, to protect privacy, we could not collect the day of birth. This, however, is unlikely to have introduced meaningful differences. Our training in sexual maturity staging and orchidometer use was designed with the input of several pediatric endocrinologists and accomplished through an instruction manual with photographs and explanatory and instructive text. As previously described, testing ensured staging proficiency among qualifying clinicians. We are aware of no large US study that has so carefully documented its training methods with a manual and testing, and shown interrater reliability among a sample of those trained. Although it would have been ideal to have assessments completed by pediatric endocrinologists with extensive experience in sexual maturity staging, this was not feasible in a study of thousands of nonreferred children across 41 states. Testicular volumes were assessed as ≤1, 2, 3, or ≥4 mL; therefore, data from studies that used >3 mL but ≤3 mL rather than >3 mL or ≥4 mL as their criteria for central pubertal takeoff are not strictly comparable. Ultrasound, regarded as a more precise method for measuring testes, is not practical for large-scale studies and is not part of the usual pediatric examination. Volume comparisons with the Prader orchidometer have been shown to be reasonably accurate.

In conclusion, our data suggest that US boys are beginning genital and pubic hair growth earlier than several decades ago in concordance with recent reports on girls. These data are consistent with recent trends from other countries, such as Denmark, Sweden, Great Britain, Italy, and China.

For example, urban Han Chinese boys achieve a testicular volume of ≥4 mL (13% by age 9) and spermarche earlier than studies conducted several decades ago; Danish boys achieve a testicular volume ≥3 mL more than 3 months earlier now than 15 years ago. Our findings are somewhat surprising, given that factors associated with earlier physical development in girls, such as overweight and certain endocrine disrupters, are not known to be associated with earlier development in boys and could even be theorized to have a delaying effect. Our data do not allow for an analysis of the possible underlying mechanisms of these observed decreases in the apparent age of onset of secondary sexual characteristics as assessed by physical examination. They do, however, demonstrate the importance in the physical examination of boys of observing the ontogeny of changes in testicular volumes along with the stage of pubic hair growth. For example, in a 7-year-old, the presence of pubic hair with concomitant testicular volume increase needs close scrutiny and endocrinologic evaluation to be sure that true sexual precocity is not occurring. In the absence of increased testicular volume or systemic changes of androgenization, the more likely process in this example would be that of “benign” premature adrenarche.

Current environmental factors, including exposure to chemicals, changes in diet, less physical activity, and other modern lifestyle changes and exposures may be related to this apparent rapid decrease in the age of onset of secondary sexual characteristics and may not reflect healthy conditions. Psychological, emotional, and behavioral affects of earlier sexual maturity may be pivotal, given the current phenomena of social and emotional delay in achieving adulthood. Longitudinal tracking is needed to clarify any impact of overweight/obesity on boys’ sexual development. The secular decrease we observed in ages of onset of secondary sexual characteristics in US boys requires further study.

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