#### Puberty

# Splitting hairs

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### Is puberty getting earlier in girls?

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There has been great recent media interest internationally in claims that puberty is occurring at younger ages, particularly in girls. Pundits extrapolate the plunging graphs of the secular trend in menarche downwards into infancy, postulate epidemics of child sexual experimentation, and bewail the loss of innocence of childhood.

Until recently, most of this debate centred on evidence from the United States, particularly the conclusions of a large national study of puberty in girls published in 1997 by Herman-Giddens and colleagues.1 The evidence was sufficient for the US Lawson Wilkins Pediatric Endocrine Society to recently revise downwards its suggested age for investigation of precocious puberty in girls,<sup>2</sup> although this has been contentious.3 Suggestions that puberty was occurring earlier received strong support from lay opinion in the UK, particularly from parents and teachers.<sup>4</sup> Further energy was given to the debate by the release of unpublished observations from the Avon Longitudinal Study of Parents and Children (ALSPAC, also known as Children of the Nineties) that approximately one in six 8 year old girls had either breast buds or some pubic hair (personal communication, Jean Golding; http:// www.ich.bris.ac.uk/alspacext/ Default.html).

However, such claims have been met with some scepticism within the field of paediatric endocrinology.3 Although some clinicians report seeing more cases of precocious puberty than a generation ago, single observer longitudinal studies of puberty show there has been little if any change since Tanner and Marshall's original work over 30 years ago.56 The well known graphs of the secular trend in age of menarche from the late nineteenth century seem to invite projections of an ever earlier age of puberty. But it is clear that in developed countries the secular trend has leveled off in the past 40 years. Indeed, there is some evidence that the average age of menarche may be rising again in some countries.78

## TRADITIONAL CONCEPTS OF PUBERTY

Our concept of the onset of normal puberty has been traditionally defined by

Tanner and Marshall's observation that the first signs of puberty appear between the ages of 8.5 and 13 years in 95% of girls.9 The study sample was 192 white British girls of primarily lower socioeconomic status who were cared for in a residential home. The early signs of puberty described by Tanner and Marshall are the appearance of a breast bud (indicating oestrogenic activity) and a small amount of fine pubic hair around the labia (indicating androgenic activity). In Marshall and Tanner's study, around 2.5% of girls developed breast buds or some pubic hair below 8.5 years. Thus standard paediatric endocrinological practice has been to define precocious puberty requiring investigation as signs of puberty under 8 years in a girl (and under 9 years in boys).<sup>10</sup>

These standards were largely unchallenged on both sides of the Atlantic until recently, although it was widely acknowledged that definitions based on white British girls resident in children's homes might not have been the most appropriate for modern ethnically diverse populations. However, more recent studies from the 1980s, in both the USA<sup>11</sup> and Britain,<sup>5 6</sup> seemed to confirm Marshall and Tanner's original data.

Let us then look at the evidence, for the truth cannot be in the middle.

## THE EVIDENCE FOR EARLIER PUBERTY

Claiming there was a lack of "up to date, geographically relevant standards", Herman-Giddens and colleagues attempted a national study of pubertal characteristics using а novel methodology.1 Two hundred and twenty five paediatricians from 65 primary care practices were recruited across the USA through the American Academy of Pediatrics Pediatric Research in Office Settings Network. The participating physicians were trained in Tanner staging by visual inspection through mailed standardised text and photographs. Physicians were tested for competency, and kappa statistics showed adequate inter-rater agreement. Subjects were girls from 3 to 12 years who presented to the practices for any complaint that might require a physical examination or for routine well child checks. Data were obtained on 17 077 girls over one year, of which 9.6% were African-American. Below age 6 years, very few white or African-American girls were reported to have any signs of sexual maturation. At age 7 years, 27.2% of African-American girls and 6.7% of white girls had evidence of breast or pubic hair development, increasing to 48.3% and 14.7% respectively at 8 years. This is dramatically greater than the 2.5% one would expect from the Tanner and Marshall data.

Interestingly, Herman-Giddens and colleagues did not identify a change in the age of menarche in white girls, reporting a mean age of menarche of 12.88 years compared to 12.8 years as the previously accepted mean.<sup>12</sup> The age of menarche had decreased only slightly in African-American girls, being 12.16 years in the recent study compared to 12.52 years in previous datasets.<sup>13</sup> The observation of earlier signs of breast and pubic hair changes, together with the lack of change in the age of menarche, led the authors to suggest that the process of puberty itself may be lengthening.

The other main body of evidence for an earlier age of puberty in girls comes from as yet unpublished information from the ALSPAC study in the UK, which suggests that at age 8 years, approximately 1 in 6 girls (18%) had reached stage 2 breast or pubic hair development (personal communication, Jean Golding). This accords with the observation from Herman-Giddens and colleagues that 14.7% of white girls aged 8 years had reached stage 2 breast or pubic hair development (the ALSPAC cohort under represents ethnic minorities, being drawn from the Avon region of the UK).

Supporting evidence for a lowering of the age of puberty comes from reports from teachers and parents that they are seeing changes in girls at a younger age. Teachers' representatives believe strongly that more girls are starting their periods in the top year of primary school than was the case 10 or 20 years ago.<sup>4</sup>

One important issue is the lack of biological plausibility for a lowering of the age of puberty, particularly when Herman-Giddens and colleagues' study agrees that the age of menarche has shifted not at all in whites and minimally in African-Americans. Candidate explanations have focused on environmentally derived oestrogens and rising levels of obesity, although there is no supportive evidence for either of these suggestions, particularly as to why they should affect the tempo of puberty as well as the timing.

## Problems with the evidence for earlier puberty

The conclusions from the British data must be treated with caution because of possible observer bias. The ALSPAC study obtained data on pubertal status at age 8 years by mailed questionnaires to mothers and daughters. The response rate has not been published and cannot be assumed to be sufficient to draw any conclusions from. The questionnaire contained line drawings and one sentence descriptions of each pubertal stage. There has been no published validation of maternal report of pubertal status against physician ratings. Attempts have been made to validate self report of pubertal stage by adolescents, but findings vary.14 15 A recent study which used the same line drawings as did ALSPAC, and was conducted in paediatric endocrine clinics where physician rating is routine and highly consistent, found that while 88% of children self rated to within 1 Tanner stage for pubic hair, only 49% correctly identified their pubic hair stage.16

The key issue for us is the accuracy of reporting the transition from stage 1 (prepubertal) to stage 2 for either breast or pubic hair development. Other studies have found that younger children tend to overestimate their development while older adolescents tend to underestimate it.14 This was reflected in the Taylor et al study<sup>16</sup> where the direction of error for the difference between stage 1 and 2 for both pubic hair and breast development was for children to markedly over-rate themselves as pubertal when they were not. Thus the direction of error in ALSPAC was likely to have been towards over-reporting of early pubertal changes by mothers and daughters. A further possible bias in the same direction was introduced by the instructions for the ALSPAC questionnaire notifying mothers that body changes could happen as early as 6 years of age.

Methodological problems with the cross-sectional study undertaken by Herman-Giddens and colleagues include both selection bias and observer bias. Cross sectional studies provide limited data on longitudinal processes such as pubertal development,<sup>17</sup> although the cross sectional status quo methodology is well accepted for calculation of median age of menarche.18 The study was not population based and included many subjects who presented for clinical problems that may have included endocrine abnormalities. Additionally, those who presented for well child checks may have included many who had concerns about their child's physical development. Of greater concern, almost 1000 girls of the original 18 549 had missing data and were excluded from analysis, although it is unclear in what direction this would bias findings. The authors acknowledge that selection bias was possible but claim that their large sample size (over 17 000) allows them to generalise their results-a surprising and statistically dubious claim.

Previous studies of puberty in the UK have used one or two highly trained expert observers to minimise interob-

server error.<sup>6 19</sup> The Herman-Giddens study used multiple self selected observers who were not experienced in assessing the pubertal status of large numbers of children. While the authors made attempts to control for bias by training and testing their observers, and quoted acceptable kappa statistics for inter-rater reliability, it is likely that the direction of observer bias in this study is similar to that of mothers and children noted above-that is, over-rating any doubtful cases as stage 2 rather than stage 1. This is particularly so in a study that was clearly set up because of concerns about a lowering of the age of pubertal changes-concerns that would have been transmitted to the participating physicians.

It is possible that the assessment of breast development on inspection alone without palpation may have resulted in an over-rating of obese prepubertal girls as breast stage 2, particularly given the rising incidence of obesity in the USA. Both inspection and palpation of breast tissue was undertaken in 39% of girls in the study, and 15% of those rated as stage 2 by inspection were found to be stage 1 by palpation (communication from authors, published in Kaplowitz and Oberfield<sup>2</sup>). This misclassification was the same in girls in the highest and lowest body mass index quartiles, suggesting that it is not fatty pseudobreasts that are at issue, but rather that visual inspection alone overestimates breast development at the transition from Tanner stage 1 to stage 2.

#### THE EVIDENCE FOR STABILITY IN THE AGE OF PUBERTY

The strongest arguments that there has been no change in the age of puberty come from detailed longitudinal studies of puberty, and from general agreement that the secular trend in age of menarche ceased in the UK and USA four decades ago. The most recent expert observer longitudinal studies of the age of puberty in the UK, undertaken through the 1980s,<sup>5</sup> <sup>6</sup> show that there has been almost no change in age of onset of puberty or progress through puberty for girls or boys since Tanner and Marshall's study in the 1960s. In the USA, recent studies of puberty in boys and girls suggest that the timing of pubertal development has changed little, if at all, since the Tanner and Marshall studies.<sup>11 20 21</sup>

As a single discrete event not subject to observational errors, age of menarche as determined by status quo or longitudinal methods is regarded as the gold standard for assessment of maturity in female populations. There is universal agreement that there has been no fall in the age of menarche in the USA, UK, and most developed countries for four decades.<sup>8 11 22</sup> Estimates of age of menarche published within the past year are 12.9 years in the UK,<sup>23</sup> and in the USA, 12.7 years for white girls and 12.0 years for black girls.<sup>20</sup>

Interestingly, Herman-Giddens and colleagues' data confirmed this yet again—suggesting that their methodology was more appropriate for the determination of age of menarche than for the timing of the beginnings of puberty.

### CONCLUSIONS

Evidence from two large but methodologically flawed studies suggests that there has been a lowering of the age at which we first see pubertal development in girls. Balanced against this is an extremely strong consensus that there has been no change in the most robust indicator of puberty (age of menarche), and evidence from smaller but methodologically sound single observer studies that there has been no change. The methodologically more robust menarche data from the Herman-Giddens and colleagues study also support the "no change" position. Thus the balance of evidence clearly suggests that there has been no change in the timing or the tempo of true puberty.

A further major problem with the hypothesis of earlier pubertal changes is the lack of biological plausibility for a lengthening of the pubertal process, given the rock solid evidence for no change in age of menarche. The mechanisms for activation of the gonadostat are not well understood, but involve genetic, nutritional, central, and possibly environmental factors.<sup>24</sup> It is well recognised that the timing and tempo of puberty in an individual are separate concepts, and the length of puberty can vary from two to four years in duration. The pubertal process may be lengthened by factors known to delay puberty that begin to operate after the initiation of puberty-these include malnutrition, chronic illness, partial gonadotrophin deficiency, gonadal failure, severe psychosocial stress, and excessive exercise.24 However, it is difficult to postulate factors that may lengthen puberty at a population level.

What then is being reported by parents, teachers, US primary care paediatricians, and mothers of the ALSPAC cohort? The first answer lies in observer error—the over interpretation of small amounts of fine hair on the pubes and the over-rating of breast development by inexperienced raters. This almost undoubtedly has occurred in both studies because of methodological inadequacies.

The second answer is that what is being reported is previously unrecognised levels of premature adrenarche (isolated pubic hair development) and premature thelarche (isolated breast development). It is important to note that breast development and pubic hair development in girls are biologically separate processes that are usually, but not inherently, congruent in timing or tempo. Isolated breast development and isolated pubic hair development become apparent when the timing of the two processes is sufficiently different to be noted by observers. Because of this, it is erroneous and misleading to lump together breast stage 2 and pubic hair stage 2 as a unified "Tanner stage 2" or "early puberty". Neither alone is fully sufficient to consider that puberty is occurring.

Isolated breast or pubic hair development are separate from true puberty, and (in their classic form) are not associated with acceleration of growth or other secondary sex characteristics. There are no population based studies of the prevalence of either condition, but premature adrenarche is more common in black and Hispanic girls and those of Mediterranean origin.<sup>25</sup> Premature development of both pubic hair and apparent breast tissue are also associated with obesity,<sup>25</sup> which may explain a rising prevalence of both conditions in populations in developed countries.

#### What now is needed?

In spite of the balance of evidence being against a lowering of the age of puberty, such beliefs are becoming widespread. New longitudinal studies of puberty and growth, using a small number of highly trained observers, are needed to robustly determine whether change is occurring. Such studies are expensive, but may also allow us to identify possible changes in the population prevalence of premature thelarche and adrenarche. The identification of premature adrenarche may be particularly important in the light of recent links to later ovarian hyperandrogenism, polycystic ovarian syndrome, and insulin resistance.26

#### PRACTICAL ADVICE FOR THE MANAGEMENT OF SUSPECTED PUBERTAL CHANGES IN YOUNG GIRLS

In the absence of strong evidence for lower norms for sexual development in young girls, we should adhere to previous recommendations that a girl under 8 years and a boy under 9 years with any signs of sexual development should be seen by a paediatric endocrinologist for assessment. This is in conflict with the recent recommendations of the American Lawson Wilkins Pediatric Endocrine Society, who suggest that investigation should only be undertaken if breast or pubic hair changes are seen before age 7 in white girls and before age 6 in black girls.<sup>2</sup>

The purpose of investigations for early sexual changes is to differentiate between relatively benign conditions such as premature thelarche or adrenarche, and those that are more serious-such as idiopathic precocious puberty; brain, gonadal, or adrenal tumour; or congenital adrenal hyperplasia. It is certainly true that, particularly in girls, onset of pubertal development after the age of 6 is relatively benign and unlikely to affect final height.27 However, it remains inappropriate for children with signs of sexual development under these ages to be dismissed as merely early developers. Thanks are extended to Mike Preece, Peter Hindmarsh, Tim Cole, Caroline Brain, and Mehul Dattani for helpful advice.

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