Pelvic ultrasonography in premenarcheal girls: relation to puberty and sex hormone concentrations

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SUMMARY Real time ultrasonography of the pelvic organs was performed on 114 normal premenarcheal girls aged between 2 years and 13 years 11 months. Values were obtained for total uterine length, anteroposterior diameters of the corpus and cervix, corpus/cervix ratio, and uterine and ovarian volumes and the resultant data were grouped according to age. It was concluded that there is no change in uterine size until approximately 7 years of age. Then the uterus begins to enlarge, both in prepubertal girls, in whom this is an age related function, and in pubertal girls, whose uterine growth is influenced not only by age but also by size and, independently of these two factors, by oestriadiol concentrations. The onset of a modification in uterine morphology with a greater enlargement of the corpus than the cervix is also seen at age 7 years. Ovarian maturation begins in the very first years of life and, even in pubertal girls, seems to be influenced by age only and not by hormonal stimuli.

Pelvic ultrasound, a rapid, accurate, and non-invasive technique, is increasingly widely used in paediatric endocrinologic gynaecology for the investigation of disorders such as precocious puberty, telarche, amenorrhoea etc. Standard for normal uterine and ovarian morphology and biometry at various ages are essential, however, if ultrasound is to be used to best effect. Although there have been several recent reports on normal values in children and adolescents, too few subjects were studied and they had not been properly selected. Furthermore, these studies are all based on static scanning methods which often do not allow proper visualisation of the ovaries.

We used a real time mechanical sector scanner to evaluate uterine and ovarian size in a large number of normal premenarcheal girls strictly grouped according to age. In addition, we studied the relation between these parameters and puberty and sex hormone concentrations.

Patients and methods

A total of 114 premenarcheal girls, whose ages ranged from 2 years to 13 years 11 months, were studied after informed parental consent had been obtained. They were all suffering from minor, non-endocrinologic, acute pathology. Each girl was evaluated for the following: weight, height, pubertal stage (breast) according to Tanner, and bone age according to Greulich and Pyle's atlas. Blood samples were also taken to determine basal concentrations of oestriadiol (EIR Switzerland); progesterone (MMI Italy); testosterone; and luteinising hormone, follicle stimulating hormone, and prolactin (BIODATA kits).

All the girls were considered normal according to the following criteria; height and weight between the 3rd and 97th centile according to Tanner, bone age retarded or advanced by less than two standard deviations according to Greulich and Pyle's atlas, and basal hormone concentrations, calculated by our laboratory, within the normal range for age. The ultrasound examinations were performed with the conventional full bladder technique, obtained by voluntary urine retention and oral administration of fluids one hour beforehand. Sedation or catheterisation were never required. A 3-5 MHz mechanical sector scanner (SRT, General Electric) with electronic calipers calibrated to a velocity of 1540 m/second was used. Longitudinal (L), anteroposterior (AP), and transverse (T) diameters of the uterus as a whole, the corpus and cervix separately, and of the ovaries were measured. The formula for a prolate ellipsoid \(V=L \times AP \times T \times 0.5233\) was used to calculate the volume of both the uterus and ovaries. The ratio AP corpus/AP cervix was also determined.

Complete or partial visualisation of the pelvic
structures was generally possible if the bladder was sufficiently filled and the patient willing to cooperate. The uterus and vaginal canal were visualised in all cases, while the ovaries were visualised on at least one side in 89·5% (93·5% in girls over 5 years and 81·1% in girls below this age).

Linear, simple, or partial regression and Student's $t$ test were used in the statistical analysis of the results. In preparing statistics only uterine and ovarian volume were considered. Although approximate these were sufficiently representative of all the diameters examined.

Results

Uterus. Table 1 shows the mean values for uterine volume grouped according to chronological age. There were no significant changes during the first years of life but between age 6 and 8 years a progressive increase in uterine size was noted. There was a significant difference between the mean volume of the uterus in girls aged 6 and 7 years considered together and that of girls aged 8 and 9 years considered together ($P<0.01$).

The growth of the uterus at this age is more evident in the corpus than in the cervix and indicates a morphological modification in the uterus itself, as is also shown by the progressive increase in the corpus/cervix ratio with age (Figure).

When prepubertal and pubertal girls over 8 years of age were considered separately (Table 1), there was a statistically significant difference in uterine volume between the two groups ($P<0.001$, in girls aged 8 to 13 years and $P<0.025$ in girls aged 9 to 11 years). In the latter group the number of pubertal and prepubertal girls was practically the same. In the age range 8 to 9 years, however, there was no difference between pubertal and prepubertal girls, but the higher number of prepubertal girls might have altered this result. From age 7 years uterine volume increased progressively with age, even in prepubertal girls.

In Table 2 pubertal girls are grouped according to pubertal stage (breast). A significant increase in uterine volume ($P<0.05$) was noted only after pubertal stage B3.

Table 3 summarises the correlations between uterine volume and chronological age, bone age, and pubertal stage. There are no significant correlations between uterine volume and bone age. The correlations between uterine volume and chronological age, bone age, and pubertal stage are statistically significant. The highest correlation is observed between uterine volume and chronological age. The correlation between uterine volume and bone age is lower than the correlation between uterine volume and chronological age. The correlation between uterine volume and pubertal stage is also statistically significant.

![Figure Ratio between anteroposterior diameter of the corpus (COAP) and the cervix (CEAP) evaluated in 114 premenarcheal girls.](http://adc.bmj.com/)

Table 1  Uterine volume in relation to chronological age and puberty (values, mean (SD))

<table>
<thead>
<tr>
<th>Chronological age (years)</th>
<th>Uterine volume (cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pubertal and prepubertal girls</td>
</tr>
<tr>
<td>2*</td>
<td>1.98 (1.58)</td>
</tr>
<tr>
<td>3</td>
<td>2.54 (1.81)</td>
</tr>
<tr>
<td>4</td>
<td>2.20 (1.57)</td>
</tr>
<tr>
<td>5</td>
<td>2.36 (1.39)</td>
</tr>
<tr>
<td>6</td>
<td>1.80 (1.57)</td>
</tr>
<tr>
<td>7</td>
<td>2.32 (1.07)</td>
</tr>
<tr>
<td>8</td>
<td>3.12 (1.52)</td>
</tr>
<tr>
<td>9</td>
<td>3.69 (1.62)</td>
</tr>
<tr>
<td>10</td>
<td>6.54 (3.78)</td>
</tr>
<tr>
<td>11</td>
<td>6.66 (2.97)</td>
</tr>
<tr>
<td>12-13</td>
<td>14.82 (7.57)</td>
</tr>
</tbody>
</table>

*This age group includes girls aged between 2.0 and 2.99 years. This grouping is also valid for subsequent ages.
Table 3  Positive correlations between uterine volume and age, growth data, and basal sex hormone concentrations according to chronological age groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Chronological age</th>
<th>Bone age</th>
<th>Growth data (weight, height, body surface)</th>
<th>Oestradiol</th>
<th>Progesterone</th>
<th>Testosterone</th>
<th>Luteinising hormone</th>
<th>Follicle stimulating hormone</th>
<th>Prolactin</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (2-7y)</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>n=55</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (8-13y)</td>
<td>r=0.687§</td>
<td>r=0.637§</td>
<td>r=0.580§</td>
<td>r=0.615§</td>
<td>r=0.422§</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>n=59</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2A</td>
<td>(prepubertal)</td>
<td>(8-13y)</td>
<td>n=25</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2B</td>
<td>(pubertal)</td>
<td>(8-13y)</td>
<td>n=34</td>
<td>r=0.612§</td>
<td>r=0.689§</td>
<td>r=0.651§</td>
<td>r=0.654§</td>
<td>r=0.407*</td>
<td>NS</td>
</tr>
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<td></td>
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</table>

*P<0.05; †P<0.01; ‡P<0.025; §P<0.01.

growth data, and basal hormone concentrations. In the 2 to 7 years age range (group 1) there were no correlations, confirming that the uterus does not enlarge until that age. Girls above the age of 8 years (group 2), however, showed a significant correlation between uterine volume and chronological age, bone age, growth data, and oestradiol, progesterone, and testosterone concentrations. When the girls in this age group were divided into pubertal and prepubertal subgroups, the same significant correlations were seen only in those who had reached puberty (group 2B), while the prepubertal girls (group 2A) showed significant correlations between uterine volume and age and growth data, but not hormone concentrations.

The application of partial linear regression analysis makes these correlations clearer; prepubertal girls aged 8 to 13 years show a correlation simply between uterine volume and age, and not growth, whereas pubertal girls show a correlation between uterine volume and both age and size. Furthermore, this latter group shows a correlation between uterine volume and oestradiol but not progesterone and testosterone. This particular correlation still exists even when the influence of age and size are excluded.

Ovaries. Table 4 gives mean ovarian volume values for the various age groups. Ovarian volume starts to increase at an early age, although it was not possible to define exactly when. There was, however, a significant difference between the mean ovarian volume of girls aged 2 to 4 years considered together and those aged 5 to 7 years considered together (P<0.005).

In girls aged 8 to 13 years, a greater number of whom were pubertal (31 pubertal and 24 prepubertal), ovarian volume was significantly greater (P<0.01) in pubertal girls (mean (SD), 2.78 (1.52)) than in prepubertal girls (1.77 (0.92)). On the other
Pelvic ultrasonography in premenarcheal girls

Table 5  Correlations between ovarian volume and age, growth data, and basal sex hormone concentrations in relation to chronological age

<table>
<thead>
<tr>
<th>Groups</th>
<th>Chronological age</th>
<th>Bone age</th>
<th>Growth data (weight, height, body surface)</th>
<th>Oestradiol</th>
<th>Progesterone</th>
<th>Testosterone</th>
<th>Luteinising hormone</th>
<th>Follicle stimulating hormone</th>
<th>Prolactin</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(2-7y) n=46</td>
<td></td>
<td></td>
<td>r=0.0-495$</td>
<td></td>
<td></td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>2</td>
<td>(8-13y) n=55</td>
<td></td>
<td></td>
<td>r=0.699$</td>
<td></td>
<td></td>
<td>r=0.0-309*</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>r=0.432†</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>2A</td>
<td>(prepubertal) (8-13y) n=24</td>
<td></td>
<td></td>
<td>r=0.609§</td>
<td></td>
<td></td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>2B</td>
<td>(pubertal) (8-13y) n=31</td>
<td></td>
<td></td>
<td>r=0.640§</td>
<td></td>
<td></td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

*P<0.05; †P<0.025; ‡P<0.01; §P<0.001.

hand, in the group aged 9 to 11 years, in which the number of pubertal girls (19) was not substantially greater than the number of prepubertal girls (16), this difference no longer existed (mean (SD), 2.27 (0.81) in pubertal girls v 2.09 (1.09) in prepubertal girls).

If the pubertal girls are divided according to pubertal stage (breast) (Table 2) a statistically significant increase (P<0.0025) in ovarian volume may be observed only after stage B3.

Table 5 shows the correlations between ovarian volume and chronological age, bone age, growth data, and basal hormone values. A statistically significant correlation is evident in the 2 to 7 years age group between ovarian volume and chronological age, bone age, and growth data. These same significant correlations were also found in the 8 to 13 years age group in which there was also a significant correlation between ovarian volume and basal oestradiol (P<0.05) and testosterone (P<0.01) concentrations. The correlation with these hormones, however, is no longer present in the 8 to 13 years age group if prepubertal and pubertal subjects are evaluated separately. If partial linear regression analysis is applied it is found that age alone is correlated with ovarian volume, both in girls aged 2 to 7 years and in those prepubertal and pubertal subjects aged 8 to 13 years.

Table 4 also shows that in a small percentage of girls functional ovarian microcysts (<9 mm) may be observed at an extremely early age. This percentage increases with age and measurable macrocysts (>9 mm) are found in girls aged 12 to 13 years, even where there is no menstrual cycle.

Discussion

According to anatomical studies,12 13 after the postnatal regression of the uterus probably caused by the interruption of hormonal stimulation from the mother, the anatomy of the uterus does not change appreciably until puberty. This was confirmed by Sample et al5 in an ultrasound study of 20 normal prepubertal girls aged 1 to 12 years, although these authors admitted that they used too few subjects to reach a totally valid conclusion. Similar findings were obtained by Ivarsson et al,7 who considered that the mean uterine size (determined by ultrasound) in a small number of 7 year old girls agreed with anatomical data. Indeed, this report7 indicated a significant correlation between uterine volume and pubertal stage (evaluated according to Tanner), although no definite information was given on the pubertal stage of the girls examined.

Our data are not in absolute agreement with those of the above authors, but we must point out that our study is not comparable in that we examined a far greater number of girls, and, importantly, grouped them into small age ranges. We were thus able to determine that there is no modification in uterine size until approximately 7 years of age. In fact there are no differences in mean uterine volume from 2 to 7 years of age. Furthermore, no correlation is apparent in this age group between uterine volume and age or size of the subject.

From age 7 years, however, there is a slow, progressive increase in the size of the uterus, as is shown by the significant differences in mean uterine

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volume and after this age and by significant correlations between this volume and the age and size of the subject, in girls over 8 years. From 7 years of age it is important to note how the uterus matures gradually in prepubertal girls, in whom no secondary sexual features have, as yet, appeared. This is shown by the partial positive correlation between uterine volume and age also seen in prepubertal girls (Table 3) over the age of 8 years. It would, therefore, seem that unlike most organs in the body, which grow with the body, the uterus, like the external genitalia, starts to increase appreciably in size only at puberty. The fact that this also occurs in prepubertal girls may mean that uterine growth is the very first sign of puberty in girls, occurring even before breast development becomes visible. When secondary sexual features, particularly breast development, appear, there is a greater increase in uterine size which is no longer solely related to age, but also to size and hormonal stimuli, above all of oestadiol. In girls over the age of 8 years there is a significant difference in uterine volume between prepubertal and pubertal subjects. Furthermore, only in pubertal girls is there a significant partial correlation between uterine volume and oestadiol concentration which is independent of age and size. The uterus grows more quickly at puberty than the body as a whole: in the space of only a few years uterine size increases by approximately five or six times. According to our data, these changes in uterine size are more striking at a particular phase of puberty, that is between stage B3 and B4. The low number of subjects studied, however, makes further investigation necessary.

The changes in uterine morphology, with an increase in the size of the corpus relative to the cervix, have already been reported in both anatomical\textsuperscript{12,13} and in ultrasound studies,\textsuperscript{5} although we believe that this modification may already be observed before puberty and not only at puberty itself. With regard to the ovaries, the high percentage of visualisation confirms the findings of Sample\textit{et al}\textsuperscript{5} but not of Ivarsson\textit{et al}\textsuperscript{7} There may be a number of reasons why the ovaries cannot be observed in certain subjects. Small, homogeneous ovaries are often indistinguishable from muscle and other echogenic pelvic structures, while the pelvis in younger patients may be of a small size. The ovaries may be stretched out of the pelvis by either a distended bladder or a full rectum, or both. Poor bladder control may also be a contributory factor. Both Simkins' anatomical data\textsuperscript{14} (although not confirmed by ultrasound data\textsuperscript{5}) and our findings show that ovarian growth is correlated with age from very first years of life. There is also a significant partial correlation between ovarian volume and chronological age in the 2 to 7 years age group. After this age, the ovaries continue to mature progressively. Ovarian maturation seems influenced solely by age and hormonal stimuli do not seem to play any important part. This is shown by the absence of correlations, even in pubertal girls, between ovarian volume and basal sex hormone concentrations.

Finally, according to our data microcysts may be normal even during the first years of life, but become much more common later in the premenarcheal period, as has been reported by others.\textsuperscript{5}

We conclude that the ovaries begin maturation in the very first years of life, apparently independently of hormonal stimuli and in line with biological maturity. The uterus does not change until approximately 7 years chronological age when it slowly increases in volume. Initially there seems to be no relation between either sex hormones present in the blood or the development of secondary sexual features, but only with age. Our study does not allow us to identify the trigger in this maturation and we can only offer two hypotheses. Firstly, it may be a question of adrenal steroids, the secretion of which begins to increase exactly at this age,\textsuperscript{15} and secondly there may be small transient peaks in the oestrogen concentration, originating from the ovaries, which we are unable to detect by a single assay and which are not sufficient to stimulate mammary tissue and give rise to breast development. At later ages, when secondary sexual features have already appeared, it is above all oestadiol which completes uterine maturation.

References
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\end{enumerate}
Pelvic ultrasonography in premenarcheal girls


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Received 12 November 1984

Fifty years ago

The early anaemia of premature infants: the haemoglobin level of immature babies in the first half-year of life and the effect during the first three months of blood injections and iron therapy


'Observations were made at the Mother's Hospital, London, on the haemoglobin level of 150 infants during the first half year of life: the lowest average haemoglobin level reached by the babies weighing three pounds odd at birth (72·2 per cent.) was only six per cent. lower than that of those weighing eight and nine pounds at birth (78·6 per cent.); the total drop of the three-pound group was, however, considerably greater than that of the eight and nine-pound group.'

'No influence on the extent of the drop in haemoglobin level in the first two to three months of life was observed as a result of giving an intramuscular injection of 15 c.c. of citrated human blood within the first three days of life, nor from the administration of iron and ammonium citrate by mouth. None of those weighing five pounds and less at birth dropped below 63 per cent.'

(Dr Helen Mackay, who was a member of the staff of the Medical Research Council, the first woman to be elected a Fellow of the Royal College of Physicians, and the first Honorary Paediatrician to the Mother's Hospital, Clapton, was renowned for her work on dietary deficiencies in infants and children. The larger numbers of very immature and small infants now surviving have led to renewed concern for the anaemia of the preterm infant and its treatment; though the mechanisms underlying the excessive fall in haemoglobin, unknown in Dr Mackay's day, are now better understood. It is perhaps fortunate she could not find an advantage for the giving of intramuscular blood, for had she done so, more infants might have become sensitised in the few remaining years before the discovery of the Rhesus factor. PAMELA A DAVIES.)
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Arch Dis Child 1985 60: 120-125
doi: 10.1136/adc.60.2.120

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