SCOLIOSIS AND FRACTURES IN YOUNG BALLET DANCERS

Relation to Delayed Menarche and Secondary Amenorrhea

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Abstract In a survey of 75 dancers (mean age, 24.3 years) in four professional ballet companies, we found that the prevalence of scoliosis was 24 percent and that it rose with increases in age at menarche. Fifteen of 16 dancers (93 percent) with scoliosis had a delayed menarche (14 years or older), as compared with 31 of 57 dancers (54 percent) without scoliosis (P < 0.04). The dancers with scoliosis had a slightly higher prevalence of secondary amenorrhea (44 percent vs. 31 percent), the mean (±SD) duration of their amenorrhea was longer (11.4 ± 18.3 vs. 4.1 ± 7.4 months; P < 0.05), and they scored higher on a questionnaire that assessed anorectic behavior.

The incidence of fractures was 61 percent (46 of 75 dancers), and it rose with increasing age at menarche. Sixty-nine percent of the fractures that were described were stress fractures (mostly in the metatarsals), and their occurrence had an even stronger correlation with increased age at menarche. The incidence of secondary amenorrhea was twice as high among the dancers with stress fractures (P < 0.01), and its duration was longer (P < 0.05) in 7 dancers in whom endocrine studies were performed. The amenorrheic intervals were marked by prolonged hypoestrogenism.

These data suggest that a delay in menarche and prolonged intervals of amenorrhea that reflect prolonged hypoestrogenism may predispose ballet dancers to scoliosis and stress fractures. (N Engl J Med 1988; 314:1353.)

Prolonged hypoestrogenism is a recognized complication of dieting, weight loss, and physical training in young women. A high incidence of delayed menarche, secondary amenorrhea, and irregular menstrual periods has been observed in young ballet dancers.1 Dieting is common among classical dancers,2,3 and restricting weight is necessary to conform to a thin body image. In addition, classical dancers begin their training early in life, usually before adolescence. Dieting and early physical training are known to delay menarche. Altered skeletal proportions have been observed in classical dancers,1 although no permanent medical problems have been reported. Because the secretion of gonadal steroids, particularly estrogen, has important physiologic effects on bone,4,5 which include stimulating epiphyseal closure and decreasing bone turnover, we examined the incidence of skeletal aberrations in ballet dancers, who may have alterations in estrogen secretion during an important phase of their growth and development.

Methods

Subjects

We surveyed 75 female dancers in four highly competitive professional ballet companies of national standing. The survey was conducted on a volunteer basis (no selection); the entire membership of the four companies was approached. The mean age (±SD) of the dancers was 24.3 ± 4.1 years (range, 18 to 36). A questionnaire requesting information on age, height, weight, age at menarche, history of amenorrhea, and hours danced per week was distributed. Amenorrhea was defined as the absence of a spontaneous menstrual period for five or more months. The dancers were also asked whether they had experienced any injuries or fractures. Forty of the 75 dancers also answered more detailed questions about the type of injury (stress or nonstress fracture) that was confirmed by the subjects' orthopedic surgeons. Stress fractures were defined as fractures that presented in the absence of acute trauma, that were diagnosed by an orthopedic surgeon on the basis of symptoms, and that were confirmed by an x-ray examination or bone scan. Fifty-one of the 75 dancers volunteered to fill out a detailed questionnaire that assessed anorectic behavior. Ten of the 75 dancers volunteered to have their endocrine status studied longitudinally.

Demographics

The educational levels of the subjects and their parents were estimated with the seven-point scale developed by Hollingshead and Redlich.6 All the dancers were white, and all were from families that were lower-middle class to upper class. Birth order and the year when dance training was begun were also determined. All subjects began dancing when they were seven to eight years old. Data about the type of dance training was obtained from two nonto companies that had similar competitive characteristics, reported rehearsal schedules, and hours danced per week.

Medical and Endocrine Studies

Ten dancers from one company had their endocrine status evaluated longitudinally. None were taking exogenous estrogens or contraceptives. Assays for luteinizing hormone, follicle-stimulating hormone, and prolactin were performed as previously described. Vaginal smears were performed as an index of estrogen secretion and medroxyprogesterone (Provera; 10 mg per day for five days) was administered to test for endogenous estrogen secretion.

Fifteen of the 18 subjects with scoliosis and all 18 known to have had stress fractures had blood samples drawn for assessments of levels of total serum calcium, inorganic phosphorus, albumin, alkaline phosphatase, N-terminal-specific parathyroid hormone, C-terminal midmolecule parathyroid hormone, 25-hydroxyvitamin D (25-OH-D), and 25-dihydroxyvitamin D (1a,25(OH)2D). The levels of parathyroid hormone were determined by a previously described radioimmunoassay,7 with the use of a chian antiserum directed against the biologically active amino terminal (N-terminal) portion of the parathyroid hormone molecule (parathyroid hormone 1-34).8,9 A C-terminal midmolecule-specific radioimmunoassay was also used; it employed an antiserum directed against a human parathyroid hormone that measures primarily fragments of parathyroid hormone.10 Levels of 25-OH-D and 1a,25(OH)2D were determined by the method of Fraher et al.11

Physical and X-Ray Examinations

Fourteen dancers with structural scoliosis were assessed by x-ray examination; an additional four dancers reported scoliosis, and al-
In an x-ray film could not be obtained, the presence of a structural scoliosis was confirmed by an orthopedic surgeon. Thus, a total of 18 subjects had scoliosis. Three subjects had previously undergone radiographic examination of the wrist to determine bone age (as part of a growth evaluation). All fractures and stress fractures were diagnosed by an orthopedic surgeon and were confirmed by an x-ray examination or a bone scan.

None of the dancers with scoliosis had a history of neurologic disease (either congenital or acquired) or of other abnormalities that have been implicated in scoliosis, including disorders of the anterior or effector pathways of the spinal cord, disorders of visual and vestibular function, midbrain dysfunction, muscle disease, and abnormalities of collagen formation.

Dieting Problems

Dieting problems were assessed in three ways. First, the subjects were asked whether they had ever had anorexia nervosa or bulimia. They were also asked about their use of laxatives and purging. Second, the subjects filled out a short version of "EAT-26," an eating-problems scale developed by Garner and Garfinkel. The EAT-26 consists of three subscales (dieting, bulimia, and oral control). The oral-control subscale measures attempts to control the intake of food, and the subjects' preoccupation with this activity. The 15-item version of EAT-26 that was used in this study included 10 items from the dieting subscale, 5 from the bulimia subscale, and 4 from the oral-control subscale. The subjects were asked to rate each item on a six-point scale by providing answers that ranged from "describes me not at all" to "describes me very well." Scores were scaled blindly for each of these subscales individually and for all of them together. Convergent validity of the scale in dancers has been obtained; this version of the EAT-26 was related to body weight and self-reported anorexia nervosa.

Third, the subjects were asked to indicate whether six types of behavior typically used to identify anorexia were characteristic of them. These included deliberate weight loss, amenorrhea, overdensity without enjoyment, feeling terrified of fat, feeling fat although others had said they were too thin, and being obsessed with thoughts of food. The presence or absence of each of these types of behavior was noted and expressed in terms of a score of 0 to 6 on a scale of anorexia. These findings were also related to the reports of anorexia nervosa. Thus, the EAT-26 and the anorectic scale were used as partly validating checks on the reports of eating problems.

Height-Weight Relations and Menarche

Ideal weights were obtained from tables of weight-height ratios for young adults (ages, 17 to 34). These tables are based on measurements of 160,000 students who entered college in the United States in 1948 to 1950. Ideal height for weight was based on data on 18-year-olds that were compiled by the National Center for Health Statistics, Health Resources Administration. Leaness was determined by weight-height ratios.

Menarche was considered delayed if it occurred at age 14 or older. The mean (+SD) reported age of menarche in the United States is 12.5±1.2 years.

Statistical Analysis

Linear-regression analyses (Pearson's r) were performed on the data with the use of a stepwise-regression computer program. The regressions were based on straight frequency distributions, rather than on relative frequency distributions. The two-tailed Student's t-test was used for statistical analysis. The chi-square test was used to determine the independence of two variables.

Results

The prevalence of scoliosis in this group was 24 percent—a almost a quarter of the sample (Table 1). Although all the dancers had undergone menarche, it had been delayed by an average of two years. The mean age at menarche of 14.5±2.1 years that we observed is considerably older than the mean of 12.9±0.1 reported for girls in the United States. The dancers with scoliosis had a significant increase in delayed menarche (14 years old or older) over those without scoliosis (83 vs. 17 percent; P<0.04). The relation between the delayed menarche and scoliosis is shown in Figure 1 and Table 2. Of the 18 dancers with scoliosis, 15 (83 percent) were 14 or older at menarche, whereas only 31 of the 57 dancers without scoliosis (54 percent) had had a delayed menarche (P<0.04). The correlation between the age at menarche and the prevalence of scoliosis was significant (r = 0.25, P<0.03); thus, the frequency distribution (Table 2) showed that the frequency of scoliosis rose with an increase in age at menarche.

More dancers with secondary amenorrhea had scoliosis (44 vs. 31 percent), but this difference did not reach statistical significance. However, those with secondary amenorrhea and scoliosis had longer inter-

Table 1: Clinical Data on 75 Dancers Surveyed.*

<table>
<thead>
<tr>
<th>Subject Group</th>
<th>No. (%)</th>
<th>Age (yr)</th>
<th>Age at Menarche (yr)</th>
<th>Weight (kg)</th>
<th>Height (cm)</th>
<th>Weight-Height Ratio</th>
<th>% of Ideal Weight</th>
<th>% of Ideal Height</th>
<th>Menarche &gt;13 Mo</th>
<th>EAT Score†</th>
<th>P&lt;0.05</th>
<th>NS</th>
<th>P&lt;0.01</th>
<th>NS</th>
<th>P&lt;0.05</th>
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<tr>
<td>Subjects</td>
<td>75</td>
<td>24.3±4.1</td>
<td>14.5±2.1</td>
<td>50.2±3.9</td>
<td>167.6±4.6</td>
<td>1.7±0.1</td>
<td>86.8±4.4</td>
<td>102.8±2.4</td>
<td>40 (53)</td>
<td>2.28±0.951</td>
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<tr>
<td>With fractures</td>
<td>18 (24)</td>
<td>22.8±4.0</td>
<td>15.2±2.0</td>
<td>51.2±5.0</td>
<td>169.7±4.1</td>
<td>1.7±0.1</td>
<td>86.5±5.8</td>
<td>103.5±2.9</td>
<td>8 (44)</td>
<td>2.59±0.381</td>
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<td>Without fractures</td>
<td>57 (76)</td>
<td>24.7±4.0</td>
<td>14.3±2.1</td>
<td>49.9±3.5</td>
<td>167.1±4.6</td>
<td>1.7±0.1</td>
<td>86.9±4.0</td>
<td>102.4±2.5</td>
<td>18 (31)</td>
<td>2.14±1.014</td>
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<td></td>
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<tr>
<td>With fractures</td>
<td>46 (61)</td>
<td>24.5±4.2</td>
<td>14.9±1.9</td>
<td>50.3±3.9</td>
<td>168.1±5.1</td>
<td>1.7±0.1</td>
<td>87.0±4.1</td>
<td>102.9±3.0</td>
<td>17 (37)</td>
<td>2.61±0.901</td>
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<tr>
<td>Without fractures</td>
<td>29 (39)</td>
<td>23.7±3.3</td>
<td>14.0±2.1</td>
<td>49.9±0.04</td>
<td>167.1±3.3</td>
<td>1.7±0.1</td>
<td>86.3±4.2</td>
<td>102.2±1.8</td>
<td>8 (27)</td>
<td>2.78±0.911</td>
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<td>With fractures</td>
<td>18 (45)</td>
<td>23.0±3.6</td>
<td>15.6±2.3</td>
<td>49.1±4.2</td>
<td>167.4±5.8</td>
<td>1.7±0.1</td>
<td>85.3±3.1</td>
<td>102.8±3.4</td>
<td>12 (67)</td>
<td>2.38±0.531</td>
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</tr>
<tr>
<td>Without fractures</td>
<td>22 (55)</td>
<td>24.0±3.2</td>
<td>14.0±1.9</td>
<td>50.9±4.3</td>
<td>168.9±4.1</td>
<td>1.7±0.1</td>
<td>85.3±3.1</td>
<td>102.8±3.4</td>
<td>6 (27)</td>
<td>2.72±0.77</td>
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</tbody>
</table>

*Plus-or-minus values are means ±SD; NS denotes not significant.†Scores are based on the four items in the oral-control subscale of the EAT scale, which measures anorectic behavior.

Based on a survey of 51 dancers.
vals of amenorrhea (11.4±1.8 vs. 4.1±1.7 months; P<0.05; Table 3) than those who did not have scoliosis. In addition, the dancers who reported both secondary amenorrhea and scoliosis had a later menarche than those with normal menstrual periods and no scoliosis (15.8±2.9 vs. 13.9±2.2 years; P<0.01).

The subjects with scoliosis were taller than those without scoliosis, with the average difference being about 2.5 cm (169.7±4.0 vs. 167.1±4.6 cm; P<0.05). Since the dancers with scoliosis were slightly heavier (51.2 vs. 49.9 kg), the ratio of the height to weight was the same in the two groups — i.e., 1.7±0.1. The incidence of scoliosis was related to height (r = 0.24, P<0.04), as well as to age at menarche (r = 0.25, P<0.03). When we used partial correlations and multiple regressions to examine the relation between age at menarche and scoliosis while controlling for height, we found that the correlation between age at menarche and scoliosis decreased (from r = 0.25 to r = 0.22) but that it remained within the range of significance (P<0.05).

There was no correlation between height and duration or incidence of amenorrhea in the dancers with scoliosis. When the dancers with neither scoliosis nor amenorrhea (n = 10) were compared with those with both scoliosis and amenorrhea (n = 8), the difference in their heights was not significant, although the dancers with scoliosis and amenorrhea were taller (168.4±4.6 vs. 171.2±2.8 cm).

In the analysis of eating attitudes, the dancers with scoliosis were found to have more deviant eating behavior than the dancers without scoliosis, as judged by the scores on the oral-control scale (2.59±0.58 vs. 2.14±1.05; P=0.05; Table 1). The scores on the other sections of the eating problems assessment showed no differences between the two groups.

The incidence of scoliosis in the families of the dancers with scoliosis was 28 percent of 18), whereas the incidence in the families of other dancers was 4 percent (2 of 57; P<0.01).

A high incidence of fractures occurred in the sample of 75 dancers (46 dancers, or 61 percent; Table 1). Forty of the 75 dancers were asked specific questions about the nature of their fractures. Thirty-two fractures were reported; of these, 27 (69 percent) were stress fractures that occurred in 18 dancers, thereby yielding an overall incidence of 45 percent (18 of 40 dancers). Most of the stress fractures were in the metatarsals (26 of 27 stress fractures), although one subject had a stress fracture of the fibula. The incidence of stress fractures among the dancers with delayed menarche was higher than that among those with normal or early menarche (52 vs. 33 percent), but this difference did not reach statistical significance. However, both the incidence of unspecified fractures among all 75 dancers and the incidence of stress fractures in the subgroup of 40 rose significantly with increasing menarchal age (Fig. 2 and Table 4). A analysis of data from the 40 subjects who were asked more specifically about their fractures revealed that the dancers with stress fractures were older at menarche than those without such fractures (15.6±2.3 vs. 14.0±1.9 years; P<0.01). There was also a relation between stress fractures and hypoestrogenic intervals; the incidence of secondary amenorrhea was more than twice as high among those with fractures than among those without fractures (Table 1), and the duration of amenorrhea was longer (Table 3). These differences were significant only in comparisons between dancers with and without stress fractures.

When the data for the entire sample of 75 dancers were analyzed without specification of the type of fracture, the results showed the same trend as the analysis of the stress fractures, but the differences between groups were not statistically significant (Table 1), despite the larger sample size. There were no differences in the number of hours of exercise per week or in the ages at which the dancers began the training between subjects with and without stress fractures.

Among the 40 dancers whose type of fracture was specified, the occurrence of only simple fractures did not show the same relation to age at menarche as to amenorrheic intervals as did the occurrence of stress fractures; however, only a small number of dancers (seven) had had simple fractures.

There was no difference in the EAT findings between dancers with and those without stress fractures.

All dancers, with inorganic alkaline- phosphatase, was no biochemistry was normal (the levels of the thyroid hormone was normal, the range for all but 25-OH- was normal, and the level of 25-OH-Vitamin D was normal). One dancer had normal range of osteoporosis, 25-OH-1-cholecalciferol.

Three subjects were found to have fusion of the vertebral column, and the levels of the thyroid hormone was normal, and the level of 25-OH-Vitamin D was normal. One dancer had normal range of osteoporosis, 25-OH-1-cholecalciferol.
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ners did not correlate with the presence of amen-
orhea or the scores on the EAT scales. The curves
were mild standard right-dorsal curves with minimal
lordoses.
All the stress fractures were in the usual locations,
regardless of whether the dancers had scoliosis.

**DISCUSSION**

Young dancers with a delay in menarche are specific-
ally at risk for scoliosis and fractures, a risk that in-
creases with an increase in age at menarche. Delayed
puberty is a known risk factor for scoliosis, and the
high incidence in our sample reflects this delay. How-
ever, the striking frequency of scoliosis (24 percent)
in this group is well above the expected frequency.
Idiopathic adolescent scoliosis occurs in approxi-
mately 1.8 percent of the general population but in 3.9
percent of white girls. The high incidence of this
problem in dancers may reflect both constitutional
(hereditary) and environmental factors. Scoliosis has a
high familial incidence, and our sample confirms this; it
occurred in 28 percent of the affected dancers' families
but in only 4 percent of the families of those not affect-
ed (P<0.01), suggesting a hereditary influence. The
differences in body type among dancers is remarkable:
the smaller number of dancers in that group.

All dancers had normal levels of serum calcium,
inorganic alkaline phosphatase, and albumin. There
was no biochemical evidence of vitamin D deficien-
cy, and the levels of 25-OH-D (33.5±14.2 ng per milli-
liter) and of 1,25(OH)²D (36.5±9.1 pg per milliliter)
were normal. The levels of both the N-terminal-
specific molecule (16.4±5.6 pg per milliliter) and the
C-terminal midmolecule (159.1±45.5 pg per millili-
ter) of the parathyroid hormone were also normal (the
normal ranges are 11 to 24 and 50 to 330 pg per mil-
aller, respectively) in all dancers except one; she
had a minimally elevated level (29 pg per milliliter)
of the N-terminal-specific parathyroid hormone but
normal levels of the C-terminal–midmolecule para-
thyroid hormone, serum calcium, albumin, phospho-
tus, 25-OH-D, and 1,25(OH)²D.

Three subjects had had radiographic studies of the
wrist for assessments of bone age, and all had been
found to have a delay in bone age of two to four years.
Although all the subjects had ceased growing, 2 of the
14 who had spinal x-ray evaluations for scoliosis had
no fusion of the iliac apophyseal plates at age 19.

There was no history or evidence of spinal anom-
alias or unusual back pain in any of the subjects with
scoliosis. The mean degree of curvature (±SD) was
16.5±8.5 degrees (range, 10 to 30). The degree of
correction
girls, with a delay in bone development, may favor long-bone growth that leads to eunuchoid proportions, such as those in persons with hypogonadotropic hypogonadism. Hypoestrogenism could also delay maturation of the osseous centers in the spine and predispose a person to vertebral instability and curvature. A delay in bone development associated with delayed menarche and secondary amenorrhea has been reported in ballet dancers who restrict their weight and exercise heavily.1 Three of the dancers in our study who had their bone ages determined had a delay in skeletal maturity, and two of the dancers with scoliosis had no fusion of the iliac apophyseal plates at age 19. Since training for the ballet begins at a young age and much of it takes place during the adolescent years, and since dieting to maintain a low body weight is common among dancers, ballet dancers as a group are most likely to have the effects of delayed sexual maturation on the growing skeleton.

The dancers with scoliosis were taller than the others, thus implicating a hereditary factor in scoliosis. Taller persons may be "at risk" for scoliosis because of prolonged growth spurts and important environmental factors. This increase in height among persons with scoliosis has been noted by others.23 A longer growth period may predispense dancers to scoliosis. The effects of the delay in maturation on the development of scoliosis appear to involve height; in our study, however, such effects could not be explained entirely by the differences in height. The slight increase in height among the dancers with scoliosis and secondary amenorrhea, although not significant, suggests that analysis of data from larger groups might show a relation between scoliosis and height. Our subjects had stopped growing, and these relations may have been attenuated.

It seems unlikely that neurologic disorders, stereotactic deficiencies, or disorders of equilibrium, all of which have been implicated in the development of scoliosis,24 could have caused the spinal curvature in this group of professional dancers, since such deficiencies would probably have hindered their performance substantially. However, a dysfunction of muscle tone, with posturing on a flexible spine during a long growth phase, in a person with a predisposition to scoliosis may have had a role. Nutritional factors may also be implicated. Dancers are known to diet to maintain the thin body form that is considered ideal in classical dance,22 and dieting is a causal factor in the development of secondary amenorrhea.25 The dancers in our study weighed a mean of 87 percent of the ideal value. Those with scoliosis also scored higher on the oral-control scale, which is a measure of dieting behavior. The higher oral-control scores suggested that the dancers with scoliosis had more rigorous dieting behavior, since the weight-height ratios of subjects with and without scoliosis did not differ. The incidence of anorexia nervosa in ballet dancers is 5 percent to 22 percent,16 a reflection of dieting behavior. Calcium and vitamin D intake is suboptimal among ballet dancers,3 and the effects of this deprivation could lead to inadequate calcification, osteopenia, and poor skeletal stability. Our blood studies showed no biochemical evidence of vitamin D deficiency or metabolic bone disease; however, bone biopsies are necessary to differentiate osteoporosis from osteomalacia. Scoliosis and fractures may be adolescent manifestations of inadequate calcification and skeletal stability during a rapid growth phase. Puerperal apposition of bone may be decreased so that at the time of maturation, bone density is lower than normal. Thus, loss of bone at even a normal rate could result in a mechanically incompetent skeleton and fractures.

The incidence of fractures among our subjects was also related to hormonal factors, since the relation between delayed menarche and stress fractures was striking. Others have found that the development of clinical fractures correlated strongly with decreased bone mass.26 The dancers with the stress fractures also had a higher incidence and a longer duration of amenorrhea than those without such fractures. Hypoestrogenic amenorrhea is associated with decreased bone density27-31 and stress fractures in young women,27-35 particularly in those with athletic amenorrhea,34 even when the intensity of exercise is controlled for.36 The findings in our sample are especially surprising because extensive physical training of the type in

Table 4. Reports of Fractures among 75 Dancers and Stress Fractures among 40 Dancers.

<table>
<thead>
<tr>
<th>Age at Menarche (Yr)</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
<th>18</th>
<th>19</th>
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<td>Fracture*</td>
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<td>4</td>
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<td>3</td>
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<td>11</td>
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<td>% of total</td>
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<td>9.3</td>
<td>26.7</td>
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<td>8.0</td>
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* p = 0.2, P<0.04 for correlation between fracture and age at menarche.
1 Fr = 0.4, P<0.01 for correlation between stress fracture and age at menarche.
which ballet dancers engage may have a protective effect on the skeleton and prevent bone loss.33,36 Our data suggest that the stress associated with regular strenuous exercise may not be sufficient to compensate for the loss in estrogen or dietary deficiencies at a critical stage.

The effects of hormonal, hereditary, and nutritional factors on the developing skeleton (particularly in adolescence) deserve further investigation. Long-term effects, such as stress fractures, are particularly important because they predispose to injury, and skeletal problems may reflect osteopenia that is not reversible. Although the relation between postmenopausal estrogen deficiency and osteoporosis is well recognized, osteopenia in young women — particularly in adolescents — with hypoestrogenism has not been studied. Confirmation of the role of estrogen in preventing skeletal deformity and osteopenia in adolescents would radically alter attitudes toward the importance of the timing of normal sexual maturation and estrogen replacement.

We are indebted to Ilana Attie, Linda Ferington, Janine Gar­giolo, Schenley Hajek, Stacey Shields, and Lily Yen for help in preparation of the manuscript; to Richard Fox for statistical analysis; to the IBM Corporation for the gift of a personal computer; to the Nichols Institute for performing the parathyroid hormone assays; to SmithKline & French Laboratories for the blood chemistry profile; to Dr. Thomas L. Clemens of the Regional Bone Center at Helen Hayes Hospital for performing the vitamin D assays; to Dr. Elizabeth什ane for her criticisms; and to the ballet companies that made this study possible.

REFERENCES

by Manson et al.,4 that represents the largest number of preg-
newborns with varicella followed prospectively. Besides the ar
the basis of the limited data presented in the report by
Infants born with defects not consistent with congenital
infection have been excluded from the analysis. The study
Enders5 included no pregnancies in which infection occurred
and the seventh month of gestation.

Table 1 shows, the point estimate of the risk of defects from first-trimester infection ranges from 0 to 9.1 percent. With
exclusion of the data from Manson et al., the 95 percent con
ance interval for the individual observed risk rates is quite wide
(maximizing a risk of 42 percent) because of the
sample sizes. When Paryani and Arvin combined their data
those from Siegel and from Enders, they reported a risk of
4.9 percent (3 of 61); but even in this case, the 95 percen
dence interval is still quite wide: 1.0 to 13.7 percent. However,
the additional data from Manson et al. are included, the
is reduced by one half, to 2.3 percent, and the confidence
the five studies, the deleted defect rates decrease further, to 0.8
cent with a 95 percent confidence interval of 0.02 to 4.2

To the Editor: Hypoestrogenic amenorrhea is associated with
decreased bone density and stress fractures in young female ath-
letes.2.4 A high incidence of delayed menarche and irregular men-
strual periods has been observed in young ballet dancers.3 The
population studies by Warren et al. strongly suggests that a prolonged hypo-
estrogenism may predispose ballet dancers to stress fractures. Our
papers support their findings.

We studied bone mineral content by dual-photon absorptiometry
(BMC-LAB 22a, NOVO) at the lumbar spine and the right femoral
neck in four women and two male ballet dancers aged 21 to 30 years.
All subjects had started dancing at 7 to 10 years of age. Three of
the four female dancers had had their menarche after age 15. We
measured the serum concentration of calcium, phosphorus, and
parathyroid hormone with a C-terminal radioimmunoassay (Byk-
Mallinkrodt) and of calcitonin with a radioimmunoassay (Byk-
Mallinkrodt). Our results are shown in Table 1. The z score is the
number of standard deviations from the sex-specific age regression
in normal American subjects.

These data show that the female ballet dancers had a decreased
bone mineral content. The dancers also had hypercalcitinaemia,
which was more pronounced in the men, in whom bone density was
reduced less than in the women. We also found mild hypercalcemia
which was more pronounced in the men, in whom bone density was

SCOLIOSIS AND FRACURES IN YOUNG BALLET DANCERS

To the Editor: Warren et al. (May 22 issue)1 suggest that the high
mortality of scoliosis in ballet dancers reflects both hereditary and
environmental factors. We also noted a high
The z score is the

Table 1. Bone Mineral Content and Serum Concentrations of Calcium, Phosphorus, Parathyroid Hormone, and Calcitonin in Young Ballet Dancers.*

<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>BONE MINERAL CONTENT</th>
<th>CALCIUM</th>
<th>PHOSPHORUS</th>
<th>PARATHYROID HORMONE</th>
<th>CALCITONIN</th>
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<tr>
<td></td>
<td>LUMBAR SPINE</td>
<td>FEMORAL NECK</td>
<td>mg/dl</td>
<td>z score</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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</tr>
<tr>
<td>6</td>
<td>1.12</td>
<td>0.98</td>
<td>2.60</td>
<td>0.72</td>
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</tr>
</tbody>
</table>

*The normal ranges are 2.2 to 2.7 mmol per liter for calcium, 1.1 to 1.4 mmol per liter for phosphorus, 0.2 to 0.6 ng per milliliter for parathyroid hormone, and 7.5 to 12 and 9 to 21 pg per milliliter for calcitonin in women and men, respectively.

...
COMPLETE HEART BLOCK DUE TO LYME DISEASE

To the Editor: An association of rhythm disturbances with Lyme disease has been described, but it is not immediately considered in the absence of a characteristic history.

A 31-year-old man presented with lethargy and complete heart block, with a sinus rate of 100 bpm and an idioventricular escape rate of 40 bpm but no hemodynamic compromise. There were no signs or symptoms of myocardial ischemia or infarction and no important cardiovascular risk factors. There were no signs or symptoms of myocarditis or congestive heart failure, and there was no evidence of drug ingestion, toxins, thyroid dysfunction, or other usual or unusual causes of heart block. The patient said he had not had a tick bite, but he had been in an endemic area. The presumptive diagnosis was degenerative disease of the conduction system. Viral and Lyme antibody titers were determined.

On the second hospital day, complete heart block was still present, but the ventricular escape rate was 25 bpm, and a temporary pacemaker was inserted. During insertion, the corrected sinus-node recovery time was measured and found to be prolonged (600 to 800 msec), indicating sinus-node dysfunction. Plans were made to place a permanent pacemaker within seven days, while awaiting laboratory data and potential recovery. The patient had evidence of occasional supraventricular captured beats on day 5, of atrioventricular Wenckebach's phenomenon on day 6, and of first-degree atrioventricular block on day 7. The temporary pacemaker was removed, and the plans for a permanent pacemaker were canceled. Had we proceeded earlier, an unnecessary procedure might have been performed. On day 7 the Lyme antibody titers were found to be high (0.469), indicating recent infection despite the lack of recognition of the concurrent infection.

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These additional data suggest that this alpha-2b human interferon preparation does not induce neutralizing antibody formation in patients with hairy-cell leukemia. The data also indicate that radioimmunoassay is an accurate technique for screening for neutralizing antibody activity to alpha-2b human interferon.

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ity of recombinant-derived interferon alpha in metastatic renal cell


Protzman WP, Jacobs SL, Miniciccozi M, Oden EM, Kelsey DK. A

NATURAL-KILLER-CELL FUNCTION AND BONE MARROW TRANSPLANTATION

To the Editor: In severe combined immunodeficiency the natural killer (NK) cells in resistance to post-thymic T-cell depletion bone marrow stem-cell engraftment is unclear. Ever, many patients with severe combined immunodeficiency have even a low level of NK-cell function have been given post-transplantation chemotherapy to "enhance" engraftment of haploidentical bone marrow. The presence of normal NK-cell function in these patients might be an important issue in conditioning regimens.

We have treated 17 infants with severe T-cell deficiency administration of haploidentical bone marrow stem cells derived from mature T-cells by soybean lectin agglutination and sheep erythrocyte rosetting. None received pretransplantation immunosuppression. Data on the 13 patients studied for NK-cell function after transplantation are shown in Table 1. (The patient number in the first four patients listed had above 50% of normal NK-cell function before transplantation. As Table 1, four of these five patients have acquired good function since haploidentical bone marrow transplantation no eighth patient had very low or absent NK-cell function before transplantation. Five of these had evidence of engraftment. The group of 13 patients, there was no evidence that the presence of normal or increased NK-cell function interfered with engraftment. By contrast, we have found that resistance to engraftment...