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 18 dancers (83 percent) with scoliosis had 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 of 10 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 1986; 314:1348-53.)

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,[4-6] 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 fractures they had sustained. Information on the location and type of injury (stress or nonstress fracture) 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 dancers volunteered to fill out a detailed questionnaire that examined the pattern of any eating disorder they may have had (see below). Ten of the 75 dancers volunteered to have their endocrine status studied longitudinally.

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Demographics

The educational levels of the subjects and their parents were estimated with the seven-point scale developed by Hollingshead and Redlich.[7] All the dancers were white, and all were from families that were lower-middle class to upper class. Birth order and age at which dance training was begun were also determined. All subjects began dancing when they were seven to eight years old. Data on stress fractures were obtained from the dancers in two national companies that had similar competitive characteristics, repertoires, 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 oral contraceptives. Assays for luteinizing hormone, follicle-stimulating hormone, and prolactin were performed as previously described.[8] 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 1,25-dihydroxyvitamin D ($1\alpha,25(OH)_2D$). The levels of parathyroid hormone were determined by a previously described radioimmunoassay,[9] with the use of a chick antiserum directed against the biologically active amino terminal (N terminal) portion of the parathyroid hormone molecule (parathyroid hormone 1-34).[10,11] A C-terminal midmolecule-specific radioimmunoassay was also used; it employed an antiserum directed against a human parathyroid hormone that measures primarily inactive fragments of parathyroid hormone.[12] Levels of 25-OH-D and $1\alpha,25(OH)_2D$ were determined by the method of Fraher et al.[13]

Physical and X-Ray Examinations

Fourteen dancers with structural scoliosis were assessed by x-ray examination; an additional four dancers reported scoliosis, and al-

though 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 efferent or efferent pathways of the spinal cord, disorders of visual and vestibular function, midbrain dysfunction, muscle disease, and abnormalities of collagen formation.

Eating Problems

Eating 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.[14] EAT-26 consists of three subscales (dieting, bulimia, and oral control).[15] The oral-control subscale measures attempts to control the intake of food and the subjects' preoccupation with this activity. The 19-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 calculated 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.[16]

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, overactivity 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.[16] Thus, the EAT-26 and the anorectic scale were used as partly validating checks on the reports of eating problems.

Weight–Height Relations and Menarche

Ideal weights were obtained from tables of average weight–height relations for young adults (ages, 17 to 34). These tables are based on measurements of 160,000 students who entered college in the United States from 1948 to 1950.[17] 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.[18] Leanness was determined by weight–height ratios.[19]

Menarche was considered delayed if it occurred at age 14 or older. The mean (±SD) reported age of menarche in the United States is 12.9±1.2 years.[20]

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 unpaired 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 — 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.[20] 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.*

Subject Group	No. (%)	Age	Age at Menarche	Weight	Height	Weight–Height Ratio	% of Ideal		Amenorrhea >5 Mo	EAT Scores†	
							Weight	Height			
		year		*kg*	*cm*				*no. (%) of subjects*		
All subjects	75	24.3±4.1	14.5±2.1	50.2±3.9	167.6±4.6	1.7±0.1	86.8±4.4	102.8±2.4	40 (53)	2.28±0.95‡	
Dancers with scoliosis	18 (24)	22.8±4.0	15.2±2.0	51.2±5.0	169.7±4.1§	1.7±0.1	86.5±5.8	103.5±2.9	8 (44)	2.59±0.58‡§	P<0.05
Dancers without scoliosis	57 (76)	24.7±4.0	14.3±2.1	49.9±3.5	167.1±4.6§	1.7±0.1	86.9±4.0	102.4±2.5	18 (31)	2.14±1.05‡§	
Dancers with fractures	46 (61)	24.5±4.2	14.9±1.9	50.5±3.9	168.1±5.1	1.7±0.1	87.0±4.1	102.9±3.0	17 (37)	2.61±0.90‡	NS
Dancers without fractures	29 (39)	23.7±3.3	14.0±2.1	49.9±0.04	167.1±3.3	1.7±0.1	86.3±4.2	102.2±1.8	8 (27)	2.78±0.91‡	
Dancers with stress fractures¶	18 (45)	23.0±3.6	15.6±2.3§	49.1±4.2	167.4±5.8	1.7±0.1	85.3±3.1	102.8±3.4	12 (67)	2.38±0.55‡	NS
Dancers without stress fractures	22 (55)	24.0±3.2	14.0±1.9§	50.9±4.3	168.9±4.1	1.7±0.1	85.3±3.1	102.8±3.4	6 (27) P<0.01	2.72±0.77	

*Plus–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. §$P<0.05$. ¶Based on a subgroup of 40 dancers.

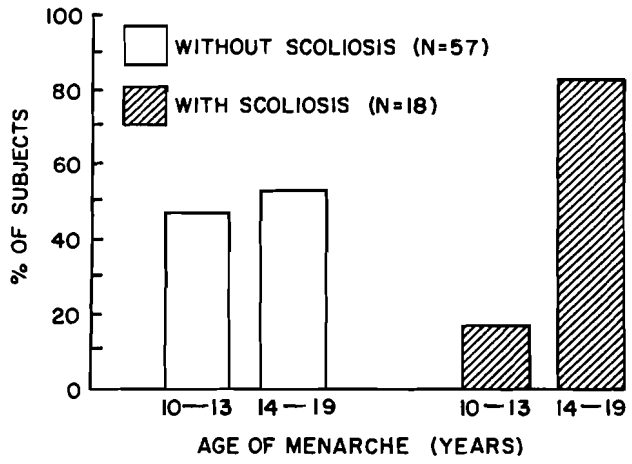

Figure 1. Relation between Age at Menarche and Scoliosis. Most of the subjects with scoliosis were 14 or older at menarche (83 vs. 17 percent; P<0.04).

vals of amenorrhea (11.4±18.4 vs. 4.1±7.4 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 ratios of the height to weight were 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 (5 of 18), whereas the incidence in the families of the other dancers was 4 percent (2 of 57; P<0.01).

A high incidence of fractures occurred in the total 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-nine 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). An 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 their 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 or 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 be-

Table 2. Age at Menarche of Dancers with and without Scoliosis.

Subject Group	Age at Menarche (Yr)					
	10–11	12–13	14–15	16–17	18–19	Row Total (%)
Without scoliosis	3	23	13	13	5	57 (76.0)
With scoliosis	—	3	7	5	3	18 (24.0)
Column total	3	26	20	18	8	75
% of total	4.0	36.0	26.7	24.0	10.7	100.0

Table 3. Mean (±SD) Duration of Amenorrhea in Subject Groups.

Subject Group of Dancers	No. of Subjects	Duration of Amenorrhea	P Value
		mo	
With scoliosis	12	11.4±18.3	<0.05
Without scoliosis	27	4.1±7.4	
With fractures	27	6.8±12.7	NS
Without fractures	12	4.5±8.9	
With stress fractures	12	13.0±7.3	<0.05
Without stress fractures	8	6.3±3.4	

*NS denotes not significant.

tween dancers with and without fractures or between those with and without stress fractures (Table 1). Twelve of the dancers with stress fractures also had scoliosis. The weights of all the dancers in the study were below the ideal levels; the mean weight was 86.7±4.2 percent of the ideal values.

Among the 10 dancers who were followed during amenorrheic intervals, marked hypoestrogenism was noted in 7, as indicated by vaginal smears that showed atrophy and a lack of withdrawal bleeding after the administration of progesterone. The endocrine profiles suggested hypothalamic amenorrhea. The levels of luteinizing hormone, follicle-stimulating hormone, prolactin, and free thyroxine were within the normal range for all but one subject, whose level of luteinizing hormone was slightly below the normal range. Seven of the 10 had no estrogen on a vaginal smear (atrophic pattern); the remaining 3 subjects had withdrawal bleeding after taking oral progesterone (10 mg per day for five days).

All dancers had normal levels of serum calcium, inorganic alkaline phosphatase, and albumin. There was no biochemical evidence of vitamin D deficiency, and the levels of 25-OH-D (33.5±14.2 ng per milliliter) and of $1\alpha,25(OH)_2D$ (36.5±9.1 pg per milliliter) were normal. The levels of both the N-terminal–specific molecule (16.4±5.8 pg per milliliter) and the C-terminal midmolecule (159.1±45.5 pg per milliliter) of the parathyroid hormone were also normal (the normal ranges are 11 to 24 and 50 to 330 pg per milliliter, 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 parathyroid hormone, serum calcium, albumin, phosphorus, 25-OH-D, and $1\alpha,25(OH)_2D$.

Three subjects had had radiographic studies of the wrists 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 anomalies or unusual back pain in any of the subjects with scoliosis. The mean degree of curvature (±SD) was 16.6±8.5 degrees (range, 10 to 30). The degree of curvature did not correlate with the presence of amenorrhea 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 specifically at risk for scoliosis and fractures, a risk that increases with an increase in age at menarche. Delayed puberty is a known risk factor for scoliosis,[21] and the high incidence in our sample reflects this delay. However, the striking frequency of scoliosis (24 percent) in this group is well above the expected frequency. Idiopathic adolescent scoliosis occurs in approximately 1.8 percent of the general population but in 3.9 percent of white girls.[22] The high incidence of this problem in dancers may reflect both constitutional (hereditary) and environmental factors. Scoliosis has a high familial incidence,[22] 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 affected (P<0.01), suggesting a hereditary influence. The decreased upper-to-lower body ratios and the long arm span previously noted in dancers[1] — features that are coveted as representing the ideal body form in classical ballet — could be inherited traits that are also associated with scoliosis. However, these physical characteristics are not as marked in the mothers and the nondancing sisters of ballet dancers.[1]

Prolonged hypoestrogenism in young adolescent

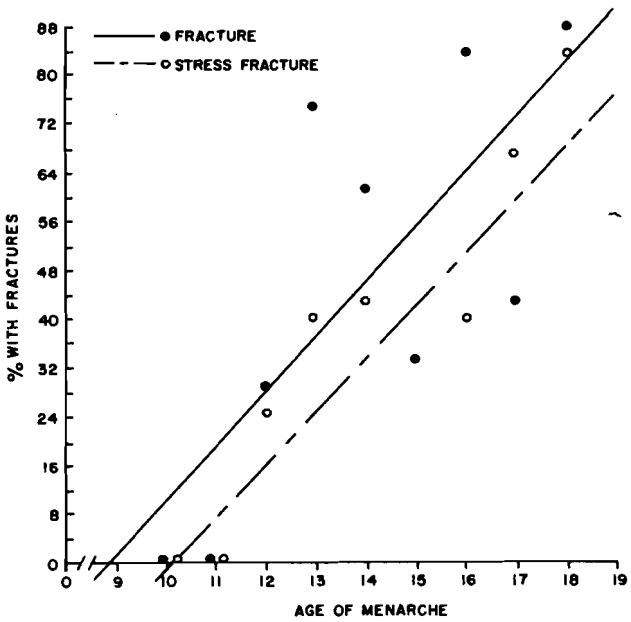

Figure 2. Relation between Age at Menarche and the Percentage of Subjects with Fractures and Stress Fractures (N = 75).
When the type of fracture was specified, the correlations for frequency distribution versus age at menarche were found to be greatest among those reporting stress fractures (n = 40), despite the smaller number of dancers in that group.

CORRECTION

In the left-hand column, the fourth line in the second full paragraph, the paren-

On page 1351,

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 predispose 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,[2,3] 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[2] 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. Pubertal 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 density[27-35] and stress fractures in young women,[27-35] particularly in those with athletic amenorrhea,[29,30,34] even when the intensity of exercise is controlled for.[34] 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.

	Age at Menarche (Yr)										
	10	11	12	13	14	15	16	17	18	19	Row total (%)
Fracture*											
No	1	2	5	5	5	4	2	4	1	—	29 (38.7)
Yes	—	—	2	15	8	2	9	3	6	1	46 (61.3)
Column total	1	2	7	20	13	6	11	7	7	1	75
% of total	1.3	2.7	9.3	26.7	17.3	8.0	14.7	9.3	9.3	1.3	100.0
Stress fracture†											
No	1		3	6	4	3	3	1	1	—	22 (55.0)
Yes	—		1	4	3	—	2	2	5	1	18 (45.0)
Column total	1		4	10	7	3	5	3	6	1	40
% of total	2.5		0.10	25.0	17.5	7.5	12.5	7.5	15.0	2.5	100.0

*$r = 0.2$, $P<0.04$ for correlation between fracture and age at menarche.

†$r = 0.4$, $P<0.01$ 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.

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OBSERVED RISK	TOTAL GESTATION 95% CONFIDENCE INTERVAL
	%
.6% (1/38)	0.1–13.8
.5% (2/135)†	0.2–5.6
— ‡	
.0% (0/288)¶	0.0–1.5
.6% (3/461)	0.1–2.1

tal abnormalities/number of
ith congenital varicella infection
seventh month of gestation
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dy by Manson et al.[4] that represents the largest number of pregnant women with varicella followed prospectively. Besides the case cribed by Paryani and Arvin, Table 1 also includes two infants med to have defects consistent with congenital varicella infection on the basis of the limited data presented in the report by el.[2] Infants born with defects not consistent with congenital cella infection have been excluded from the analysis. The study Enders[3] included no pregnancies in which infection occurred ond the seventh month of gestation.

s Table 1 shows, the point estimate of the risk of defects following first-trimester infection ranges from 0 to 9.1 percent. With exception of the data from Manson et al., the 95 percent confidence interval for the individual observed risk rates is quite wide proaching a maximal risk of 42 percent) because of the ll sample sizes. When Paryani and Arvin combined their data h those from Siegel and from Enders, they reported a risk of 4.9 percent (3 of 61); but even in this case, the 95 percent fidence interval is still quite wide: 1.0 to 13.7 percent. However, he additional data from Manson et al. are included, the is reduced by one half, to 2.3 percent, and the confidence val becomes relatively narrow. (If the two cases from the el study are deleted, the defect rate decreases further, to 0.8 cent with a 95 percent confidence interval of 0.02 to 4.2 cent.)

lthough none of the four studies identified any infants with cella-related defects following second-or third-trimester infec- case reports document their existence.[5,6] Thus, Table 1 in- es data for the overall risk of defects throughout gestation. If considers only the second and third trimester, the observed risk none of 353, with a 95 percent confidence interval of 0 to 1.1 cent.

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SCOLIOSIS AND FRACTURES IN YOUNG BALLET DANCERS

the Editor: Warren et al. (May 22 issue)[1] suggest that the high lence of scoliosis in ballet dancers reflects both hereditary and ronmental factors. We also noted a high lence of scoliosis in our study of pa with hypomastia and mitral-valve pro- 2] In addition, many of our subjects ballerina-type body builds. This con- tion of anatomical findings seen in bal- ancers may have a mesenchymal and yologic foundation similar to that of mastia and mitral-valve prolapse.

uring the sixth week of development, s of chondrification begin to form in vertebrae, and a scoliotic curve can be cted in the anlagen of the spinal column. mesenchymal components of the breast mitral valve are also actively developing ng this period. An influence, either ge- or environmental, on growth patterns g the sixth week of development may t formation of the vertebral column. phenotypic manifestation of this influence shows tissue specificity for certain commonly derived mesenchymal lines — i.e., the vertebral column, leading to scoliosis, a tall stature, and the decreased upper-body:lower-body ratio referred to by Warren et al. in regard to ballerinas.

We believe that the frequently coexisting findings of thoracoskeletal abnormalities (scoliosis or straight back), a ballerina-like stature, hypomastia, and mitral-valve prolapse are linked through their common mesenchymal origin and simultaneous embryologic differentiation during the sixth week of embryologic life. Recognition of these associated clinical findings offers valuable information to the astute clinician.

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To the Editor: Hypoestrogenic amenorrhea is associated with decreased bone density and stress fractures in young female athletes.[1,2] A high incidence of delayed menarche and irregular menstrual periods has been observed in young ballet dancers.[3] The paper by Warren et al. strongly suggests that a prolonged hypoestrogenism may predispose ballet dancers to stress fractures. Our observations 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 female 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 hypercalcitoninemia, which was more pronounced in the men, in whom bone density was reduced less than in the women. We also found mild hypercalcemia and suppressed parathyroid function in these subjects.

We think that calcitonin may protect the bone from demineralization in young ballet dancers. We could not exclude the role of vigorous exercise in the observed hormonal changes. Aloia et al.[4] have recently reported that short-term exercise causes mild hypercalcemia and a transient decrease in parathyroid hormone and an increase in calcitonin concentration in the blood. During a 20-minute rest period, the levels of each of these variables returned to

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

Subject No.	Bone Mineral Content				Calcium	Phosphorus	Parathyroid Hormone	Calcitonin
	Lumbar Spine		Femoral Neck					
	g/cm²	*z score*	*g/cm²*	*z score*	*mmol/liter*	*mmol/liter*	*ng/ml*	*pg/ml*
Women								
1	0.94	−1.8	0.96	−2.1	2.62	0.94	0.27	22
2	1.20	+0.4	1.07	−1.1	2.45	1.00	0.28	26
3	0.87	−2.1	0.84	−2.5	—	—	—	—
4	1.01	−1.2	1.03	−1.6	2.61	0.94	0.24	35
Men								
5	1.03	−0.5	1.12	−0.3	2.65	1.05	0.23	50
6	1.12	+0.2	0.98	−1.2	2.60	0.72	0.21	50

*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.

base line. Our investigations were always started a few hours after the subjects had stopped dancing.

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COMPLETE HEART BLOCK DUE TO LYME DISEASE

To the Editor: An association of rhythm disturbances with Lyme disease has been described,[1-4] 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 recent exposure.

This case is important because Lyme disease is becoming more common, it may be associated with serious rhythm disturbances that are transient, and it must be included in the differential diagnosis, even if it is not suggested by a characteristic history. Penicillin therapy is recommended for the infection. The heart block usually resolves within 7 to 10 days. We have seen two such cases within a four-week period.

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ANTIBODIES IN PATIENTS WITH HAIRY-CELL LEUKEMIA RECEIVING ALPHA-2b INTERFERON

To the Editor: In June 1986 Intron A, alpha-2b human inter was approved for use in the treatment of hairy-cell leukemia. Intron A is a recombinant-derived protein produced in *Esch coli*, we considered the possibility that this particular prepa might induce antibody formation and, theoretically, beneficial effects in patients with hairy-cell leukemia.[1]

In a previous study of 423 patients with cancer who were tre parenterally with Intron A, an overall incidence of neutral antibody induction of 2.4 percent was detected with use of ra immunoassay.[2] In our study, 270 serum samples from 109 pati with hairy-cell leukemia were assayed with a bioassay and a se tive radiometric assay[3] to detect antibody to alpha-2b human in feron. All the patients were treated by subcutaneous injection wi dose of 2×10^6 IU per square meter of body-surface area three ti weekly. The samples were obtained at intervals from 1 to 13 mo after the start of treatment. Most of the patients (82 percent) been treated for at least three months. Only 1 of the 270 sam was positive in either assay, and this particular sample was pos in both assays. However, it came from a patient from whom pretreatment sample was available; a determination canno made regarding whether the activity had been induced or whet had existed before therapy.

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

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NATURAL-KILLER-CELL FUNCTION AND BONE MARROW TRANSPLANTATION

To the Editor: In severe combined immunodeficiency the re natural killer (NK) cells in resistance to post-thymic T-cell dep haploidentical 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 pre plantation chemotherapy to "enhance" engraftment of haploi cal marrow cells. There is an increased morbidity and mor associated with such conditioning regimens.

We have treated 17 infants with severe T-cell deficienci administration of haploidentical bone marrow stem cells dep of mature T cells by soybean lectin agglutination and sheep ery cyte rosetting.* None received pretransplantation immunosup sion. Data on the 13 patients studied for NK-cell function i transplantation are shown in Table 1. (The patient numbers re those in our article.*) The first five patients listed had above-n to half-normal NK-cell function before transplantation. As sho Table 1, four of these five patients have acquired good im function since haploidentical bone marrow transplantatio next eight patients had very low or absent NK-cell function transplantation; five of these had evidence of engraftment. T this group of 13 patients, there was no evidence that the pres normal or increased NK-cell function interfered with engraf By contrast, we have found that resistance to engraftme

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Table 1. Effec

PATIENT No.	
	P
1	72
14	59
13	45
16	22
4	20
10	7
5‡	5
9	5
3	2
8	2
6	1
2	1
7‡	0

*NK activity was measured for Patients 1, 2, 3, and 14, an tive data at an E:T ratio of 5(
†Plus signs indicate good r
‡Deceased

correlate with the pr T-cell function.*

A second reason gi pression in patients NK-cell activity has function delays the d depleted bone marro within four months o We observed a later this series. Patients I NK-cell function) did months after transpl between NK-cell fun function.

Thus, the results of tion in these 13 pati presence of normal N ance to engraftment o tion. Until data are pu ence of NK-cell funct justification for patie and NK-cell functio suppression.

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*Buckley RH, Schiff S human severe primary T c stem cell transplantation.

SYNOVIAL-FLU IN DI

To the Editor: Amyl of long-term hemodia carpal-tunnel and syn cursor protein of this globulin.[1] Whereas se raised in patients on ated amyloid do not are no data on synov arthropathy. Amyloid is also deposited at t