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Christine M. Snow

Sex differences in bone mass and size are thought to contribute to the greater incidence of vertebral fractures in women. While these sex differences are widely recognized, the relative contributions of bone mass, bone density, and bone size to the differences in vertebral strength and fracture risk between men and women have not been fully delineated. Furthermore, it is unknown whether the roles of each of these factors in determining vertebral strength change differently with age in men and women. We studied the bone content, density and geometry as well as vertebral loading and the factor of risk of the L3 vertebra in a sample of prepubertal males and females. Our first aim was to assess differences in vertebral bone dimensions, bone density, vertebral loading patterns and fracture risk, as measured by the factor of risk, in prepubertal children. Our second aim was to determine whether pre-pubertal growth affects the geometry and density of L3 differently in boys and girls. We measured vertebral dimensions, cross-sectional area and volumetric BMD of the third lumbar vertebral body in 93 prepubertal children (54 boys and 39 girls), using dual-energy X-ray absorptiometry scans obtained in the posterior-anterior and lateral projections. We also employed basic biomechanics to estimate vertebral loading during upright standing and forward bending. Bone strength and loading data were used to assess sex differences in the factor of risk in prepubertal children. Twenty

children (11 boys and 9 girls) were assessed at baseline and seven months later to examine the effects of growth on bone size and vBMD. At baseline, boys and girls were similar for age, height, weight and calcium intake. L3 width and depth were 6.7% and 5.8% greater in boys than girls, respectively ($P$ <0.001 and $P$ =0.01, respectively). In contrast, vertebral height was 3.5% greater in girls than boys ($P$ = 0.04). While vertebral loading was similar between sexes, stresses on the spine were 12.2% lower in boys during upright standing and 12.0% lower in boys during forward bending at both 50° and 90°, as compared to girls ($P < 0.001$, $P < 0.01$ and $P < 0.01$, respectively). The factor of risk was similar between boys and girls under each loading condition. During growth, changes in vertebral size and density were not different between boys and girls. Our results indicate that even prior to puberty, sex differences in vertebral size contribute to differences in vertebral stress during standing and forward bending. Furthermore, before the onset of puberty, growth does not result in disparate changes between sexes.

# Sex Differences in Vertebral Bone Characteristics, Loading Patterns and the Factor of Risk in Prepubertal Children

by
Arwen A. Fuller

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I understand that my thesis will become part of the permanent collection of Oregon State University libraries. My signature below authorizes release of my thesis to any reader upon request.

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Arwen A. Fuller, Author

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# CONTRIBUTION OF AUTHORS

Dr. Toby Hayes is the President and CEO of Hayes and Associates, Inc., in Corvallis, Oregon. His area of specialty is biomechanics and injury reconstruction. Dr. Hayes provided countless hours of assistance in determining the engineering principles that underlie the materials and methods section of Chapter 2 and assisted in editing all components of this thesis.

Dr. Robyn Fuchs, as part of her dissertation work, collected all of the anthropometric data, calcium intake data, Tanner Stage data and a majority of the bone data for this study, with the exception of the data on bone size.

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# DEDICATION

*To my mom and dad*

# CHAPTER 1: INTRODUCTION

## BACKGROUND

### Consequences of Osteoporosis and Fractures of the Spine

Osteoporosis is an increasingly critical public health problem. According to the National Osteoporosis Foundation's 2000 census information, nearly 44 million Americans over the age of 50 are currently subject to developing osteoporosis (1). At this time, upwards of 17 billion dollars are spent to treat the 1.5 million fractures that are reported each year in the United States (1, 2). With the graying of America, these numbers are expected to double, if not triple, in coming years if effective preventive measures are not implemented (1, 3).

More than half of all age-related fractures reported in the U.S. occur at the spine and account for more than $746 million in annual health care costs (1). Unlike hip fractures, fractures of the spine are often unreported or untreated and it is estimated that only a third of all vertebral fractures receive medical attention (1). Furthermore, the estimated survival rate at 5 years following vertebral fracture diagnosis is lower than the 5-year survival rate after a hip fracture (9). Since the risk for a fragility fracture in later life is greater for women than men, vertebral fractures are particularly prevalent in women (1-7). While the lifetime risk of a hip fracture for women is twice that for men, in the United States the lifetime risk for a clinically diagnosed vertebral fracture for women is more than three-times that for men (16% and 5% respectively) (8). Though it is known that more women than men suffer from problems associated with skeletal fragility, the causes underlying these sex-differences are not well understood.

### Etiology of Fractures of the Spine

Unlike the bones of the appendicular skeleton that are composed primarily of cortical bone, the axial skeleton, including the vertebrae, consists mainly of cancellous

bone. In comparison to cortical bone, which is dense in structure, cancellous bone is characterized by a sponge-like arrangement of trabeculae. The structural advantage of cancellous bone is its high surface area to volume ratio that equates to a high strength to weight ratio. For example, during activities of daily living, a lumbar vertebra with a mass of approximately 7 g (ash weight) can withstand compressive loads ranging from 50% to over 300% of one's body weight (data for relaxed standing and lifting 15 kg from the floor with arms straight down, respectively) (3).

A disadvantage of trabecular bone stems from the inverse relationship between fracture risk and bone mass. The mass of trabecular bone is only one-fourth that of cortical bone (10). Therefore, any damage to the trabecular architecture or reduction in its density greatly compromises the loading capacity of the bone such that a decline in number and/or thickness of trabeculae is associated with a reduction in compressive strength (6). In addition, the strength of trabecular bone is closely related to its apparent density such that a slight decrease in vertebral density can result in a significant reduction in strength (3, 11). Trabecular deterioration is characteristic of the normal aging process and reductions in apparent density of approximately 50% have been reported from the 3$^{rd}$ to the 8$^{th}$ decade (11).

## Factor of Risk

Spinal fractures occur when the load applied to the vertebra exceeds its load-bearing capacity (3, 8, 11, 12). The ability to resist fracture is determined by the ratio of the applied load to the load required to cause fracture and is termed the "Factor of Risk" ($\Phi$ = applied load/fracture load) (12). If the applied load is less than the failure load, then fracture is unlikely. However, if the applied load exceeds the loading capacity of the bone, then fracture is probable. Vertebral loading results from an individual's body weight, height and the external forces applied during activity (3, 11). Additionally, the magnitude of applied loading depends on the biomechanical characteristics of the specific activity (3, 12). In some cases, and depending on individual bone mass, even everyday actions such as bending and lifting can exceed the vertebral failure load and result in spinal fracture (6, 3, 11).

The denominator of the factor of risk, failure load, is calculated as the product of the cross-sectional area (CSA) and volumetric density (vBMD) of the vertebra (3, 6, 11). Increases in the cross-sectional area and cross-sectional moment of inertia serve to improve the vertebral body's resistance to compressive and bending loads, respectively (11). Consequently, the load per unit area, or stress, is reduced which thereby decreases the risk for fracture. In clinical settings, however, measurement of CSA is not practical and areal BMD (aBMD) values are the sole indication of fracture risk. Although spinal BMD values correlate with vertebral compressive loads, relying strictly on density neglects the important and potentially dominant influences of loading. Moreover, disregarding the interaction of bone geometry and density may result in under- or overestimation of fracture risk (12, 13).

## Assessing Bone Strength

Bone mineral content, or BMC (measured in grams), is readily evaluated using dual-energy x-ray absorptiometry (DXA). DXA is also used to assess the area (measured in $cm^2$) of a given bone structure and, in turn, BMC and area values can be combined to give a measure of areal bone mineral density (BMD, BMD = BMC/area, measured in $g/cm^2$). BMD is traditionally used to assess and describe susceptibility to fracture. Specifically, the World Health Organization's definition of osteoporosis is a BMD value of 2.5 standard deviations below the average value for healthy young adult women (2, 4). Although fracture risk is reportedly inversely related to BMD, there is an indisputable overlap in the distribution of BMD values in patients with and without fractures (6, 7, 11, 14, 15), calling into question the validity of BMD as a clinically diagnostic tool.

DXA is the most widely used instrument for the assessment of bone mass both in research and clinical settings. However, BMD data obtained with DXA has been limited to areal or two-dimensional evaluations of density that fail to accurately account for variations in bone size. DXA-derived BMD values are reported as BMC/ projected area, $g/cm^2$ and thus, do not assess the three-dimensional structure of bones.

The two-dimensional nature of DXA is of particular concern when assessing the vertebrae. Frequently, scans of the spine are performed in the posterior-anterior projection (PA), which incorporates the posterior elements (the spinous and transverse processes) and is unable to isolate the body of the vertebra. While lateral scanning capabilities can better identify the clinically relevant vertebral bodies, research has produced mixed-reviews regarding the improved ability of lateral scans to identify individuals with elevated bone loss (16-18). More recent DXA technology, however, permits three-dimensional evaluations of the spine through the coupling of data from the posterior-anterior (PA) scans with those in the lateral projection. This combination yields a "width-adjusted" assessment of BMD (wa-BMD) that is calculated by dividing the BMD value from the lateral scan by the average width of the vertebra obtained from the PA scan. The validity of these measures as an assessment of volumetric BMD, however, has yet to be thoroughly examined.

## Peak Bone Mass: A primary determinant of osteoporosis-related fracture risk

Peak bone accrual during growth and adolescence is a major determinant of fracture risk in later life (19-21) and maximizing peak bone mass has been recommended as a potential strategy in preventing osteoporosis (4). Peak bone mass is the maximum amount of bone acquired prior to the beginning of the age-related decline. It has been estimated that the lifetime risk of fracture incidence declines approximately 40% for each 5% gain in peak bone mass (21). While the age at which peak mass is achieved is site-specific, it is estimated that more than 90% of peak bone mass is acquired by the age of 18 (21). Vertebral mass, however, is reported to increase throughout the third decade of life (22).

During growth, vertebrae increase in both size and mineral content. However, the relative rates of accrual in size and mass differ depending on pubertal status, sex, race, nutrition and physical activity (19-21, 23). Most studies in children have failed to detect sex differences in BMD prior to the onset of puberty (19, 23-26, 28), but vertebral cross-sectional area and BMC are reported to be greater in boys across all stages of development (23). Furthermore, this discrepancy between males

and females increases with age; with the greatest disparities observed in subjects classified as Tanner stage V (pubertal maturation) (25). However, it isn't clear whether boys have greater vertebral width, depth or both. Vertebral height, is not reported to differ between boys and girls, thus, DXA measures of areal BMD that adjust for vertebral height may be insensitive to gender differences in vertebral size that are reflected only in width and cross-sectional area (19, 23).

## Summary

While peak bone mass has been established as an important determinant of the lifetime risk for osteoporosis, it is hypothesized that smaller bone size in girls relative to boys may be a significant contributor to the observed sex differences in vertebral fracture incidence later in life (6, 20, 21, 23). Whether or not vertebral density values are similar in boys and girls, ultimately, larger bones have a greater CSA that results in a greater resistance to compressive loads. Moreover, little is known about what role the growth process plays in contributing to osteoporosis and osteoporosis-related fracture risk in adulthood or how sex differences during growth and development influence fracture risk in adulthood. If bone size, as well as density, can be enhanced during growth, then we can design and implement bone-building strategies during development that may function to prevent osteoporosis and fractures during aging. Furthermore, if sex differences in bone are inherent, it is possible that these bone-building strategies should be different for boys and girls.

# PURPOSE

The primary purpose of this study was to further delineate the role of vertebral bone size and its relative contribution to the factor of risk in young children. Specifically, we wanted to determine if sex differences exist in bone size and composition in prepubertal children and to explore how these sex differences may influence bone strength under different loading conditions. Additionally, we wanted to examine the effect of growth on the size, composition and strength of bone to determine if growth affects vertebral bone differently in boys and girls.

# RESEARCH QUESTIONS, HYPOTHESES AND AIMS

## Research Question One

Are sex differences in vertebral bone dimensions, bone density, vertebral loading patterns, or factor of risk present in prepubertal children?

### Hypothesis One:

Vertebral width and depth are greater in prepubertal boys than girls, but vertebral height does not differ between sexes. Furthermore, bone mineral density, loading patterns and factor of risk are not different between prepubertal (Tanner stage I) boys and girls.

### Aim One:

Vertebral bone dimensions and bone mineral density values for L3 will be evaluated using posterior-anterior and lateral spine absorptiometry data. Vertebral loading patterns and factor of risk will be calculated using standard engineering methods. We will use one-way univariate analysis of variance to determine the significance of any differences between males and females.

## Research Question Two

Does growth affect the geometry as well as the density of the vertebral bodies of L3 differently in boys and girls?

### Hypothesis Two:

The effects of growth of the vertebral bodies of L3 will not differ in prepubertal boys and girls.

## Aim Two:

A subgroup of subjects assessed at baseline and 7 months will be evaluated for changes in L3 vertebral bone geometry and BMD values using previously collected posterior-anterior and lateral spine data from DXA measurements. Difference scores will be calculated and analysis of variance will be used to evaluate differences between boys and girls.

# CHAPTER 2: SEX DIFFERENCES IN VERTEBRAL BONE CHARACTERISTICS, LOADING PATTERNS AND THE FACTOR OF RISK IN PREPUBERTAL CHILDREN

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## ABSTRACT

Sex differences in bone mass and size are thought to contribute to the greater incidence of vertebral fractures in women. While these sex differences are widely recognized, the relative contributions of bone mass, bone density, and bone size to the differences in vertebral strength and fracture risk between men and women have not been fully delineated. Furthermore, it is unknown whether the roles of each of these factors in determining vertebral strength change differently with age in men and women. We studied the bone content, density and geometry as well as vertebral loading and the factor of risk of the L3 vertebra in a sample of prepubertal males and females. Our first aim was to assess differences in vertebral bone dimensions, bone density, vertebral loading patterns and fracture risk, as measured by the factor of risk, in prepubertal children. Our second aim was to determine whether pre-pubertal growth affects the geometry and density of L3 differently in boys and girls. We measured vertebral dimensions, cross-sectional area and volumetric BMD of the third lumbar vertebral body in 93 prepubertal children (54 boys and 39 girls), using dual-energy X-ray absorptiometry scans obtained in the posterior-anterior and lateral projections. We also employed basic biomechanics to estimate vertebral loading during upright standing and forward bending. Bone strength and loading data were used to assess sex differences in the factor of risk in prepubertal children. Twenty children (11 boys and 9 girls) were assessed at baseline and seven months later to

examine the effects of growth on bone size and vBMD. At baseline, boys and girls were similar for age, height, weight and calcium intake. L3 width and depth were respectively 6.7% and 5.8% greater in boys than girls ($P$ <0.001 and $P$ =0.01, respectively). In contrast, vertebral height was 3.5% greater in girls than boys ($P$ = 0.04). While vertebral loading was similar between sexes, stresses on the spine were 12.2% lower in boys during upright standing and 12.0% lower in boys during forward bending at both 50° and 90°, as compared to girls ($P < 0.001$, $P < 0.01$ and $P < 0.01$, respectively). The factor of risk was similar between boys and girls under each loading condition. During growth, changes in vertebral size and density were not different between boys and girls. Our results indicate that even prior to puberty, sex differences in vertebral size contribute to differences in vertebral stress during standing and forward bending. Furthermore, before the onset of puberty, growth does not result in disparate changes between sexes.

# INTRODUCTION

While osteoporosis is characterized as a major health problem that is neither age nor sex dependent, discrepancies in the prevalence of osteoporosis-related fractures between men and women are well documented (1-10, 14, 29). It is estimated that 30-50% of all women vs. 15-30% of men will experience at least one osteoporosis-related fracture over their lifetime (5,6). Furthermore, while women's lifetime risk of a hip fracture is twice that of men, in the United States, the lifetime risk for a clinically diagnosed vertebral fracture for women is more than three times that for men (8).

Vertebral strength is a function of the volumetric density and cross-sectional area of the vertebra. Measures of the spine in healthy individuals have demonstrated that volumetric bone mineral density does not differ between sexes during childhood and young adulthood (6, 7, 30). However, vertebral cross-sectional area and bone mass are greater in men than women regardless of age (6, 7, 14, 19, 20, 23, 30-32). Accordingly, it is theorized that differences in bone size contribute to the difference in vertebral fracture incidence in men and women.

Fractures of the spine occur when the loads applied to the vertebra exceed the load-bearing capacity of the bone. Thus, bone mass and vertebral geometries provide information on only one component of fracture incidence. Without considering potential variations in loading, sex differences in vertebral fracture prevalence cannot be thoroughly assessed. Few studies, however, have examined the relationship between loading and bone strength and its contribution to the discrepancy in fracture risk between men and women; moreover, the data that do exist are conflicting (6, 7, 30). Larger bones in men are thought to sustain correspondingly higher loads such that the load per unit area, or stress on the vertebrae is equal between sexes (6, 7). Evidence from computed tomography, however, demonstrates that when subjected to equivalent loads and when matched for age, height, weight and vertebral height, the mechanical stress on the vertebra is greater in women than men under both axial compression and bending loads (30).

Vertebral cross-sectional area in children has also been shown to be greater in boys than girls during growth (23). Cortical and trabecular densities, however, do not vary between sexes throughout development (23). Still, the biomechanical influences of loading and bone size on vertebral stress in children have yet to be determined. Furthermore, sex differences in vertebral strength and fracture risk prior to peak bone mass accrual are poorly understood.

In this study, we hypothesized that while boys have larger vertebrae than girls during childhood, sex differences in vertebral bone density, loading patterns and fracture risk are not evident prior to puberty. We also hypothesized that, prior to the onset of puberty, growth does not affect boys and girls differently with regards to the geometry and density of the vertebral bodies.

To address these hypotheses, we studied the bone content, density and geometry of the bodies of the L3 vertebra as well as vertebral loading and the factor of risk in a sample of prepubertal males and females. We first asked, are differences in vertebral bone dimensions, trabecular bone density, vertebral loading patterns and fracture risk that have been reported in older adults, present in prepubertal children? Secondly, we asked, does growth affect the geometry as well as the density of the vertebral bodies differently in boys and girls?

# MATERIALS AND METHODS

## Subjects

We studied children recruited from two local elementary schools to participate in a prospective randomized controlled trial examining the effects of a jumping intervention on bone mass at the hip and spine. The parent of each child completed a standard health history questionnaire to determine study inclusion (Appendix C). Exclusion criteria included disorders or medications known to affect bone metabolism, thyroid disease, diabetes, chronic diseases, orthopedic problems that could limit participation in the exercise intervention or testing, and body weight that exceeds 20% of the recommended weight for height and age. Of the 100 children recruited in 1998, one child exceeded 20% of the recommended weight for height and age and was excluded. Thirty children had illegible bone scan data. From a second cohort of 90 children who were tested in 2001, complete scan data was available for only 24 subjects.

Data from 93 healthy children (54 boys and 39 girls) were evaluated cross-sectionally in this study. Additionally, 20 subjects (11 boys and 9 girls) from the cross-sectional cohort who did not participate in the jumping intervention and had valid baseline and 7-month test data were evaluated longitudinally to assess the effects of growth. The study was approved by the Oregon State University Institutional Review Board and the Oregon Board of Radiology. Parents of all children gave written informed consent prior to participation (Appendix B). All testing was conducted at the Bone Research Laboratory in Corvallis, Oregon.

Each child's height and weight were measured in lightweight clothing and without shoes. Height was recorded to the nearest 0.1 cm using a wall-mounted stadiometer and weight was recorded to the nearest 0.1 kg using an electronic scale. Body fat was estimated with skinfold measurements according to the protocol and prediction equations formulated by Williams et al. (33). Tanner stages were used to assess sexual maturation (34) (Appendix E). Parents were given line drawings and written explanations of each developmental stage that were classified by pubic hair in

boys and both pubic hair and breast development in girls. A researcher knowledgeable with Tanner stage criteria was available to answer questions. To determine average calcium intake, the parent of each child completed a Harvard Youth Food Frequency Questionnaire (35) (Appendix D). Mean data (± standard deviation) for subject age, anthropometric measures and calcium intake is given in Table 1.1. All subjects showed no signs of sexual maturation and were classified as prepubertal (Tanner Stage I).

**Table 1.1.** Age, anthropometric measures and calcium intake in prepubertal boys and girls [data are given as mean ± standard deviation (SD)]

| | Boys (n=54) | Girls (n=39) | *P*-value |
|---|---|---|---|
| Age (y) | 8.02 ± 1.24 | 8.01 ± 1.29 | 0.97 |
| Height (cm) | 129.0 ± 8.6 | 128.6 ± 10.16 | 0.81 |
| Weight (kg) | 28.7 ± 6.6 | 28.7 ± 6.5 | 0.97 |
| Avg. Calcium (mg) | 1256 ± 431 | 1230 ± 370 | 0.82 |

## Study Design

We wanted to determine if there are sex differences in the components of fracture risk (vertebral loading and strength) in prepubertal children. To evaluate the material and structural properties of the lumbar spine, we used dual-energy x-ray absorptiometry (DXA) to assess the bone mass, density and geometry of the body of the L3 vertebra. To examine how sexes might differ in the distribution of forces at the lumbar spine, we evaluated the stresses incurred by L3 under three different loading scenarios: upright standing, spinal flexion of 50° and spinal flexion of 90°. By determining the strength of the bone and the loads applied to the vertebra, we could then examine if sex differences in the factor of risk existed in each loading scenario. Finally, we examined bone size and volumetric density longitudinally to determine whether growth caused disparate changes in boys and girls.

## Methods

### Failure Load: Measurement of vertebral strength

Failure load is a function of the cross-sectional area and volumetric density of the vertebra (3, 6, 11). To estimate cross-sectional area, vertebral body dimensions were obtained using DXA (Hologic QDR/4500-A; Hologic Inc., Waltham, MA, USA). The same trained technician performed all DXA scan analyses. The lateral projection was used in conjunction with the posterior-anterior (PA) projection to isolate the clinically relevant anterior body of the L3 vertebra. Vertebral body width was determined from the PA projection while height and depth of L3 were evaluated using the lateral projection. Vertebral height was calculated as the average of the anterior, middle and posterior heights (6). Average depth was calculated as lateral area divided by average height (6). Cross-sectional area (CSA) of L3 was calculated as

(Eq.1) $[\pi \times \text{width}/2 \times \text{avg. depth}/2]$

and was assumed to be ellipsoidal in shape (6, 36). Vertebral body BMC (g), bone area ($cm^2$) and areal BMD ($g/cm^2$) of L3 were also evaluated by DXA.

The compressive strength of lumbar vertebrae depends on bone mass and the structural arrangement of the trabecular and cortical bone (37). Bone mass is best evaluated with ashing, and the strength ($S$) of the vertebral body has been given as,

(Eq.2) $$S = 8515\rho_{ash}^{1.6},$$

where $\rho_{ash}$ is the volumetric ash density of the vertebral centrum excluding the endplates (6). vBMD of the vertebral body centrum, as evaluated with DXA, was substituted for $\rho_{ash}$ in this equation such that vertebral body strength was evaluated as

(Eq.3) $$S = [8515 \times (\text{mid-vBMD}^{1.6})],$$

where mid-vBMD is the volumetric density of the vertebral centrum without the endplates. We were unable to isolate and exclude the endplates from our measurements due to DXA software limitations; thus, we assessed mid-vertebral BMC, mid-volume and mid-vBMD under the assumption that the material properties of L3 were uniform throughout the entire vertebral body. Accordingly, mid-BMC was evaluated as one-third lateral BMC

(Eq.4) Mid-BMC = Lateral BMC/3.

Mid-volume was calculated as cross-sectional area divided by one-third average height

(Eq.5) Mid-volume= [CSA/ (Avg. Ht/3)].

This volume estimation is based on the assumption that the vertebral body is a cylinder with an ellipsoidal cross-section, which has been validated to predict vertebral volume against submersion in vitro (6, 7, 15, 36, 38). Mid-volumetric BMD was estimated as mid-BMC divided by mid-volume. (6). The in-house precision error for the qualitative bone measurements of the lumbar spine is 1-1.5% based on adult scans.

## Applied Load: Estimation of internal and external forces

Static analyses were performed to estimate the contraction forces of the erector spinae and the compressive loads on the lumbar spine during upright standing, forward flexion of 50° and forward flexion of 90°. These analyses were based on the assumption of static equilibrium such that the sum of all forces and moments along the x and y-axes was equal to zero (equations 6, 7 and 8, respectively).

(Eq. 6) $\Sigma F_X = 0$

(Eq. 7) $\Sigma F_Y = 0$

(Eq. 8) $\circlearrowleft \Sigma M_O = 0$

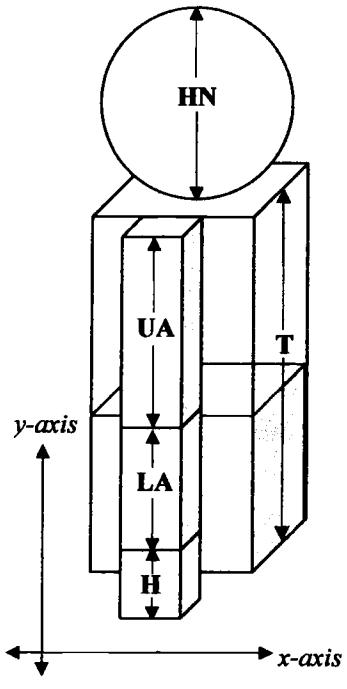
Vertebral loading results from a combination of body weight forces and muscular forces. In the first loading scenario, upright standing, we assumed that the center of gravity of the upper body was located directly over L3 and that no muscle forces or bending moments were generated to maintain postural equilibrium. Therefore, the compressive force acting on the vertebral body during upright standing was estimated to be equivalent to the resultant weight ($W_R$) of the upper body segments, which can be determined by simply summing the weights of the body segments of the head + neck, trunk and upper extremities (Eq. 9, Fig. 1).

(Eq. 9) $\text{Force}_{0^\circ} = W_R,$

*where* $W_R$ is the resultant weight equal to the sum of the weights of each upper body segment: the Head + Neck segment (HN), Trunk segment (T), Upper and Lower Arm segments (UA and LA) and the Hand segment (H). $W_R$ takes into consideration the mass of both arms (Eq. 10, Fig. 1)

(Eq. 10) $W_R = [W_{HN} + W_T + 2 \times (W_{UA} + W_{LA} + W_H)]$

The masses of the upper-body segments were calculated from linear regression equations developed for children by R.K. Jensen (1986) (39). Equations for the different segment masses were based upon whole body mass data collected during testing.




**(Fig. 1)** During upright standing, spinal muscle forces and forward bending moments are assumed to be equal to zero such that the estimated compression forces on the third lumbar vertebral body during upright standing were equal to the sum of the weight of the head + neck (HN), trunk (T), and upper extremities (UA, LA & H).

The compressive force on L3 during spinal flexion results from the combined forces of gravity acting on the upper body and the muscle forces generated to resist gravity at the angle of forward bending (Fig. 2). During spinal flexion, the weight of the upper body generates a forward bending moment that must be resisted by the spinal extensor muscles in order to maintain static equilibrium. The forces applied by the erector spinae muscles must balance the moments applied by the upper body weight acting at its center of gravity. Therefore, to assess the compressive force on L3, we first determined the distance between L3 and the center of gravity of the upper body ($\overline{X}$). The center of gravity of any system of segments can be found by summing the moments applied by each individual segment around an arbitrary axis (40). To employ this approach, we used anthropometric measures to determine individual segment weights, lengths and locations of center of gravity. These values were then

used in standard engineering formulae for finding the center of gravity of a system consisting of multiple particles (41) (Eq. 11).

(Eq. 11)
$$\overline{X}_{\theta} = \frac{[(\overline{X}_{HN} \times W_{HN}) + (\overline{X}_{T} \times W_{T}) + (\overline{X}_{A} \times 2W_{A})]}{W_{R}}$$

*where* $\overline{X}_{HN} = [(L_T + L_{HN} - r_{HN}) \times \sin\theta] \times W_{HN}$,

$\overline{X}_{T} = [(L_T - r_T) \times \sin\theta] \times W_T$ and,

$\overline{X}_{A} = [L_T \times \sin\theta] \times [2 \times W_A]$ (26).

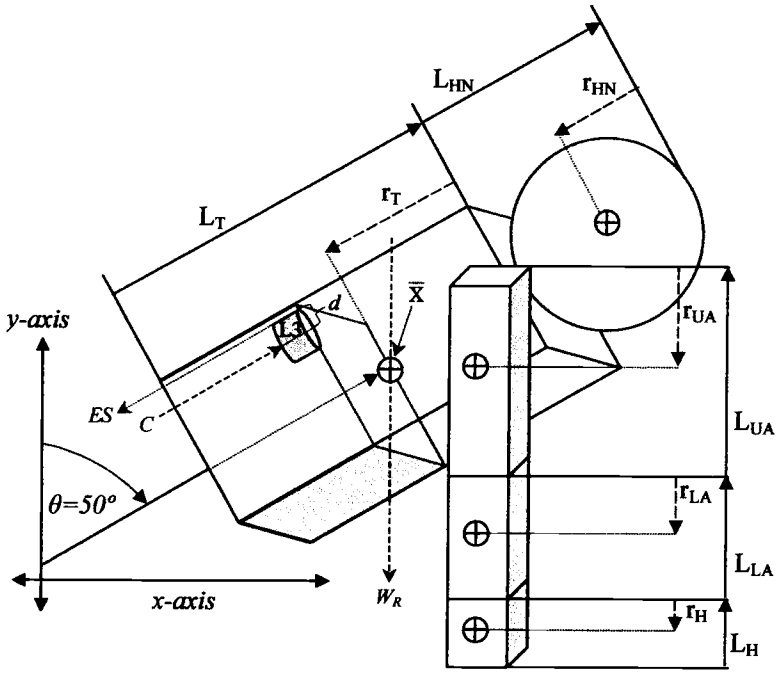
$\overline{X}_{HN}$, $\overline{X}_{T}$ and $\overline{X}_{A}$ represent the locations along the x-axis of the center of gravity for each segment: the head + neck, trunk, and composite arm segments, respectively. $W_R$ is the resultant weight equal to the sum of the weights of each upper body segment (Eq. 10). $L_{HN}$ and $L_T$ represent the lengths, in centimeters, for the head + neck and trunk segments. $r_{HN}$ and $r_T$ are the radii to the center of mass for the head + neck and trunk segments. The location along the x-axis of the center of mass of each arm segment was assumed to lay in-line vertically with the superior border of the trunk segment. $\theta$ represents the angle of forward bending, either 50 or 90 degrees. To confirm the accuracy of our derivations and their implementation in equations, we checked our predictions against known values determined from known segment parameters and bending angles (see Appendix F).

The radius to the center of mass for each segment was calculated from linear regression equations designed specifically for children (39). The equations used to determine the length of the radius to the segment centers of mass were calculated using segment lengths that were estimated from the 1977 AnthroKids database (40). Appropriate AnthroKids data were determined according to each subject's age. Segment length was derived as a proportion of subject height measured during testing. Segment proportions were determined according to the corresponding AnthroKids age group.

The mass, length and radius to the center of mass of the head segment included both the head and neck, extending from the superior surface of the sterno-clavicular joint to the top of the subject's head. This "head + neck" segment length was established by subtracting the average distance from the standing surface to the sterno-clavicular joint, as estimated from age-appropriate AnthroKids data, from the subject's measured height.

Available pediatric data for estimating trunk segment lengths, masses and radii to centers of mass included the portion of the body that extends from the greater trochanter to the superior surface of the sterno-clavicular joint. Therefore, our reference point for the estimation of forces on L3 was at the level of the greater trochanter and, for the purpose of comparison to force data available in the literature, we made the assumption that forces on L3 are equal to forces at this reference point. The distance to the subject's greater trochanter as well as the distance to the sterno-clavicular joint was estimated using data from AnthroKids. Individual trunk segment lengths were determined by subtracting the height of the subject's greater trochanter from the height to their sterno-clavicular joint.

Upper-arm, lower-arm and hand segment lengths were estimated directly from the AnthroKids data that coincided with each subject's age. These segment lengths were then used to calculate the radius to the center of mass for these segments during the bending scenarios.




**(Fig. 2)** Spinal flexion creates a forward bending moment. As a result, compressive forces (*C*) acting on the vertebra must equal both the erector spinae muscle forces (*ES*) and the forces generated by the weight of the upper body.

The force imposed at L3 is therefore equal to the resultant weight about the x-axis at the given forward bending angle, $\theta$ (Eq. 12) (41).

(Eq. 12) $$\text{Force}_\theta = [W_R \times (_\theta / d)],$$

where $\overline{X}_\theta$ represents the location of the center of mass of the upper body along the x-axis at angle $\theta$. $d$ is the length of the moment arm of the spinal extensor muscles acting on L3, which was measured according to the protocol of Duan et al. (6, 7) (Eq. 13):

(Eq.13) $d$ = [(length 1 + length 2) – mid-vertebral body depth/2]

where length 1 is the distance from the anterior edge of the vertebral body to the anterior edge of the high density region that indicates the location of the transverse processes. Length 2 is the distance from the anterior edge of the vertebral body to the posterior edge of the high-density region (6, 7).

## Vertebral Stress

Stress is a measure of the force per unit area that develops within a structure in response to applied loads (42). Consequently, the stress on L3 is determined by the forces generated from the weight of the upper body and the extensor muscles divided by the cross-sectional area of L3. Therefore, the stress on L3 during each of the three standing positions was calculated according to the following equations (eq. 14, 15 and 16, respectively):

(Eq. 14) $\text{Stress}_{0^\circ} = \text{Force 1} / \text{CSA}$,

(Eq. 15) $\text{Stress}_{50^\circ} = [\text{Force 1} * [\cos 50^\circ + (\overline{X}_{50^\circ} / d)] / \text{CSA}]$ and,

(Eq. 16) $\text{Stress}_{90^\circ} = [\text{Force 1} * [\cos 90^\circ + (\overline{X}_{90^\circ} / d)] / \text{CSA}]$(41, 42).

## Factor of Risk

The Factor of Risk describes the ratio of the applied load to the load required to cause fracture (12) and is calculated as

(Eq. 17) $\text{Factor of Risk} = \text{Stress} / [8515 * \text{vBMD}^{1.6}]$ (6).

## Data Analysis

All data are reported as the mean $\pm$ the standard deviation. Univariate ANOVA was used to determine the significance of any differences between groups (54 boys and 39 girls) on each dependent variable. Difference scores were calculated to examine the effect of a 7-month growth period on the vertebral dimension and bone density of L3 in 20 subjects (11 boys and 9 girls). Univariate ANOVA was also used to determine the significance of any differences in the effects of growth between boys and girls. A *P*-value of 0.05 was used to establish statistical significance unless otherwise noted.

# RESULTS

## Sex Differences: A Cross-sectional Analysis

### Vertebral Strength

We first asked if vertebral bone dimensions and bone density were different between sexes in prepubertal children. We found that L3 geometry was different between sexes (Table 2.1). Specifically, L3 was 6.7% wider ($P < 0.001$) and 5.8% deeper ($P = 0.01$) in boys than girls. Vertebral height, however, was 3.5% greater in girls than boys ($P = 0.04$). In accordance with the differences in width and depth, the corresponding cross-sectional area was 12% greater in boys ($P < 0.001$). The volume of the middle portion of L3 (Mid-Volume) was 7.8% greater in boys than girls, but this difference did not reach statistical significance ($P = 0.07$)(Table 2.1).

**Table 2.1**. Vertebral geometry as evaluated by the height, width, depth, cross-sectional area and mid-volume of L3

| | Boys (n= 54) | Girls (n= 39) | *P*-value |
|---|---|---|---|
| L3 Height (cm) | 1.96 ± 0.17 | 2.03 ± 0.19 | 0.04* |
| L3 Width (cm) | 3.76 ± 0.24 | 3.51 ± 0.29 | <0.001‡ |
| L3 Depth (cm) | 2.78 ± 0.31 | 2.62 ± 0.32 | 0.01† |
| CSA ($cm^2$) | 8.25 ± 1.24 | 7.26 ± 1.34 | <0.001‡ |
| Mid-Volume ($cm^3$) | 5.39 ± 0.99 | 4.97 ± 1.22 | 0.07 |

* = significant @ $P \leq 0.05$; † = significant @ $P \leq 0.01$; ‡ = significant @ $P \leq 0.001$

We also found that bone area, BMC and BMD of L3, as evaluated by posterior-anterior and lateral DXA projections, were not different between boys and girls (Table 2.2). Volumetric BMD of the middle portion of L3 was 4.6% higher in girls than boys, but did not reach statistical significance with *P*-values of 0.07. Accordingly,

estimated of compressive strength (*S*) was greater in girls by 7.3%, but like vBMD, was not statistical significant (Table 2.2).

**Table 2.2**. Bone area, BMC and BMD from posterior-anterior and lateral DXA scans of L3

| | Boys (n= 54) | Girls (n= 39) | *P*-value |
|---|---|---|---|
| Lateral Area ($cm^2$) | 5.45 ± 0.82 | 5.36 ± 1.02 | 0.63 |
| Lateral BMC (g) | 3.02 ± 0.73 | 2.91 ±0.78 | 0.51 |
| Mid-vBMD ($g/cm^3$) | 0.186 ± 0.02 | 0.195 ± 0.02 | 0.07 |
| Strength ($g/cm^3$) | 583 ± 119 | 629 ± 121 | 0.07 |

## Vertebral Loading and Stress

We also asked whether prepubertal boys and girls differed in their vertebral loading patterns. When we examined the components of vertebral loading, we found that, while upper body mass was not different between boys and girls [188.8 ± 41.4 vs. 189.2 ± 41.4 N, respectively; $P = 0.96$], segment lengths did differ. Girls' head + neck segments were 5.3% longer than boys' ($P < 0.001$). In contrast, boys had 3.5% longer trunks ($P = 0.02$), 4.8% longer upper arm segments ($P < 0.01$), and 5.8% longer lower arm segments ($P < 0.001$) than girls. Hand lengths were not different between boys and girls ($P = 0.65$). As a result of the differences in segment lengths, during forward bending, the location of the upper body center of mass ($\overline{X}$) was located more anterior along the x-axis in boys than girls by 2.6% at 50° of flexion ($P = 0.03$) and by 2.7% at 90° of flexion ($P = 0.03$). Compressive forces on L3 were not different between prepubertal boys and girls. However, the compressive stress (load per unit area) on L3 was 12% greater in girls than boys in all three loading conditions (Table 2.3).

**Table 2.3.** Sex-differences in vertebral loading and stress

| | Boys (n=54) | Girls (n=39) | *P*-value |
|---|---|---|---|
| Force @ 0° (N) | 189 ± 41.4 | 189 ± 41.4 | 0.96 |
| Force @ 50° (N) | 1485 ± 395 | 1482 ± 387 | 0.98 |
| Force @ 90° (N) | 1938 ± 515 | 1935 ± 505 | 0.98 |
| Stress @ 0° ($N/cm^2$) | 23 ± 4.2 | 26 ± 4.3 | <0.001‡ |
| Stress @ 50° ($N/cm^2$) | 195 ± 39.2 | 221 ± 42.1 | <0.01† |
| Stress @ 90° ($N/cm^2$) | 235 ± 48.0 | 267 ± 52.0 | <0.01† |

† = significant @ $P \leq 0.01$; ‡ = significant @ $P \leq 0.001$

## Factor of Risk

We asked whether prepubertal boys and girls differed for the factor of risk during standing and forward bending. We report that there were no sex differences in the factor of risk for upright standing, spinal flexion of 50° or spinal flexion of 90° (Table 2.4).

**Table 2.4.** The factor of risk during upright standing and spinal flexion of 50° and 90°

| | Boys (n=54) | Girls (n=39) | *P*-value |
|---|---|---|---|
| F.O.R @ 0° | 0.04 ± 0.01 | 0.04 ± 0.01 | 0.21 |
| F.O.R. @ 50° | 0.34 ± 0.08 | 0.36 ± 0.08 | 0.27 |
| F.O.R. @ 90° | 0.41 ± 0.09 | 0.44 ± 0.10 | 0.29 |

## Sex-Differences in Growth: A Longitudinal Analysis

The effect of growth on subject height, weight and calcium intake was not different between boys and girls over the seven-month period (Table 3.1). No subjects reported any changes in sexual maturation characteristics and thus remained classified as Tanner stage I.

**Table 3.1.** Effects of age on anthropometric measures and calcium intake

| | Boys (n=11) | Girls (n=9) | *P*-value |
|---|---|---|---|
| Height (cm) | 3.30 ± 1.71 | 2.44 ± 1.50 | 0.25 |
| Weight (kg) | 1.42 ± 0.83 | 1.86 ± 1.35 | 0.38 |
| Calcium (mg) | -50.9 ± 392.6 | 20.0 ± 93.1 | 0.63 |

## Vertebral Strength

We asked whether growth affects the geometry as well as the density of the vertebral bodies differently in boys and girls. We report that there were no sex differences in the effects of growth on the components of vertebral strength during 7 months of prepubertal growth (Table 3.2). Mid-vBMD of L3 did not change differently in boys vs. girls during this growth period. Additionally, no disparate changes between sexes were seen in vertebral cross-sectional area, width, average depth or average height (Table 3.2).

**Table 3.2.** Effects of age on volumetric BMD and bone size

| | Boys (n=11) | Girls (n=9) | *P*-value |
|---|---|---|---|
| Mid-vBMD ($g/cm^3$) | -0.007 ± 0.010 | 0.000 ± 0.018 | 0.31 |
| CSA ($cm^2$) | -0.12 ± 0.59 | 0.05 ± 0.50 | 0.51 |
| Width (cm) | 0.04 ± 0.14 | 0.20 ± 0.11 | 0.72 |
| Depth (cm) | -0.07 ± 0.17 | 0.01 ± 0.20 | 0.37 |
| Height (cm) | 0.08 ± 0.15 | 0.06 ± 0.09 | 0.69 |

# DISCUSSION

Our primary question asked whether sex differences exist among prepubertal children with regards to vertebral bone dimensions, bone density, vertebral loading patterns and the factor of risk. The data supported our hypothesis that boys have larger vertebrae than girls during childhood. Even prior to the pubertal growth spurt, L3 vertebral width and depth is greater in boys than girls, which corresponds to a larger cross-sectional area in boys. Conversely, vertebral height in girls is greater than boys. Sex differences in volumetric BMD ($g/cm^3$) and strength ($S$) were not statistically significant in our population with alpha = .05. It is probable, however, that low power inhibited our ability to detect a true difference between boys and girls (power = 0.44 and 0.45, respectively). Consequently, we believe that the same analyses of a larger population would support the trends in this study and indicate that girls have greater vBMD and estimated vertebral strength than boys at Tanner stage I.

As expected, we report that forces on L3 do not differ between sexes during upright standing and forward bending of 50° and 90°. However, since these forces are distributed over a greater cross-sectional area in boys, vertebral stresses are lower in boys than girls under each of these loading conditions. Furthermore, we determined that forward bending of 50° and 90° resulted in spinal loading at 34% and 41% of the fracture threshold for L3, respectively.

We also asked whether growth affects the geometry as well as the density of the vertebral bodies differently in boys and girls. As expected, our data demonstrate that, in our small population, seven months of growth does not result in disparate changes between prepubertal boys and girls in the geometry and volumetric density of the L3 vertebral body.

Our study has several strengths. To our knowledge, ours is the first to examine the relationship between bone size and loading at the lumbar spine in children. Moreover, we believe this is the first study to assess biomechanical implications of the sex differences in vertebral size in prepubertal children. Additionally, we employed lateral DXA scans to assess the BMC and BMD in this study. As compared with

traditional PA scans, lateral scans facilitate the isolation of the posterior elements and thus provide more accurate bone measures of the clinically relevant vertebral bodies. Finally, we used subject-specific anthropometric data to estimate the effects of vertebral loading in kids. As in previous work (6), rather than simply using a single estimate of upper body weight to calculate vertebral loads, we used anthropometric data and engineering statics to determine the center of gravity of the upper body as a system composed of multiple segments.

We make several assumptions that limit our results. First, in efforts to assess bone strength we assume that vertebral BMC is an accurate surrogate for the ash weight of the third lumbar vertebra. Vertebral compressive strength is dependent on bone mass and the trabecular and cortical bone structure (37). Bone mass is best assessed through ashing, and vertebral cancellous ash density has been correlated highly with compressive stress (43). For obvious reasons, ashing is not an appropriate method for assessing bone strength in vivo. Fortunately, DXA measures of vertebral BMC and BMD are also highly correlated to vertebral load and stress (43). Moreover, Ebbesen et al. (43) found that the ash weight of the total vertebral body of L3 is correlated to the DXA BMC value with an $r^2 = 0.91$. Consequently, we believe that our use of BMC to estimate vertebral strength is a suitable application and should be considered valid.

We also assume that the shape of the third lumbar vertebra approximates a cylinder with an ellipsoidal cross-section. Therefore, vertebral volume is calculated in the same way that one would calculate the volume of an ellipsoidal cylinder [$\pi \times$ width/2 $\times$ depth/2 $\times$ height]. Consequently, the calculation used to determine bone strength is also dependent upon the validity of this assumption. Vertebral body volume is best assessed by submersion (36). Tabensky et al. (36) demonstrated that lumbar vertebral volume estimated with the above calculation was similar to the volume derived from submersion, an assumed gold standard.

Another limitation was our assumption that forces incurred at L3 are equal to those estimated at our point of reference, the greater trochanter. We chose to make this assumption because we wanted to evaluate the influence of body segment mass and

size on spinal loads as accurately as possible. Due to limitations in the availability of data on body segment mass and size in children, we were unable to determine the relative location of L3 within the overall trunk segment in children. Schultz and Andersson (44) indicate that, based upon body segment weight data in adults, the portion of the trunk that lies above L3 carries 36% of a subject's total body weight. The weight of the head is approximated as 5% of total body weight and the weights each arm are said to be 4.5% of body weight (44). The corresponding weight of the upper body above L3 is then approximately 50% of the subject's total weight. In their analysis of the biomechanics of standing and forward bending, Duan et al. (6) indicate that 45.5% of total body weight is located above L3. The body proportions of children, however, are different from adults (45). R.K. Jensen's regression equations clearly indicate that changes in segment mass proportions occur with age, which "preclude the simple adaptation of adult proportions" (45). The proportion of body weight reported to lie in the upper bodies of children ranges from 62-67% of total body weight and the definition of "upper body" varies between studies (46, 47). Using equation parameters for the entire trunk, which was measured from the greater trochanter to the sterno-clavicular joint, enabled us to more accurately estimate the loads imposed during standing and forward bending for each subject. For the purpose of determining the presence of sex-differences, we believe that this was a more appropriate estimation considering that differences in the body segments of boys and girls may contribute to variations in loading and stresses at the spine between sexes.

In addition to our assumptions, our small sample size in the prospective observation limited this study. While the longitudinal results support our hypothesis that prepubertal growth does not affect bone size and density differently between sexes, these results should be interpreted with caution because of our limited sample size. Furthermore, we report that, in boys, Mid-vBMD, CSA and vertebral depth values went down following a 7-month growth period. Decreases in bone density and size in a growing population are physiologically improbable in the absence of disease. Therefore, we believe these results are indicative of problems regarding sample size, measurement technique, and/or study design. Again, low power may have inhibited

our ability to detect true differences between prepubertal boys and girls. And although all aspects of scanning were performed according to the manufacturer's instructions, lateral DXA scans may be particularly sensitive to minute changes in subject positioning from one assessment to another as compared to PA scans. Additionally, seven months may have been too short a duration to provide a true assessment of vertebral growth. The duration of the complete remodeling cycle is estimated to take about 3-6 months to complete (48). However, during normal growth, the magnitude of bone change during the formation phase dominates the effects of the resorption phase. Finally, the retrospective nature of the study design prohibited us from directly measuring body segment parameters and limited the number of individuals who had complete baseline and seven-month data. Further examination with a larger, more diverse sample population is clearly warranted.

Our results support reports in the literature that, across the lifespan, boys have larger lumbar vertebrae than girls (6, 7, 23, 25, 26, 30, 49). However, our data vary from findings in the literature that state that vertebral height is greater in males or does not differ between sexes throughout growth and aging (7, 23, 25, 26, 30). In children, the discrepancy in data regarding vertebral height may stem from differences in measurement technique and the use of CT vs. DXA scanning technology. Results regarding sex differences in the lumbar spine bone mineral density of children are varied. However, variability in the methodology used to assess BMD may account for these differences. Gilsanz et al. used CT scanning to assess cortical and trabecular vBMD ($g/cm^3$) and found no differences in boys and girls across all stages of pubertal development (23, 25, 26). Studies using DXA measures of areal BMD suggest that during the onset of the pubertal growth spurt in girls, which occurs prior to that in boys, girls have higher vertebral density ($g/cm^2$) than boys (19, 27). It is likely that the planar nature of the absorptiometry data failed to account for differences in the three dimensional geometry of the vertebrae that was captured by the CT scans.

Our data on sex differences in vertebral cross-sectional area are largely supported in the literature. Gilsanz et al. (23) reported that boys had larger vertebral size in the transverse plane than girls across the all stages of development. The authors did not,

however, examine the biomechanical implications of these sex differences. Duan et al. (6, 7) found that in adults aged 18-92 years, forces acting on L3 are greater in men than women because men have greater stature and thus greater compressive loads. They also report that in the young adults (18-43y), vertebral stresses are not different between sexes because in men, higher loads are distributed across a greater vertebral cross-sectional area than in women (6,7). Consequently, the factor of risk does not differ between sexes in young adults (6). With aging, however, they found that women have less gain in cross-sectional area and a greater loss of vertebral bone density such that elderly women (60-92y) incurred greater stresses at the spine than elderly men (6,7). The authors suggest that these changes were the result of higher rates of endosteal resorption in women and slower rates of periosteal expansion as compared to men (7). As a result, the factor of risk increased by only 21% in men during aging vs. a 102% increase in women. Gilsanz et al. examined the biomechanical implications of vertebral size in young adults (25-45y) and found that when matched for age, weight, trabecular vBMD and vertebral height, the stress incurred at the lumbar spine is 33% greater during axial compression and 39% greater during bending in women than in men when subjected to equivalent loads (30). Since prepubertal females and males were not different for height and weight, our data confirm that the vertebral stress on L3 in boys is less than in girls when loads are equivalent because, in boys vertebral loads are distributed over a greater cross-sectional area. Prepubertal girls, however, appear to compensate for their smaller bones by having higher vertebral strength, or higher vBMD. While differences between sexes in vBMD did not reach statistical significance, we believe that elevated vBMD in girls provides the best explanation for the subsequent equivalency between sexes for the factor of risk. So, while the factor of risk is equivalent between young adult men and women because larger bones carry greater loads in men, the factor of risk is equivalent between prepubertal boys and girls because girls have stronger vertebrae, which offsets the load distribution advantage of boys.

Subjects in the present study did not advance in pubertal status over the seven-month growth period. Gilsanz et al. (23) found that the magnitude of the difference in

vertebral cross-sectional area between boys and girls increased when moving from Tanner stage I to Tanner stage V. This would suggest that hormonal variations during puberty exert some influence on the discrepancy in bone size between sexes. However, it is clear that this discrepancy is present even prior to puberty and may therefore have genetic origins. Tabensky et al. (50) examined the relative contribution of reduced peak accrual vs. age-related bone loss to osteoporosis by assessing women with vertebral fractures and their adult daughters. Since the daughters of women with vertebral fractures had reduced vBMD vs. the daughters of women without fracture, the authors suggest that the vBMD deficit in women with fractures may be the result of a genetically predetermined reduction in peak vBMD (50). Women with vertebral fractures were also characterized by reduced vertebral volume in comparison to non-fractured controls. However, their daughters did not share these reductions in bone size, which suggests that reduced vertebral size results during the aging process rather than during growth (50). In a study looking at sets of twins, Naganathan et al. (32) demonstrated that the genetic influence on the variance in BMD is similar between men and women. At the forearm, however, they found that there were lower correlations between the bone densities of the opposite-sex dizygotic twin pairs as compared to same-sex dizygotic twin pairs (32). The authors suggest that this may indicate that there is some degree of association between sex and the influence of genetics on bone density (32).

This study has several implications. Our findings in prepubertal children, suggest that the factor of risk is comparable between prepubertal boys and girls because girls have stronger vertebrae, which probably offsets the load distribution advantage seen in boys. Furthermore, during growth, increases in vertebral width and depth may be more important than increases in vertebral height with regards to maximizing failure load and preventing fracture of the lumbar vertebrae. Finally sex-differences in vertebral failure loads that become clinically relevant following an osteoporosis-related fracture probably have genetic origins that are evident even before puberty such that there is some sort of genetic preparation in boys for the higher loads they will incur in adulthood.

We have shown that boys have larger vertebral cross-sectional area than girls prior to puberty. Consequently, compressive stresses imposed on the vertebra are lower in boys than girls when loaded equally. The factor of risk, however, is similar between sexes most likely because girls have higher vBMD than boys. Finally, we found no differences in the effects of growth upon the geometry or vBMD of the vertebra between boys and girls. Since the amount of bone accrued during growth is a determinant of the risk for fracture in later life, and larger bones appear to be better suited for preventing fracture we recommend that studies be done to examine the ability to modify bone size as well as bone content during growth. If bone size can be increased through intervention, a reduction in the greater prevalence of vertebral fractures among women may be achieved.

# CHAPTER 3: CONCLUSION

Osteoporosis is a critical public health problem that results in at least 1.5 million fractures in the United States each year. While osteoporosis is not a gender-specific disease, the risk for fracture in later life is greater for women than men (1-7). With regards to osteoporosis of the spine, sex differences in the mass and size of the vertebrae are thought to contribute to the greater occurrence of fractures in women. Though sex differences are widely recognized, the relative contributions of bone mass, bone density and bone size to the differences in vertebral strength and fracture risk between men and women have not been fully delineated. Moreover, it is not clear when these factors begin to contribute to the discrepancy in fracture risk between sexes or how their influence changes differently with age in men and women.

Our study has provided preliminary evidence that the relative contribution of vertebral size and strength to failure load varies between males and females even prior to puberty. While differences between sexes in strength did not reach statistical significance, we believe that elevated vBMD in girls provides the best explanation for the subsequent equivalency between sexes in the factor of risk. Our findings suggest that the factor of risk is comparable between prepubertal boys and girls because girls have stronger vertebrae, which offsets the load distribution advantage seen in boys. Furthermore, we found that before the onset of puberty, a growth period of seven months does not result in disparate changes between sexes in the density and size of the third lumbar vertebra.

Peak bone accrual during growth and adolescence is a major determinant of fracture risk in later life (19-21) and maximizing peak bone mass has been recommended as a potential strategy in preventing osteoporosis (4). While optimal peak bone mass depends upon adequate nutrition and normal hormonal balance, physical activity is also advocated as a way to maximize bone accrual during growth (4). Since larger bones appear to be better suited for preventing fracture we recommend that studies be done to examine the modifiability of bone size during growth. If bone size, like bone mass can be increased through intervention, this may

provide a new strategy in the reduction of osteoporosis-related vertebral fractures in women.

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# APPENDICES

# APPENDIX A: LITERATURE REVIEW

# LITERATURE REVIEW

While osteoporosis is not a gender specific disease, the discrepancy in its prevalence and related fracture incidence between men and women is attracting progressively more public and research interest. Although the exact mechanisms that result in these inconsistencies are not known, it has been hypothesized that sex-differences in the skeletal response to growth and development may provide the foundation for the greater occurrence of osteoporosis and fractures in women. To further explore this topic, it is the aim of this proposal to do the following: 1) Review the etiology of osteoporosis and the significance of gender discrepancies with specific regards to fractures of the spine, 2) To examine how growth may influence gender differences in fracture incidence, and 3) To propose future research to further delineate this area of interest.

***Consequences of Osteoporosis and Fractures of the Spine:*** Osteoporosis is an increasingly critical public health problem. According to the National Osteoporosis Foundation's 2000 census information, nearly 44 million Americans over the age of 50 are currently subject to developing osteoporosis (1). Amazingly, this means that more than half of all individuals 50 years of age or older and living in the United States are at a significant risk for increased bone fragility and the fractures that are inherent to this aging-related disease (1). Currently, upwards of seventeen billion dollars are spent to treat the 1.5 million fractures that are reported each year in the United States (1, 2). Sadly, these numbers are expected to double, if not triple, in coming years if effective preventive measures are not implemented (1, 3). Moreover, the consequences these fractures represent at the level of the individual are more devastating than simple monetary costs. Fracture sufferers are subject to increased mortality rates, chronic pain, significant psychological burden and an overwhelming decrease in quality of life, as exemplified by increased levels of fear, anxiety and depression often reported in osteoporosis sufferers (1-4).

More than half of all age-related fractures reported in the U.S. occur at the spine and account for more than $746 million in annual health care costs (1). Furthermore, unlike hip-fractures, fractures of the spine are often unreported or untreated and it is estimated that only a third of all vertebral fractures receive medical attention (1). Although the prevalence of osteoporosis increases for both sexes with advancing age, the risk for a fragility fracture in later life is greater for women than men (1-7). It is estimated that 30-50% of all women and 15-30% of men will experience at least one osteoporosis-related fracture over their lifetime (5, 6). While women's lifetime risk of a hip fracture is twice that of men, in the United States the lifetime risk for a clinically diagnosed vertebral fracture for women jumps to more than three-times that for men (16% and 5% respectively) (8). Moreover, at any given age, women are 1.9 times more likely than men to experience a fracture of the spine (9). While it is obvious that more women suffer from problems associated with skeletal fragility than men, the causes underlying these sex-differences are not well understood.

***Etiology of Fractures of the Spine:*** Unlike the bones of the appendicular skeleton that are composed primarily of cortical bone, the axial skeleton, including the vertebrae, consists mainly of cancellous bone. In comparison to cortical bone, which is dense in structure, cancellous bone is characterized by a sponge-like arrangement of trabeculae. While still under investigation, it is generally accepted that the specific alignment of these trabeculae correlates to (and remodels to adapt to) the directions in which the bone is habitually stressed (3). The structural advantage of cancellous bone is its high surface area to volume ratio, which equates to a high strength to weight ratio. For example, during activities of daily living (ADLs) a lumbar vertebra with a mass of approximately 7 g (ash weight) is capable of withstanding compressive loads ranging from more than 50% to over 300% of one's body weight (data for relaxed standing and lifting 15 kg from the floor with arms straight down, respectively) (3).

While healthy trabecular bone is quite strong, it is much more metabolically active than cortical bone and is readily susceptible to certain endocrine changes (i.e.

menopause), exposure to different medications, various metabolic disorders and changes in loading patterns. Indeed, the turnover rate of cancellous bone is about twice that of cortical bone, 4% vs. 2% per year (10), with a remodeling rate of 5-10 times that of cortical bone (11). These elevated rates of turnover and remodeling may work to restrict the strength capacity of trabecular bone by limiting its peak accrual.

Another liability of trabecular bone stems from the inverse relationship between fracture risk and bone mass. When comparing equal sizes of cortical and trabecular bone samples, it is clear that cortical bone has far more mass for any given size. In fact, the mass of trabecular bone is approximately one-fourth that of cortical bone (12). Therefore, the structural arrangement, or trabecular architecture, is a potentially vital contributor to cancellous bone strength. Likewise, any damage to this architecture or reduction in its density greatly compromises the loading capacity of the bone such that a decline in number and/or thickness of trabeculae is associated with a reduction in compressive strength (6). In addition, the strength of trabecular bone is closely related to its apparent density such that a slight decrease in vertebral density can result in a significant reduction in strength (3, 13). For example, Hayes and Bouxsein described this phenomenon using values from elderly cadaveric vertebrae and found that a 25% decrease in vertebral density was associated with a 44% reduction in strength (3). Similarly, Ebbesen et al. (14) reported that decreases with age in vertebral compressive strength were twice as large as decreases in vertebral density. However, trabecular deterioration is characteristic of the normal aging process and reductions in apparent density of approximately 50% have been reported from the 3$^{rd}$ to the 8$^{th}$ decade (13). In men, this loss is characterized by a thinning of the vertical trabecular struts while women have been shown to experience more loss of entire trabeculae (15). Additionally, with menopause, estrogen deficiency results in the preferential resorption of the horizontal structures resulting in reduced support to the vertical, load bearing trabeculae. This deterioration has been reported to result in an average diminution in compressive failure force of 75% from ages 25 to 75y with losses of more than 93% in extreme cases (13).

***Factor of Risk:*** Spinal fractures occur when the load applied to the vertebra exceeds its load-bearing capacity (3, 8, 13, 16). The ability to resist fracture is determined by the ratio of the applied load to the load required to cause fracture and is termed the "Factor of Risk" ($\Phi$; $\Phi$ = applied load/fracture load) (17). If the applied load is less than the failure load, then fracture is unlikely. However, if the applied load exceeds the loading capacity of the bone, then fracture is probable. Vertebral loading results from an individual's body weight, height and the external forces applied during activity (3, 13). Additionally, the magnitude of applied loading depends on the biomechanical characteristics of the specific activity. For example, while vertebral compressive forces for forward flexion of 20° with a 10-kg weight in each hand have been estimated at 1850 N, after considering the attenuation by intra-abdominal pressure and the load carried by the facet joints, the corrected estimation of force is closer to 1100 N (17). In some cases, and depending on an individual's skeletal health, even everyday actions such as bending and lifting can exceed the vertebral failure load and result in spinal fracture (6, 3, 13).

The denominator of the Factor of Risk, failure load, is calculated as the product of the cross-sectional area (CSA) and volumetric density (vBMD) of the vertebrae (3, 6, 13). Vertebral CSA functions to increase the vertebral moment of inertia, which provides a biomechanical advantage by decreasing the load incurred per unit area and thus diminishes the risk for fracture (18). Gilsanz et al. reported a 25% reduction in vertebral CSA in women vs. men that was associated with 30%-40% greater mechanical stress (18). In clinical settings, however, measurement of CSA is often neglected and areal BMD (aBMD) values are given as the sole indication of an individuals fracture risk. Although spinal BMD values have been shown to correlate with vertebral compressive loads, relying strictly on density neglects the important and potentially dominant influences of loading. Moreover, disregarding the interaction of bone geometry and density may result in under- or overestimation of fracture risk (19, 20). This premise is supported by the significant overlap seen in the BMD values of individuals with and without fragility fractures (6, 7). Seeman (5) recently reported

that while persons with aBMD values below that at which osteoporosis is diagnosed (2.5 SD below the young normal mean) are at the highest risk for fracture, 50-75% of all fractures occur in the portion of the population with BMD values that place them only at moderate or even mild fracture risk. So, although low bone mass is a primary risk factor for fractures of the spine, both the geometry and the mineral content of the vertebrae account for vertebral strength and determine fracture resistance.

***Assessing Bone Strength:*** Bone mineral content, or BMC (measured in grams), is readily evaluated using dual-energy x-ray absorptiometry (DXA). DXA is also used to assess the area (measured in $cm^2$) of a given bone structure and, in turn, BMC and area values can be combined to give a measure of areal bone mineral density (BMD, BMD = BMC/area, measured in $g/cm^2$). BMD is traditionally used to assess and describe susceptibility to fracture. Specifically, the World Health Organization's definition of osteoporosis is a BMD value of 2.5 standard deviations below the average value for healthy young adult women (2, 4). Although fracture risk is reportedly inversely related to BMD, there is an undisputable overlap in the distribution of BMD values in patients with and without fractures (6, 7, 10, 13, 21), calling into question the validity of BMD as a clinically diagnostic tool. To address this concern, a recent Consensus Development Conference proposed a new working definition of osteoporosis as a disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to increased bone fragility and elevated fracture risk (4). While BMD is still readily used to predict an individual's risk for fracture, this new definition conveys the importance of structural contributions to osteoporosis.

DXA is, perhaps the most widely used instrument in bone densitometry both in research and clinical settings. However, BMD data obtained by DXA has been limited to areal or two-dimensional evaluations of density that fail to accurately account for variations in bone size. Because of the two-dimensional nature of DXA, BMD values are given as (BMC/ projected area) or ($g/cm^2$) which do not fully account for the three-dimensional nature of bones. Carter et al. (22) demonstrated this limitation by

assessing the effect of doubling the linear dimensions of a hypothetical bone specimen. While both samples have equal apparent densities (BMC/volume), DXA cannot capture true volumetric density with areal measures and DXA-derived BMD (BMC/ projected area) is overestimated in the larger sample as twice that of the smaller sample. In turn, the authors conclude that areal assessments of BMD may under- or overestimate the actual bone densities of tall or short persons (22).

The two-dimensional nature of DXA is of particular concern when assessing the vertebrae. Frequently, scans of the spine are performed in the posterior-anterior projection (PA), which incorporates the posterior elements (the spinous and transverse processes) and is unable to isolate the anterior body of the vertebra. While lateral scanning capabilities can better identify the clinically relevant bodies of the vertebrae, research has produced mixed-reviews regarding the improved ability of lateral scans to identify individuals with elevated bone loss (23, 24, 25).

Until recently, the ability to thoroughly and accurately evaluate vertebral structure has been limited to computed tomography (CT) scanning. However due to the costliness of CT scanning and its inherent high radiation exposure, CT technology may not be ethically appropriate for longitudinal studies with healthy subjects or studies in children. In contrast, DXA utilizes low-dose radiation and is less expensive than CT scanning. However, until recently, DXA has been limited to two-dimensional assessments. The latest DXA software, however, permits three-dimensional evaluations of the spine by means of the coupling of data from scans in the posterior-anterior (PA) and lateral projections. This combination yields a "width-adjusted" assessment of BMD (WA-BMD) that is calculated by dividing the BMD value from the lateral scan by the average width of the vertebra obtained from the PA scan. Despite the novelty of this technique and the need for more comparison studies, width-adjusted BMD is reportedly comparable to QCT measures in premenopausal women (26). Additionally, the use of lateral BMD data facilitates the exclusion of the posterior and transverse processes from analysis and thus isolates the clinically relevant vertebral bodies.

***Peak Bone Mass- A Primary Determinant of Osteoporosis-Related Fracture Risk:*** Peak bone accrual during growth and adolescence is a major determinant of fracture risk in later life (27-29) and maximizing peak bone mass has been recommended as a potential strategy in preventing osteoporosis (4). Peak bone mass (PBM) is the maximal amount of bone acquired prior to the beginning of the age-related decline. It has been estimated that the lifetime risk of fracture incidence declines approximately 40% for each 5% gain in PBM (29). While the age at which PBM is achieved is site-specific, it is estimated that more than 90% of PBM is acquired by the age of 18 (29). Vertebral mass, however, is thought to continue growing throughout the third decade of life (30). While the rate of skeletal growth has been shown to be greatest during adolescence, peak bone mineral content velocity (a measure of the rate of accrual) has been shown to lag behind peak height velocity (28, 29). Moreover, it has been suggested that this dissociation between linear growth and skeletal accretion results in a brief period of relative skeletal weakness that may be associated with the increased fracture incidence observed during adolescence (28, 29).

Most studies in children have failed to detect any sex differences prior to the onset of puberty (31-37). Bonjour and colleagues (31) reported no sex-differences in vertebral BMD or size between boys and girls in age groups 9-10 and 10-11 years. However, at about age 12, girls began to experience the "growth spurt" that accompanies the onset of puberty, and for age groups 12-13 and 14-15 years, girls had greater BMD values than boys. In contrast, boys experienced their pubertal growth spurt between the ages of 13 and 17 years (31). The authors concluded that the majority of gain in BMC and BMD from age 9 to 18y, for both boys and girls is accumulated between the ages of 11 and 15 years, suggesting that puberty may provide a limited window of opportunity for the accrual of vertebral bone mass. Accordingly, Glastre et al. (36) showed no sex differences in BMD until the onset of puberty in girls and, Theintz et al. (32) reported that the rate of bone accretion at the spine and femoral neck increases by four to six-fold over a 3-year period, ages 11-14y, in girls and over a 4-year period, ages 13-17y, in boys. In contrast, Gilsanz and colleagues reported no sex differences at any Tanner stage of development (37).

During growth, vertebrae increase in both size and mineral content. However, the relative rates of accrual in size and mass differ depending on pubertal status, sex, race, nutrition and physical activity (29, 38-40). Bonjour et al. found that although boys were shown to have similar BMD values as their female counterparts by the age of 17, when examined more closely, they had significantly greater vertebral area values and trends towards greater mean BMC values (31). Additionally, at any given Tanner stage of development, boys were shown to have greater BMC as well as greater vertebral area. So, although girls had a higher BMD between the ages of 12 and 15, it was the contribution of an elevated BMC in the ratio of BMC to area that accounted for this significance in BMD (BMD = BMC/area). Boys, however, had similar increases in both contributors to BMD (BMC and area) (31). In contrast, Bailey et al. (28) reported a significant gender effect on peak BMC accrual at the femoral neck and for total body BMC values, but not for BMC of the lumbar spine.

Gilsanz et al. (33) studied 196 boys and girls representing each Tanner stage of development (Stages I-V). Although no sex differences were seen for spinal trabecular BMD values, boys had substantially larger vertebrae (17%), as evaluated by CSA, at all stages of development. Furthermore, this discrepancy between males and females was shown to increase with age, with the greatest disparities seen in subjects classified as Tanner stage V. The vertebral volume was also greater in boys than girls beginning at Tanner stage III. Vertebral height however did not differ between boys and girls, which supports findings by Bonjour and colleagues (31). Thus, DXA measures of aBMD that adjust for vertebral height may be insensitive to gender differences in vertebral size that are reflected in width and CSA.

In summary, while peak bone mass has been established as an important determinant of the lifetime risk for osteoporosis, it is hypothesized that diminished bone size in girls relative to boys may be a significant contributor to the observed sex differences in vertebral fracture incidence later in life (6, 28, 29, 33). Whether or not vertebral density values are similar in boys and girls, ultimately, larger bones have greater mineral content, a greater CSA and greater strength. Still, little is known about

what role the growth process plays in contributing to osteoporosis and osteoporosis-related fracture risk and more research necessary.

***Summary and Proposal for Future Research:*** The discrepant effect of gender on the growth of the axial skeleton may account for sex differences in the incidence of fragility fractures of the spine in later life. We know that both skeletal health and fracture resistance are functions of many interrelated factors including, but not limited to age, sex, endocrine factors, mechanical loading, genetics, nutritional habits, lifestyle patterns, medication exposure, bone geometry and density and loading magnitude (1-4, 38-40). With the ultimate goal of absolute osteoporosis prevention, we must work to gain a more thorough understanding of the individual contribution of these factors as well as their interactions.

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# APPENDIX B: INFORMED CONSENT

## EFFECTS OF JUMPING ON GROWING BONES IN CHILDREN

*Informed Consent For Jumping Group*

### INTRODUCTION

My child has been invited by Dr. Christine Snow (Principal Investigator) to participate in this study looking at how jumping exercises effect bone growth in children. In this exercise study we will be exploring the effect that jumping and stretching exercises have on increasing bone mass, and muscle power.

### PROGRAM DETAILS

I am aware that this study will take place over a 12-month period, from September (1998) to September (1999). An explanation of the exercise program and the testing measurements that will be used are explained below.

### MEASUREMENTS

It has been explained to me that as the parent I will be asked to bring my child in for testing in September (1998), May (1999), and September (1999) to the Oregon State University Bone Research Laboratory. Information regarding all tests was provided to me at the informational meeting, and in the information packet. The approximate time that it will take to complete all tests will be one hour and include the following:

**1. Bone Mineral Density Testing:**

- It has been explained to me that the bone mineral testing will require my child to lie quietly on an x-ray table for a total of six minutes for the hip and spine.
- The radiation dose is considered safe to administer and has been used in many studies, resulting in the development of standard values for children.
- The amount of radiation that my child will receive is comparable to what they would be exposed to during a plane trip across the country, or from a day outside in the sun.

**2. Physical Fitness Tests:**

- I understand that my son/daughter will be asked to perform two tests to measure physical fitness:
    1. Leg press test: to measure muscular power
    2. Sit and reach test: to measure flexibility

**3. Body Composition Testing:**

- It has been explained to me that my child will have his/her body composition measured using skinfold calipers.
- My child and I have been shown how the calipers work, and it has been explained to me that this procedure will not hurt my child.
- Measurements will only be taken on the arm and shoulder.
- The way in which my child's body composition will be measured has been used in other children of this age group and has been demonstrated as a safe and reliable way to measure body fat.

**4. Physical Activity Questionnaires:**

- It has been explained to me that I will help my child complete a questionnaire that will ask questions about the types of activities my son/daughter participates in on a regular basis.
- My child will also be asked questions regarding the amount of TV watched on a weekly basis, and the types of organized sports my son/daughter may be involved in.

**5. Food Questionnaire:**

- I will be recording my child's food intake on a food questionnaire that will take approximately 20 minutes to complete.
- This questionnaire will require me to answer questions based on the types of foods my son/daughter consumes on an annual basis.

**EXERCISE INTERVENTION**

**1. Training**

- It has been explained to me that if my child is in the exercise program he/she will perform jumping exercises that will take approximately 15 minutes to complete.
- The jumping exercises will take place from October (1998) to May (1999), 3x per week at a regularly schedule time.
- All exercise classes will be led by a qualified instructor from this research project.
- Alternative activities will be provided if my child is unable to participate in the jumping exercises.

**2. Detraining**

- It has been explained to me that my child will be asked to come back in for testing in September (1999), 6-months after the conclusion of the jumping class.
- During this 6-month time period my child will not participate in jumping exercises at the elementary school , and will be asked not to perform these exercises at home.

**BENEFITS & RISK OF INJURY**

- It has been explained to me that this study will include a wellness curriculum that will provide my child with an opportunity to learn about topics such as osteoporosis, nutrition, and physical activity.
- My child will receive valuable information regarding his/her bone mineral density, body composition, and muscular power as a result of my child participate in this study.
- Information obtained form this study will aid in providing rationale for the economic support of physical education in public schools as a preventive strategy for osteoporosis.
- It has been explained to me that the possibility of injury from either the jumping exercises or the physical fitness tests may occur; however, the risk for injury is minimal. It is the investigators experience that children performing these exercises and tests have not been injured as a result of participation. I understand that the University does not provide a research subject with compensation or medical treatment in the event a subject is injured, or as a result of participation in the research project.

**CONFIDENTIALITY**

It has been explained to me that confidentiality will be maintained for my child by a number coding system and that only the researchers will have knowledge of my child's name. I have been informed that the results of this study may be published in scientific literature, and that these data will not reveal the identity of my child.

**INVESTIGATOR INFORMATION**

I have been informed and understand the nature and purpose of this research study. The researchers have offered to answer any questions that I may have. I understand that my child's participation in this study is voluntary and that I may remove my child from the study at any time without sacrificing of benefits to which my child is entitled. Questions about the research or any aspect of my child's participation should be directed to Dr. Christine Snow at 737-6788 or Robyn Fuchs at 737-5935. I have read the above information and agree for my child to participate.

Please check the box that indicates what you will allow your child to participate in this year.
*Jumping exercises and completing all tests would give your son/daughter full participation in the exercise class and study.

| | |
|---|---|
| *Jumping/Bone scan, physical fitness tests, body composition | ☐ |
| Jumping/Bone scan, physical fitness tests, no body composition | ☐ |
| Jumping/No testing | ☐ |
| My child will not participate in this study | ☐ |

Subject Signature_____Date_____

Parent/Guardian Signature_____Date_____

Investigators Signature_____Date_____

## EFFECTS OF JUMPING ON GROWING BONES IN CHILDREN

*Informed Consent for Stretching Group*

### INTRODUCTION

My child has been invited by Dr. Christine Snow (Principal Investigator) to participate in this study looking at how jumping exercises effect bone growth in children. In this exercise study we will be exploring the effect that jumping and stretching exercises have on increasing bone mass, and muscle power.

### PROGRAM DETAILS

I am aware that this study will take place over a 12-month period, from September (1998) to September (1999). An explanation of the exercise program and the testing measurements that will be used are explained below.

### MEASUREMENTS

It has been explained to me that as the parent I will be asked to bring my child in for testing in September (1998), May (1999), and September (1999) to the Oregon State University Bone Research Laboratory. Information regarding all tests was provided to me at the informational meeting, and in the information packet. The approximate time that it will take to complete all tests will be one hour and include the following:

**1. Bone Mineral Density Testing:**

- It has been explained to me that the bone mineral testing will require my child to lie quietly on an x-ray table for a total of six minutes for the hip and spine.
- The radiation dose is considered safe to administer and has been used in many studies, resulting in the development of standard values for children.
- The amount of radiation that my child will receive is comparable to what they would be exposed to during a plane trip across the country, or from a day outside in the sun.

**2. Physical Fitness Tests:**

- I understand that my son/daughter will be asked to perform two tests to measure physical fitness:
    1. Leg press test: to measure muscular power
    2. Sit and reach test: to measure flexibility

**3. Body Composition Testing:**

- It has been explained to me that my child will have his/her body composition measured using skinfold calipers.
- My child and I have been shown how the calipers work, and it has been explained to me that this procedure will not hurt my child.
- Measurements will only be taken on the arm and shoulder.
- The way in which my child's body composition will be measured has been used in other children of this age group and has been demonstrated as a safe and reliable way to measure body fat.

**4. Physical Activity Questionnaires:**

- It has been explained to me that I will help my child complete a questionnaire that will ask questions about the types of activities my son/daughter participates in on a regular basis.
- My child will also be asked questions regarding the amount of TV watched on a weekly basis, and the types of organized sports my son/daughter may be involved in.

5. Food Questionnaire:

- I will be recording my child's food intake on a food questionnaire that will take approximately 20 minutes to complete.
- This questionnaire will require me to answer questions based on the types of foods my son/daughter consumes on an annual basis.

EXERCISE INTERVENTION

1. Training

- It has been explained to me that if my child is in the exercise program he/she will perform stretching exercises that will take approximately 15 minutes to complete.
- The stretching exercises will take place from October (1998) to May (1999), 3x per week

at a regularly schedule time.

- All exercise classes will be led by a qualified instructor from this research project.
- Alternative activities will be provided if my child is unable to participate in the stretching exercises.

2. Detraining

- My child will be asked not participate in jumping exercises at the elementary school, or at home between May 1999-Septebmer 1999.
- It has been explained to me that my child will be asked to come back in for testing in September (1999), 6-months after the conclusion of the jumping class.

BENEFITS & RISK OF INJURY

- It has been explained to me that this study will include a wellness curriculum that will provide my child with an opportunity to learn about topics such as osteoporosis, nutrition, and physical activity.
- My child will receive valuable information regarding his/her bone mineral density, body composition, and muscular power as a result of my child participate in this study.
- Information obtained form this study will aid in providing rationale for the economic support of physical education in public schools as a preventive strategy for osteoporosis.
- It has been explained to me that the possibility of injury from either the stretching exercises or the physical fitness tests may occur; however, the risk for injury is minimal. It is the investigators experience that children performing these exercises and tests have not been injured as a result of participation. I understand that the University does not provide a research subject with compensation or medical treatment in the event a subject is injured, or as a result of participation in the research project.

CONFIDENTIALITY

It has been explained to me that confidentiality will be maintained for my child by a number coding system and that only the researchers will have knowledge of my child's name. I have been informed that the results of this study may be published in scientific literature, and that these data will not reveal the identity of my child.

INVESTIGATOR INFORMATION

I have been informed and understand the nature and purpose of this research study. The researchers have offered to answer any questions that I may have. I understand that my child's participation in this study is voluntary and that I may remove my child from the study at any time without sacrificing of benefits to which my child is entitled. Questions about the research or any aspect of my child's participation should be directed to Dr. Christine Snow at 737-6788 or Robyn Fuchs at 737-5935. I have read the above information and agree for my child to participate.

Please check the box that indicates what you will allow your child to participate in this year.
*Stretching exercises and completing all tests would give your son/daughter full participation in the exercise class and study.

| | |
|---|---|
| *Stretching/bone scan, physical fitness tests, body composition | ❑ |
| Stretching/bone scan, physical fitness tests, no body composition | ❑ |
| Stretching /no testing | ❑ |
| My child will not participate in this study | ❑ |

Subject Signature_____Date_____

Parent/Guardian Signature_____Date_____

Investigators Signature_____Date_____

# APPENDIX C: HEALTH HISTORY AND PHYSICAL ACTIVITY QUESTIONNAIRE

**OREGON STATE UNIVERSITY BONE RESEARCH LABORATORY**
**Heath and Physical Activity History**
**NIH KIDS STUDY**

_____ _____
Child's last name First Middle Date of birth

_____ _____
Address, Street Home phone

_____
City, State

_____ _____
Parent/Guardian's last name First Middle Home phone

_____ _____
Address, Street Work phone

_____
City, State

_____ _____
Person to contact in case of emergency Home phone/ Work phone

**********

_____pounds _____ft_____inches
Child's Weight Child's Height Male Female (circle one)

**********

Race/ethnic background of your child (Please check as many as apply)

Caucasian (white) ☐
Asian (Oriental ) ☐
African (black) ☐
Mexican, Hispanic, or Latino ☐
American Indian ☐
Pacific Islander ☐
If none of the above choices apply to you,
please use your own description._____

_____

**PAST HISTORY (Check if yes)**
**Has your child ever had?**

| | |
|---|---|
| Diabetes | _____ |
| Heart murmur | _____ |
| Heart defect | _____ |
| Asthma | _____ |
| Epilepsy | _____ |
| Back injury | _____ |
| Serious illness | _____ |
| Operations | _____ |
| Other musculoskeletal injury or problems | _____ |

**FAMILY HISTORY (Check if yes)**
**Have you, or your other children had?**

| | |
|---|---|
| Diabetes | _____ |
| Heart attacks | _____ |
| High blood pressure | _____ |
| High cholesterol | _____ |
| Congenital heart disease | _____ |
| Heart operations | _____ |
| Other | _____ |
| | _____ |
| | _____ |

**PRESENT SYMPTOMS REVIEW (Check if yes)**
**Has your child recently had?**

| | |
|---|---|
| Chest pain | _____ |
| Shortness of breath | _____ |
| Heart palpitations | _____ |
| Cough on exertion | _____ |
| Coughing blood | _____ |
| Back pain | _____ |
| Painful, stiff or swollen joints | _____ |

Other_____
_____

**MEDICAL/HEALTH AND PHYSICAL ACTIVITY QUESTIONS**

Date of your child's last medical exam?

Please list your child's present medications and dosages here (include vitamins):

Child's Physician:_____

How would you rate you son/daughter's present level of health?

Does your child experience any pain or shortness of breath with moderate exercise?

How physically fit do you feel your child is at the present time? (Circle one) poor / moderate / active / very active /

## HEALTH HABITS

Consumption of calcium-rich daily products

How many 8 oz glasses of milk does your child drink per day?_____ per week?_____
How many servings of cheese (1 oz) does your child eat per day?_____ per week?_____
How many servings of yogurt (1 cup) does your child eat per week?_____

Body Weight

What was your child's weight 1 month ago? _____
What was your child's weight 6 months ago? _____

Cola Beverages

How many cola beverages does your child drink daily?_____
How many years has your child been drinking cola beverages on a regular basis?_____

## PHYSICAL ACTIVITY

List all sports or activities in which your child has participated during the past year: (Examples include aerobics, tennis, soccer, softball, dance, football, hiking, swimming, biking, etc.) Use the back of this paper if necessary.

| ACTIVITY | AVE # HR./WK | AVE # MONTHS/YR. |
|---|---|---|
| Ex. Soccer | 1 | 6 |

## OSTEOPOROSIS RISK FACTORS

Please circle true or false for the following. If you think a statement may apply to your child but are not sure, place a question mark (?) by that statement.

1. true false My child has been treated with cortisone or similar drugs.
2. true false My child has a history of the blood tumor, leukemia.
3. true false My child has lactase deficiency (inability to digest milk).
4. true false My child takes anabolic steroids now or has in the past.
5. true false My child avoids milk and other dairy products.
6. true false My child usually eats meat at least twice a day.
7. true false On average, my child usually drinks 2 or more soft drinks daily.
8. true false My child is very physically active most of the time.
9. true false My child has been treated with chemotherapy for cancer.
10. true false My child has received an organ transplant
11. true false My child has had trouble with anorexia nervosa or bulimia.

_____ _____
Parent/Guardian Signature Date

# APPENDIX D: HARVARD YOUTH FOOD FREQUENCY QUESTIONNAIRE

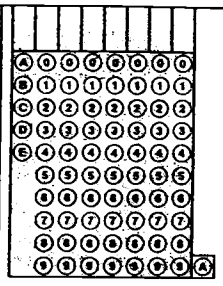
PAGE ONE EATING SURVEY K-95-1 HARVARD MEDICAL SCHOOL

## MARKING INSTRUCTIONS

- Use a **NO. 2 PENCIL** only.
- Do not use ink or ballpoint pen.
- Darken in the circle completely.
- Erase cleanly any marks you wish to change.
- Do not make any stray marks on this form.

The RIGHT way ● to mark your answer!

The WRONG way ⊘ ⊗ ◒ ⊙ to mark your answers!

**1. What is your AGE?**

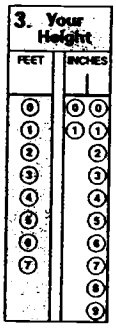
- ○ Less than 9
- ○ 9
- ○ 10
- ○ 11
- ○ 12
- ○ 13
- ○ 14
- ○ 15
- ○ 16
- ○ 17
- ○ 18 or older

**2. Are you:**

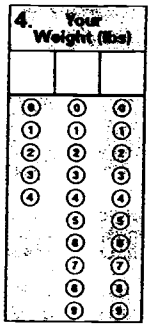
- ○ Male
- ○ Female

**3. Your Height**

FEET | INCHES



**4. Your Weight (lbs)**



## Questionnaire refers to what you ate over the past year.

**5. Do you now take vitamins (like Flintstones, One-A-Day, etc.)?**

○ No ○ Yes → **If yes)** **a) How many vitamin pills do you take a week?**

- ○ 2 or less
- ○ 3 - 5
- ○ 6 - 9
- ○ 10 or more

**b) For how many years have you been taking them?**

- ○ 0 - 1 years
- ○ 2 - 4
- ○ 5 - 9
- ○ 10+ years

**6. How many teaspoons of sugar do you ADD to your beverages or food each day?**

- ○ None/less than 1 teaspoon per day
- ○ 1 - 2 teaspoons per day
- ○ 3 - 4 teaspoons per day
- ○ 5 or more teaspoons per day

**7. Which cold breakfast cereal do you usually eat?**

○ Never eat cold breakfast cereal

**8. Where do you usually eat breakfast?**

- ○ At home
- ○ At school
- ○ Don't eat breakfast
- ○ Other

**9. How many times each week (including weekdays and weekends) do you usually eat breakfast prepared away from home?**

- ○ Never or almost never
- ○ 1 - 2 times per week
- ○ 3 - 4 times per week
- ○ 5 or more times per week

**10. How many times each week (including weekdays and weekends) do you usually eat lunch prepared away from home?**

- ○ Never or almost never
- ○ 1 - 2 times per week
- ○ 3 - 4 times per week
- ○ 5 or more times per week

**11. How many times each week do you usually eat after-school snacks or foods prepared away from home?**

- ○ Never or almost never
- ○ 1 - 2 times per week
- ○ 3 - 4 times per week
- ○ 5 or more times per week

**12. How many times each week (weekdays and weekends) do you usually eat dinner prepared away from home?**

- ○ Never or almost never
- ○ 1 - 2 times per week
- ○ 3 - 4 times per week
- ○ 5 or more times per week

**13. How many times per week do you prepare dinner for yourself (and/or others in your house)?**

- ○ Never or almost never
- ○ Less than once per week
- ○ 1 - 2 times per week
- ○ 3 - 4 times per week
- ○ 5 or more times per week

**14. How often do you have dinner that is ready made, like frozen dinners, Spaghetti-O's, microwave meals, etc.**

- ○ Never/less than once per month
- ○ 1 - 2 times per week
- ○ 3 - 4 times per week
- ○ 5 or more times per week

**15. How many times each week (including weekdays and weekends) do you eat late night snacks prepared away from home?**

- ○ Never/less than once per month
- ○ 1 - 2 times per week
- ○ 3 - 4 times per week
- ○ 5 or more times per week

**16. How often do you eat food that is fried at home, like fried chicken?**

- ○ Never/less than once per week
- ○ 1 - 3 times per week
- ○ 4 - 6 times per week
- ○ Daily

**17. How often do you eat fried food away from home (like french fries, chicken nuggets)?**

- ○ Never/less than once per week
- ○ 1 - 3 times per week
- ○ 4 - 6 times per week
- ○ Daily

# DIETARY INTAKE

**How often do you eat the following foods:**

**Example If you drink one can of diet soda 2 - 3 times per week, then your answer should look like this:**

**E1. Diet soda (1 can or glass)**

- ○ Never
- ○ 1 - 3 cans per month
- ○ 1 can per week
- ● 2 - 6 cans per week
- ○ 1 can per day
- ○ 2 or more cans per day

PAGE THREE Questionnaire refers to what you ate over the past year. HARVARD MEDICAL SCHOOL

## BEVERAGES

**FILL OUT ONE BUBBLE FOR EACH FOOD ITEM**

**18. Diet soda (1 can or glass)**
- ○ Never/less than 1 per month
- ○ 1 - 3 cans per month
- ○ 1 can per week
- ○ 2 - 6 cans per week
- ○ 1 can per day
- ○ 2 or more cans per day

**19. Soda - not diet (1 can or glass)**
- ○ Never/less than 1 per month
- ○ 1 - 3 cans per month
- ○ 1 can per week
- ○ 2 - 6 cans per week
- ○ 1 can per day
- ○ 2 or more cans per day

**20. Hawaiian Punch, lemonade, Koolaid or other non-carbonated fruit drink (1 glass)**
- ○ Never/less than 1 per month
- ○ 1 - 3 glasses per month
- ○ 1 glass per week
- ○ 2 - 4 glasses per week
- ○ 5 - 6 glasses per week
- ○ 1 glass per day
- ○ 2 or more glasses per day

**21. Iced Tea - sweetened (1 glass, can or bottle)**
- ○ Never/less than 1 per month
- ○ 1 - 3 glasses per month
- ○ 1 - 4 glasses per week
- ○ 5 - 6 glasses per week
- ○ 1 or more glasses per day

**22. Tea (1 cup)**
- ○ Never/less than 1 per month
- ○ 1 - 3 cups per month
- ○ 1 - 2 cups per week
- ○ 3 - 6 cups per week
- ○ 1 or more cups per day

**23. Coffee - not decaf. (1 cup)**
- ○ Never/less than 1 per month
- ○ 1 - 3 cups per month
- ○ 1 - 2 cups per week
- ○ 3 - 6 cups per week
- ○ 1 or more cups per day

**24. Beer (1 glass, bottle or can)**
- ○ Never/less than 1 per month
- ○ 1 - 3 cans per month
- ○ 1 can per week
- ○ 2 or more cans per week

**25. Wine or wine coolers (1 glass)**
- ○ Never/less than 1 per month
- ○ 1 - 3 glasses per month
- ○ 1 glass per week
- ○ 2 or more glasses per week

**26. Liquor, like vodka or rum (1 drink or shot)**
- ○ Never/less than 1 per month
- ○ 1 - 3 drinks per month
- ○ 1 drink per week
- ○ 2 or more drinks per week

**Example** If you eat:

3 pats of margarine on toast
1 - 2 pats of margarine on sandwich
1 pat of margarine on vegetables

5 - 6 pats total all day

then answer this way →

**E2. Margarine (1 pat) - not butter**
- ○ Never
- ○ 1 - 3 pats per month
- ○ 1 pat per week
- ○ 2 - 6 pats per week
- ○ 1 pat per day
- ○ 2 - 4 pats per day
- ● 5 or more pats per day

## DAIRY PRODUCTS

**27. What TYPE of milk do you usually drink?**
- ○ Whole milk
- ○ 2% milk
- ○ 1% milk
- ○ Skim/nonfat milk
- ○ Don't know
- ○ Don't drink milk

**28. Milk (glass or with cereal)**
- ○ Never/less than 1 per month
- ○ 1 glass per week or less
- ○ 2 - 6 glasses per week
- ○ 1 glass per day
- ○ 2 - 3 glasses per day
- ○ 4+ glasses per day

**29. Chocolate milk (glass)**
- ○ Never/less than 1 per month
- ○ 1 - 3 glasses per month
- ○ 1 glass per week
- ○ 2 - 6 glasses per week
- ○ 1 - 2 glasses per day
- ○ 3 or more glasses per day

PAGE FOUR — Questionnaire refers to what you ate over the past year. — HARVARD MEDICAL SCHOOL

**30. Instant Breakfast Drink (1 packet)**

- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**31. Whipped cream**

- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**32. Yogurt (1 cup) - Not frozen**

- ○ Never/less than 1 per month
- ○ 1 - 3 cups per month
- ○ 1 cup per week
- ○ 2 - 6 cups per week
- ○ 1 cup per day
- ○ 2 or more cups per day

**33. Cottage or ricotta cheese**

- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

**34. Cheese (1 slice)**

- ○ Never/less than 1 per month
- ○ 1 - 3 slices per month
- ○ 1 slice per week
- ○ 2 - 6 slices per week
- ○ 1 slice per day
- ○ 2 or more slices per day

**35. Cream cheese**

- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

**36. What TYPE of yogurt, cottage cheese & dairy products (besides milk) do you use mostly?**

- ○ Nonfat
- ○ Lowfat
- ○ Regular
- ○ Don't know

**37. Butter (1 pat) - NOT margarine**

- ○ Never/less than 1 per month
- ○ 1 - 3 pats per month
- ○ 1 pat per week
- ○ 2 - 6 pats per week
- ○ 1 pat per day
- ○ 2 - 4 pats per day
- ○ 5 or more pats per day

**38. Margarine (1 pat) - NOT butter**

- ○ Never/less than 1 per month
- ○ 1 - 3 pats per month
- ○ 1 pat per week
- ○ 2 - 6 pats per week
- ○ 1 pat per day
- ○ 2 - 4 pats per day
- ○ 5 or more pats per day

**39. What FORM and BRAND of margarine does your family usually use?**

- ○ None
- ○ Stick
- ○ Tub
- ○ Squeeze (liquid)

WHAT SPECIFIC BRAND AND TYPE (LIKE "PARKAY CORN OIL SPREAD")?

Leave blank if you don't know.

**40. What TYPE of oil does your family use at home?**

- ○ Canola oil
- ○ Corn oil
- ○ Safflower oil
- ○ Olive oil
- ○ Vegetable oil
- ○ Don't know

## MAIN DISHES

**41. Cheeseburger (1)**

- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ One per week
- ○ 2 - 4 per week
- ○ 5 or more per week

**42. Hamburger (1)**

- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ One per week
- ○ 2 - 4 per week
- ○ 5 or more per week

**43. Pizza (2 slices)**

- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**44. Tacos/burritos (1)**

- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ One per week
- ○ 2 - 4 per week
- ○ 5 or more per week

**45. Which taco filling do you usually have:**

- ○ Beef & beans
- ○ Beef
- ○ Chicken
- ○ Beans

**46. Chicken nuggets (6)**

- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**47. Hot dogs (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ One per week
- ○ 2 - 4 per week
- ○ 5 or more per week

**48. Peanut butter sandwich (1) (plain or with jelly, fluff, etc.)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ One per week
- ○ 2 - 4 per week
- ○ 5 or more per week

**49. Chicken or turkey sandwich (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ One per week
- ○ 2 or more per week

**50. Roast beef or ham sandwich (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ One per week
- ○ 2 or more per week

**51. Salami, bologna, or other deli meat sandwich (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ One per week
- ○ 2 or more per week

**52. Tuna sandwich (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ One per week
- ○ 2 or more per week

**53. Chicken or turkey as main dish (1 serving)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**54. Fish sticks, fish cakes or fish sandwich (1 serving)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

**55. Fresh fish as main dish (1 serving)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**56. Beef (steak, roast) or lamb as main dish (1 serving)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**57. Pork or ham as main dish (1 serving)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**58. Meatballs or meatloaf (1 serving)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**59. Lasagna/baked ziti (1 serving)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

**60. Macaroni and cheese (1 serving)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

**61. Spaghetti with tomato sauce (1 serving)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**62. Eggs (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 eggs per month
- ○ One egg per week
- ○ 2 - 4 eggs per week
- ○ 5 or more eggs per week

**63. Liver: beef, calf, chicken or pork (1 serving)**
- ○ Never/less than 1 per month
- ○ Less than once per month
- ○ Once per month
- ○ 2 - 3 times per month
- ○ Once per week or more

**64. Shrimp, lobster, scallops (1 serving)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

**65. French toast (2 slices)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

**66. Grilled cheese (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

**67. Eggrolls (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

## MISCELLANEOUS FOODS

**68. Brown gravy**
- ○ Never/less than 1 per month
- ○ Once per week or less
- ○ 2 - 6 times per week
- ○ Once per day
- ○ 2 or more times per day

**69. Ketchup**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**70. Clear soup (with rice, noodles, vegetables) 1 bowl**
- ○ Never/less than 1 per month
- ○ 1 - 3 bowls per month
- ○ 1 bowl per week
- ○ 2 or more bowls per week

**71. Cream (milk) soups or chowder (1 bowl)**
- ○ Never/less than 1 per month
- ○ 1 - 3 bowls per month
- ○ 1 bowl per week
- ○ 2 - 6 bowls per week
- ○ 1 or more bowls per day

**72. Mayonnaise**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 6 times per week
- ○ Once per day

**73. Low calorie/fat salad dressing**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 6 times per week
- ○ Once or more per day

**74. Salad dressing (not low calorie)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 6 times per week
- ○ Once or more per day

**75. Salsa**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 6 times per week
- ○ Once or more per day

**76. How much fat on your beef, pork, or lamb do you eat?**
- ○ Eat all
- ○ Eat some
- ○ Eat none
- ○ Don't eat meat

**77. When you have chicken or turkey, do you eat the skin?**
- ○ Yes
- ○ No
- ○ Sometimes

## BREADS & CEREALS

**78. Cold breakfast cereal (1 bowl)**

- ○ Never/less than 1 per month
- ○ 1 - 3 bowls per month
- ○ 1 bowl per week
- ○ 2 - 4 bowls per week
- ○ 5 - 7 bowls per week
- ○ 2 or more bowls per day

**79. Hot breakfast cereal, like oatmeal, grits (1 bowl)**

- ○ Never/less than 1 per month
- ○ 1 - 3 bowls per month
- ○ 1 bowl per week
- ○ 2 - 4 bowls per week
- ○ 5 - 7 bowls per week
- ○ 2 or more bowls per day

**80. White bread, pita bread, or toast (1 slice)**

- ○ Never/less than 1 per month
- ○ 1 slice per week or less
- ○ 2 - 4 slices per week
- ○ 5 - 7 slices per week
- ○ 2 - 3 slices per day
- ○ 4+ slices per day

**81. Dark bread (1 slice)**

- ○ Never/less than 1 per month
- ○ 1 slice per week or less
- ○ 2 - 4 slices per week
- ○ 5 - 7 slices per week
- ○ 2 - 3 slices per day
- ○ 4+ slices per day

**82. English muffins or bagels (1)**

- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ 1 per week
- ○ 2 - 4 per week
- ○ 5 or more per week

**83. Muffin (1)**

- ○ Never/less than 1 per month
- ○ 1 - 3 muffins per month
- ○ 1 muffin per week
- ○ 2 - 4 muffins per week
- ○ 5 or more muffins per week

**84. Cornbread (1 square)**

- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more per week

**85. Biscuit/roll (1)**

- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ 1 per week
- ○ 2 - 4 per week
- ○ 5 or more per week

**86. Rice**

- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**87. Noodles, pasta**

- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**88. Tortilla - no filling (1)**

- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ 1 per week
- ○ 2 - 4 per week
- ○ 5 or more per week

**89. Other grains, like kasha, couscous, bulgur**

- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

**90. Pancakes (2) or waffles (1)**

- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

**91. French fries (large order)**

- ○ Never/less than 1 per month
- ○ 1 - 3 orders per month
- ○ 1 order per week
- ○ 2 - 4 orders per week
- ○ 5 or more orders per week

**92. Potatoes - baked, boiled, mashed**

- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

# FRUITS & VEGETABLES

**93. Raisins (small pack)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ 1 per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**94. Grapes (bunch)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**95. Bananas (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ 1 per week
- ○ 2 - 4 per week
- ○ 5 or more per week

**96. Cantaloupe, melons (1/4 melon)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ 1 per week
- ○ 2 or more times per week

**97. Apples (1) or applesauce**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ 1 per week
- ○ 2 - 6 per week
- ○ 1 or more per day

**98. Pears (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ 1 per week
- ○ 2 - 6 per week
- ○ 1 or more per day

**99. Oranges (1), grapefruit (1/2)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ 1 per week
- ○ 2 - 6 per week
- ○ 1 or more per day

**100. Strawberries**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

**101. Peaches, plums, apricots (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ 1 per week
- ○ 2 or more per week

**102. Orange juice (1 glass)**
- ○ Never/less than 1 per month
- ○ 1 - 3 glasses per month
- ○ 1 glass per week
- ○ 2 - 6 glasses per week
- ○ 1 glass per day
- ○ 2 or more glasses per day

**103. Apple juice and other fruit juices (1 glass)**
- ○ Never/less than 1 per month
- ○ 1 - 3 glasses per month
- ○ 1 glass per week
- ○ 2 - 6 glasses per week
- ○ 1 glass per day
- ○ 2 or more glasses per day

**104. Tomatoes (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ 1 per week
- ○ 2 - 6 per week
- ○ 1 or more per day

**105. Tomato/spaghetti sauce**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**106. Tofu**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**107. String beans**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**108. Beans/lentils/soybeans**
- ○ Never/less than 1 per month
- ○ Once per week or less
- ○ 2 - 6 times per week
- ○ Once per day

**109. Broccoli**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**110. Beets (not greens)**
- ○ Never/less than 1 per month
- ○ Once per week or less
- ○ 2 or more times per week

**111. Corn**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**112. Peas or lima beans**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**113. Mixed vegetables**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**114. Spinach**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once a week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**115. Greens/kale**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**116. Green/red peppers**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once a week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**117. Yams/sweet potatoes (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once a week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**118. Zucchini, summer squash, eggplant**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**119. Carrots, cooked**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**120. Carrots, raw**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**121. Celery**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**122. Lettuce/tossed salad**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 6 times per week
- ○ One or more per day

**123. Coleslaw**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

**124. Potato salad**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

**Think about your usual snacks. How often do you eat each type of snack food.**

**Example** If you eat poptarts rarely (about 6 per year) then your answer should look like this:

**E3. Poptarts (1)**
- ● Never/less than 1 per month
- ○ 1 - 3 per month
- ○ 1 - 6 per week
- ○ 1 or more per day

## SNACK FOODS/DESSERTS

**125. Fill in the number of snacks (food or drinks) eaten on school days and weekends/vacation days.**

| Snacks | School Days | | | | | Vacation/Weekend Days | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | NONE | 1 | 2 | 3 | 4 OR MORE | NONE | 1 | 2 | 3 | 4 OR MORE |
| Between breakfast and lunch | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| After lunch, before dinner | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| After dinner | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

**126. Potato chips (1 small bag)**
- ○ Never/less than 1 per month
- ○ 1 - 3 small bags per month
- ○ One small bag per week
- ○ 2 - 6 small bags per week
- ○ 1 or more small bags per day

**127. Corn chips/Doritos (small bag)**
- ○ Never/less than 1 per month
- ○ 1 - 3 small bags per month
- ○ One small bag per week
- ○ 2 - 6 small bags per week
- ○ 1 or more small bags per day

**128. Nachos with cheese (1 serving)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 or more times per week

**129. Popcorn (1 small bag)**
- ○ Never/less than 1 per month
- ○ 1 - 3 small bags per month
- ○ 1 - 4 small bags per week
- ○ 5 or more small bags per week

**130. Pretzels (1 small bag)**
- ○ Never/less than 1 per month
- ○ 1 - 3 small bags per month
- ○ 1 small bags per week
- ○ 2 or more small bags per week

**131. Peanuts, nuts (1 small bag)**
- ○ Never/less than 1 per month
- ○ 1 - 3 small bags per month
- ○ 1 - 4 small bags per week
- ○ 5 or more small bags per week

**132. Fun fruit or fruit rollups (1 pack)**
- ○ Never/less than 1 per month
- ○ 1 - 3 packs per month
- ○ 1 - 4 packs per week
- ○ 5 or more packs per week

**133. Graham crackers**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ 1 - 4 times per week
- ○ 5 or more times per week

**134. Crackers, like saltines or wheat thins**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ 1 - 4 times per week
- ○ 5 or more times per week

**135. Poptarts (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 poptarts per month
- ○ 1 - 6 poptarts per week
- ○ 1 or more poptarts per day

**136. Cake (1 slice)**
- ○ Never/less than 1 per month
- ○ 1 - 3 slices per month
- ○ 1 slice per week
- ○ 2 or more slices per week

**137. Snack cakes, Twinkies (1 package)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ Once per week
- ○ 2 - 6 per week
- ○ 1 or more per day

**138. Danish, sweetrolls, pastry (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ 1 per week
- ○ 2 - 4 per week
- ○ 5 or more per week

**139. Donuts (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 donuts per month
- ○ 1 donut per week
- ○ 2 - 6 donuts per week
- ○ 1 or more donuts per day

**140. Cookies (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 cookies per month
- ○ 1 cookie per week
- ○ 2 - 6 cookies per week
- ○ 1 - 3 cookies per day
- ○ 4 or more cookies per day

**141. Brownies (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ 1 per week
- ○ 2 - 4 per week
- ○ 5 or more per week

**142. Pie (1 slice)**
- ○ Never/less than 1 per month
- ○ 1 - 3 slices per month
- ○ 1 slice per week
- ○ 2 or more slices per week

**143. Chocolate (1 bar or packet) like Hershey's or M & M's**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ 1 per week
- ○ 2 - 6 per week
- ○ 1 or more per day

**144. Other candy bars (Milky Way, Snickers)**
- ○ Never/less than 1 per month
- ○ 1 - 3 candy bars per month
- ○ 1 candy bar per week
- ○ 2 - 4 candy bars per week
- ○ 5 or more candy bars per week

**145. Other candy without chocolate (Skittles) (1 pack)**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**146. Jello**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**147. Pudding**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

**148. Frozen yogurt**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

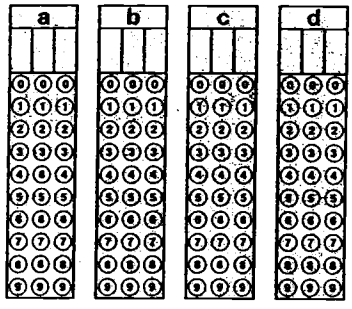
**149. Ice cream**
- ○ Never/less than 1 per month
- ○ 1 - 3 times per month
- ○ Once per week
- ○ 2 - 4 times per week
- ○ 5 or more times per week

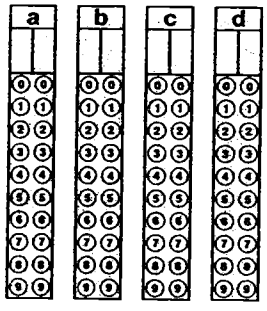
**150. Milkshake or frappe (1)**
- ○ Never/less than 1 per month
- ○ 1 - 3 per month
- ○ 1 per week
- ○ 2 or more per week

**151. Popsicles**
- ○ Never/less than 1 per month
- ○ 1 - 3 popsicles per month
- ○ 1 popsicle per week
- ○ 2 - 4 popsicles per week
- ○ 5 or more popsicles per week

**152. Please list any other foods that you usually eat at least once per week that are not listed (for example, coconut, hummus, falafel, chili, plantains, mangoes, etc. . .)**

| FOODS | HOW OFTEN? |
|---|---|
| a) _____ | a) _____ |
| b) _____ | b) _____ |
| c) _____ | c) _____ |
| d) _____ | d) _____ |




# THANK YOU FOR COMPLETING THIS SURVEY!

# APPENDIX E: TANNER PUBERTAL STAGE CLASSIFICATION QUESTIONNAIRES

OREGON STATE UNIVERSITY BONE RESEARCH LABORATORY
Tanner Stage Sheet: Girls
NIH KID STUDY


*Girls go through normal changes as they get older. One of these changes is to grow larger breasts. Please LOOK at the drawings and READ the sentences below each of them. Then choose the drawing closest to your stage of breast development and FILL IN THE CIRCLE above it.*

**STAGE 1**

- *The nipple is raised a little.*
- *The rest of the breast is still flat.*

**STAGE 2**

- *The breast is a little larger and the nipple is raised more than in Stage 1.*
- *The area around the nipple (areola) is larger than in Stage 1.*

**STAGE 3**

- *The area around the nipple (areola) and the breast are both larger than Stage 2.*
- *The areola does not stick out away from the breast.*

**STAGE 4**

- *The area around the nipple (areola) and the nipple stick up above the shape of the breast.*

**STAGE 5**

- *Only the nipple sticks out in this stage.*
- *The area around the nipple (areola) has moved back down to the breast.*

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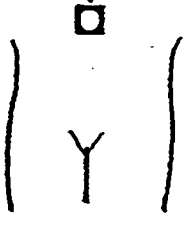
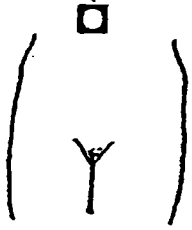
*Another change is to grow pubic hair. Please LOOK at the drawings and READ the sentences below each of them. Then choose the drawing closest to your stage of hair development and FILL IN THE CIRCLE above it.*

**STAGE 1**



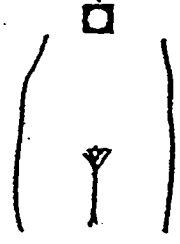
- *There is no pubic hair.*

**STAGE 2**



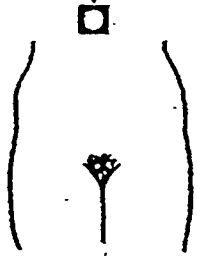
- *There is a little, long, lightly colored hair.*
- *This hair may be straight or a little curly.*

**STAGE 3**



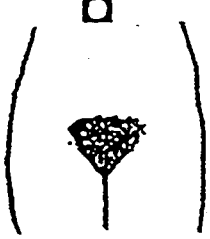
- *The hair is darker, coarser, and more curled.*
- *It has spread out and thinly covers a larger area.*

**STAGE 4**



- *The hair is now as dark, curly, and coarse as that of a grown woman.*
- *The hair has not spread out to the legs.*

**STAGE 5**



- *The hair is now like that of a grown woman.*
- *The hair often forms a triangle (▽) as it spreads out to the legs.*

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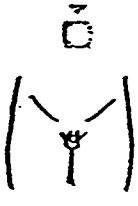
Tanner Stage Sheet: Boys
NIH KID STUDY

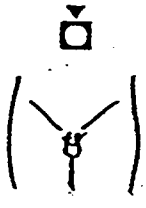

***Boys go through normal changes as they get older. Please look at the drawings and read the sentences below each of them. Then choose the drawing closest to your stage of hair development and fill in the circle above it.***

**STAGE 1**



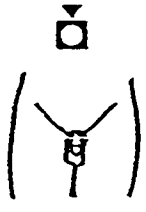
- *There is no pubic hair.*

**STAGE 2**



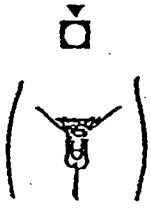
- *There is a little soft, long, lightly colored hair.*
- *Most of the hair is at the base of the penis.*
- *This hair may be straight or a little curly.*

**STAGE 3**



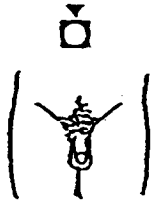
- *The hair is darker, coarser and more curled.*
- *It has spread out and thinly covers a larger area.*

**STAGE 4**



- *The hair is now as dark, curly, and coarse as that of a grown man.*
- *The hair has not spread out to the thighs.*

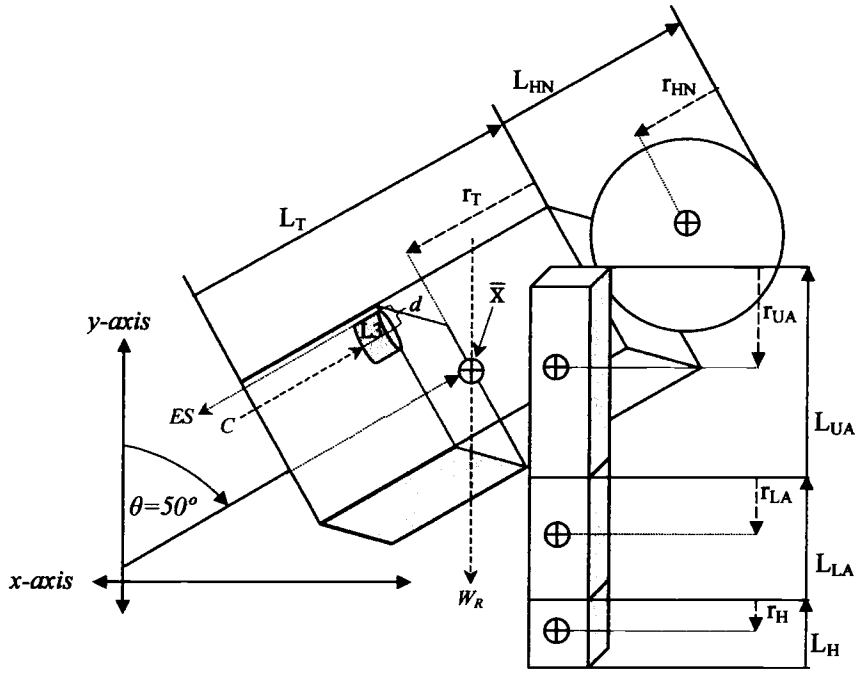
**STAGE 5**



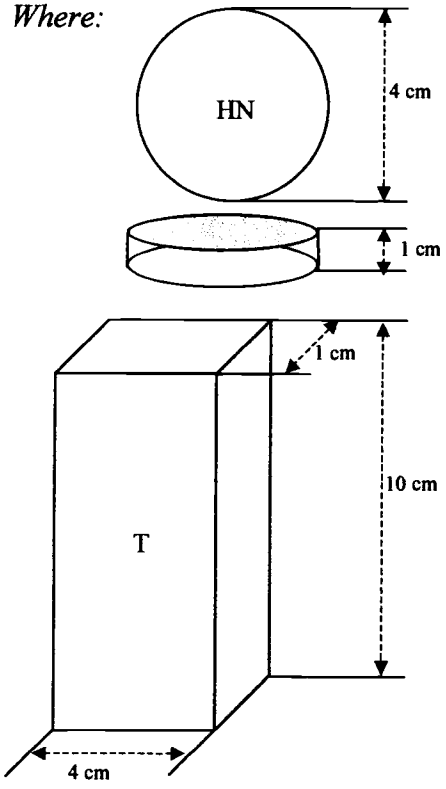
- *The hair has spread out to the thighs, like a grown man.*

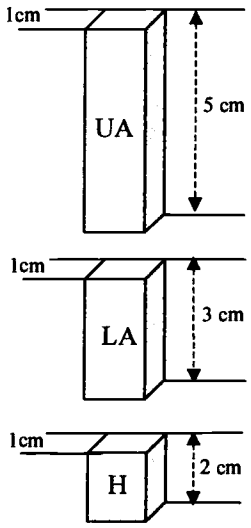
# APPENDIX F: EXAMPLE OF THE PROCEDURE FOR DERIVING $\overline{X}$

## Procedure for determining $\overline{X}$:




*Where:*



## Procedure for determining $\overline{X}$ (cont.):

*And:*

- Density of all Segments = $2N/cm^3$
- Volume of Trunk and Arm Segments

  (UA, LA and H) = *length* × *width* × *height*
- Volume of Head + Neck Segment (HN) = $\pi r^2 \times$ *height*
- sine $\theta = 0.766$, *where* $\theta = 50°$

The equation for $\overline{X}$ is:

$$\overline{X}_{\theta} = \frac{[(\overline{X}_{HN} \times W_{HN}) + (\overline{X}_{T} \times W_{T}) + (\overline{X}_{A} \times 2W_{A})]}{W_R}$$

*where* $\overline{X}_{HN} = [(L_T + L_{HN} - r_{HN}) \times \sin\theta] \times W_{HN}$,

$\overline{X}_{T} = [(L_T - r_T) \times \sin\theta] \times W_T$ and,

$\overline{X}_{A} = [L_T \times \sin\theta] \times [2 \times W_A]$

Therefore, $\overline{X}$ calculated as:

$$\overline{X} = \frac{[80N\ (10/2) + 25.13N\ (10 + 4/2) + 20N\ (10)] \times 0.766}{125.13}$$

$\overline{X} = 5.52$ cm