Bone Health and Distress in Young Individuals

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“Exercise is Medicine™”

- More should be done to address physical activity and exercise in healthcare settings
- ACSM and the AMA are making efforts to bring a greater focus on physical activity and exercise in health care settings
  www.exerciseismedicine.org

Dr. Barbara Drinkwater

Bone Health
What is Bone Health?

“Children are NOT little adults”

Osteoporosis:
“a pediatric disease with geriatric consequences”
“A silent epidemic”

Osteoporosis

“A skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture”

BONE STRENGTH:
“reflects the integration of bone density and bone quality”

Risk Factors for Osteoporosis

- Race
- Sex (female)
- Family history
- Early menopause
- Slender/fair skin
- Nulliparity
- Sedentary lifestyle
- Smoking
- EtOH > 3 drinks/day
**Bone Development**

**Bone Modelling Unit (BMU)**

- During growth:
  - Bone mass increases by:
    - linear growth
    - cortical apposition
    - cancellous modification
  - Process of MODELLING

- In adults:
  - Bone formation and resorption are coupled
  - Process of REMODELLING

**Physical activity during childhood and adolescence**
- 5-10% higher bone mass
- Associations between daily physical activity (PA) and BMC in older children
- How to best measure?
  - Self-report vs accelerometry
  - Iowa Bone Development Study
  - 3-5 days of activity
  - using Actigraph vs. PAQ-C
**Pathophysiology**

- Bones adapt to mechanical stimuli:
  - High rate
  - High magnitude
  - From uncommon directions

Lanyon LE, Rubin CT. Static vs. dynamic loads as an influence on bone remodeling. J Biomech. 1984;17(12):897-905

**Exercise and Bone Health**

- Athletes (jumpers, volleyball players, hurdlers)
- Stronger bones than controls at loaded skeletal sites

Pathophysiology

- Running – 3-5 times body weight GRF
- Resistance exercise and weight-lifting – osteogenic (muscle strength)
- Pre-pubertal soccer (football) – beneficial (♀,♂)

Pathophysiology

- Rowing – positive effects on lumbar spine; lightweights – negative effect
- Pre-pubertal gymnasts – higher BMD despite menstrual irregularity, low energy & Ca intake – persists into older age

Cyclists??

- 2006 World Master Track Championships, Manchester (103 ♀, ages 30-82)
- Sprint cyclists (n=52) and to a lesser extent distance cyclists (n=19) had greater tibia and radius bone strength surrogates (from pQCT) than controls (n=32)
- Sprint cyclists had 10% greater grip strength

Muscular Forces

- Tennis and squash players – greater cortical thickness in dominant arm
- Effect greater if start pre-pubertal
- Force magnitude is more osteogenic than rate

Exercise and Bone Mass

- Longitudinal study of 80 white women over 10 years, Penn State Young Women’s Health Study
- BMD, body composition, estimated proximal femur section modulus (bone bending strength); calcium intake (45 days prospective food records), exercise history and OC use (questionnaire)
- Only exercise during adolescence significantly associated with increased BMD and bone bending strength


Effects of Weight Cycling

- 48♂, 2♀ judoists
- DEXA, cortisol, osteocalcin, C-terminal telopeptide, bone uncoupling index (UI)
- 4% weight change – loss or gain - altered bone metabolic balance


Bone Metabolism

- Young Female Athletes
Effects of Medications on Bone

NEGATIVE EFFECTS:

- NSAIDs (Cox-2 inhibitors)
- DMARDs
- Psychotropics
- Anti-epileptics
- Corticosteroids:
  - Chronic disease
    - IBD
    - RA
    - Asthma
  - Inhalers
- Depot medroxyprogesterone Acetate (DMPA)
  - 2% of Canadian women using contraception
  - Transient decrease in BMD – 2.44-6.53% in adolescents; 5-6% in adult women 5 year use
  - Proportional to duration of use, reversible
  - November 2004 - FDA – Black Box warning
  - 2005 – Health Canada Advisory
  - Effects on “occurrence of fracture” unknown
  - Routine BMD testing not advised
  - Counsel on “bone health”

Female Athlete Triad Update 2010

Effects of Medications on Bone: OCPs?

- Few prospective studies
- Lots of variables
- DMPA ↓ BMD
- OC in adolescents may prevent attainment of maximal BMD
- OC in peri- or menopausal women may maintain BMD
- Lower dose OC may cause slight ↓ BMD

Canadian Contraceptive Consensus Update
The Female Athlete Triad

Disordered Eating, Amenorrhea and Osteoporosis

Health Benefits of Exercise

1. What do we know?
2. What do we do?
3. Where do we go from here?
Disordered Eating (Including Eating Disorders)

- Amenorrhea (Menstrual Dysfunction)
- Osteoporosis (Osteopenia)
- Low Energy Availability and/or Eating Disorder

Sports categories:
- Aesthetic sports
- Endurance sports
- Sports with weight categories for competition
EDNOS - Eating Disorders Not Otherwise Specified

- All criteria for AN are met except amenorrhea
- All criteria for AN are met except that, despite significant weight loss, the individual’s current weight is within normal range
- All criteria for BN are met except that binge and purge cycles are $< 2x/week$ for $< 3$ months
- An individual of normal body weight regularly uses purging behavior after eating small amounts of food
- An individual repeatedly chews and spits out, but does not swallow, large amounts of food

Prevalence of Triad

- Does it exist?
  - Khan et al., BJSM 36:10-13, 2002
  - 423 active military personnel (17-53)
    - DSM-IV criteria for ED, or “at risk”
      - 33 (6%) had ED, 109 (26%) “at risk”
      - “menstrual irregularities”
      - Then had DEXA – only 6 subjects had osteopenia
        - Lauder, MC and TBM, 1999

- Prevalence of Triad
  - 91 Runners - $> 40$ miles/week
  - 6% of oligomenorrheic and/or amenorrheic runners were osteoporotic, and 48% were osteopenic
  - 26% overall had BMD that could be called osteopenic
  - Even in runners who were menstruating – low BMD scores were observed if they had evidence of disordered eating

Anorexia Athletica

- Female athletes must exhibit the following criteria:
  - Excessive fear of becoming obese
  - Restriction of caloric intake
  - Weight loss
  - No medical disorder
  - Gastrointestinal complaints

- Cobb et al., MSSE 35:711-718, 2003
- Sundgot-Borgen, MSSE 26:414-419, 1994
“Anorexia Athletica”

- Plus one or more of the following:
  - Disturbance in body image
  - Compulsive exercising
  - Binge eating
  - Use of purging methods
  - Delayed puberty
  - Menstrual dysfunction

Additional Risk Factors

- Personality factors
- Pressure to lose weight
- Frequent weight cycling
- Early start of sport-specific training
- Being injured
- Overtraining
- Coaching behavior

Menstrual dysfunction occurs in different forms:

- Delayed menarche
- Secondary amenorrhea
- Oligomenorrhea
- Anovulation
- Luteal phase deficiency
Menstrual Dysfunction

- **Primary amenorrhea** – absence of menstrual cycles by age 16, despite other changes of puberty
  
  American Society of Reproductive Medicine, Fertil Steril 82:266-272, 2004

- **Eumenorrhea** – cycles of 25-34 days
- **Oligomenorrhea** – longer than 35 days
- **Secondary Amenorrhea** – 3 or more months of missed cycles
- **Luteal suppression** – < 10 days

Health Consequences

- **Amenorrhea**
- **Impaired endothelium-dependent arterial vasodilatation** which reduces perfusion of working muscle and increases risk of cardiovascular disease.
  
  Zeni Hoch et al., MSSE 35:377-383, 2003

- **Impaired skeletal muscle oxidative metabolism**
  
  Harber et al., CJP 23:219-225, 2000

- **Elevated LDL cholesterol**
  
  O'Donnell & De Souza Sports Med 34(9):601-627, 2004

Menstrual Dysfunction

- "**Low energy availability**, NOT the stress of exercising
- **Disruption of LH pulsatility**
  
  Loucks JAP 84:37-46, 1998

- **Role of Leptin?**

Energy Availability

- **Dietary energy intake**
  
  Exercise energy expenditure

  Energy Availability

- **Body activates mechanisms that reduce amount of energy for cellular maintenance, thermoregulation, growth and reproduction**
Energy Availability

- In healthy sedentary eumenorrheic women, resting metabolism consumes an EA of \( \sim 30 \text{ kcal/kgFFM/day} \).
- Low energy availability disrupts LH pulsatility.
- Restoration of low BMD may require raising EA > 45 kcal/kgFFM/day.

Hypometabolic State

Reductions in:
- Resting BMR
- Total T
- Leptin
- Insulin
- Glucose
- IGF-1
- IGFBP-3

Elevations in:
- AGFBP-1
- Ghrelin
- Growth hormone
- Cortisol

Hypometabolic State

- Crash dieting
- Weight cycling
- Disordered eating, including subclinical DE with “normal” menstrual function!

Osteoporosis - Definition

Normal:
- Bone density no less than 1 SD below mean for young adult women (T-score above -1)

Osteopenia:
- Bone density 1.0 - 2.5 SD below mean

Osteoporosis:
- Bone density 2.5 SD or more below mean

World Health Organization
International Society for Clinical Densitometry

- 2003 Position Development Conference
- New “guidelines” for diagnosis of osteoporosis in men, premenopausal women, and children:
  - T-scores of −2.5 SD or less in men > 65, or men from 50-65 if other risk factors are present
  - WHO classification – NOT to be used for premenopausal women
  - Children and adolescents (<20) – if Z-scores are −2.0 or less ⇒ “low bone density for chronological age”

ACSM and IOC Guidelines

- “low BMD for age” used for female athlete with risk factors and a Z score between -1 and -2
- “osteoporosis” used for a Z score below -2 in combination with clinical risk factors for fracture

Three Spectrums

- The population of athletes is distributed along three spectrums.
- These spectrums are linked by endocrine mechanisms.
- Each athlete travels along these spectra one way or the other.
- An athlete travels at different rates on each spectrum.

“Window of Opportunity”
Optimal BMD is achieved by maintaining:
- Physiologic estrogen levels
- Adequate nutrition
- Load-bearing exercise

**“New” Female Athlete Triad**

Nutrition and Athletic Performance: Nutrition and Athletic Performance:
"It is the position of the American Dietetic Association, Dietitians of Canada, and the American College of Sports Medicine that physical activity, athletic performance and recovery from exercise are enhanced by optimal nutrition."


**Exercise and Nutrition Recommendations**

**Adequate Energy Needs**

- Needed to maintain body weight, maximize training effects and maintain health
- Low-energy intakes lead to:
  - Loss of muscle mass
  - Menstrual dysfunction
  - Loss or failure to gain BMD
  - Risk of fatigue, injury, illness
Adequate Energy Needs

Male endurance athletes:
3000-5000 kcal/day

Female athletes with energy intakes < 1800-2000 kcal/day at risk

WHO classifies BMI < 18.5 kg/m² as underweight (≥18y)

Protein Requirements

Adult requirement:
- 0.8 g/kg of body weight per day

Endurance sports:
- 1.2 to 1.4 g/kg/day

Strength sports:
- 1.6 to 1.7 g/kg/day

“Ideal” Body Composition for the Athlete

No valid scientific rationale
Better to define a “range” of values, and monitor both health and performance
Limitations of current methods of measurement
May precipitate disordered eating behaviors

Body Weight and Sport Participation

- Daily weigh-ins should be discouraged
- If weight (fat) loss is required, it should start before the competitive season and involve a trained health and nutrition professional
**Caloric Restriction and BMD**
- Estrogen-dependent and estrogen-independent pathways
- Energy-deficit induced metabolic changes in bone trophic factors (IGF and leptin)
- Micronutrient deficiencies:
  - Calcium
  - Others?

**Evidence??**
- Bone formation markers decrease:
  - N-terminal pro-peptide of type I collagen (P1NP)
  - Osteocalcin
- Bone resorption markers don’t change:
  - Deoxypyridinoline (DPD)
  - N-terminal telopeptide
- Dose-response effect
  - Need severe energy restriction before bone resorption increases (also involves 18% suppression of serum estrogen)
  - Ihle and Loucks J Bone Min Res 2004

**Nutrition and BMD**
- Osteogenic aids???
  - Calcium
  - Vitamin D
  - Vitamin K
  - Bone-building nutrients:
    - Role of bone morphogenic proteins (BMPs)
    - Statins and flavonoids (phytoestrogens)

**Levels of Evidence, with Fracture as Outcome**

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Calcium Requirements

Age 1-3 – 500 mg; Age 4-8 – 800 mg
Adolescents and young adults:
- at least 1200 mg/day
Adults over age 24:
- 800-1000 mg/day
Women with menstrual dysfunction:
- 1500 mg/day
Post-menopausal women:
- 1200-1500 mg/day

Calcium Supplements

- Calcium carbonate (Tums, Os-Cal, Caltrate) and calcium carbonate (Citrical) equal in bioavailability
- Take in divided doses
- Caution with calcium from bone meal, dolomite and oyster shells

Evidence??

- Overall positive effect
  - Lanou et al. Pediatrics 2005
  - Lumbar and hip BMD increases of 1.5%
  - Addition of 800 mg/day calcium to diet of young distance runners with intake of 1000 mg/day prevents cortical but not trabecular bone loss
    - Winters-Stone & Snow Int J Sport Nutr and Exerc 2004

3-5 helpings of dairy foods/day:
- 8 oz glass of milk = 300 mg
- Container of yoghurt = 415 mg

Good sources:
- Canned fish with bones
- Kidney beans, almonds
- Dark green leafy vegetables
Effect of Other Nutrients?

- Phosphorus is critical – need 2:1 Ca++:PO₄
- Phytates, oxalates form insoluble compounds
- High dietary animal protein intake, sodium, caffeine can cause hypercalciuria
- Potassium will decrease urinary calcium excretion
- Magnesium not necessary

Vitamin D

- 85% of usual daily Vitamin D input is from the skin
- Vitamin D 400-800 IU/day reduces risk of hip and nonvertebral fractures
  - Bischoff-Ferrari et al. JAMA 2005
- Lowest acceptable level of blood 25-OH Vitamin D: 75-80 nmol/L (90-100??)
- >50% of adults may need > or = 1000 IU/day

Vitamin D and Bone Health

- Edmonton 53 degrees 33’N
- Edinburgh 55 degrees 57’N

Vitamin D in Europe

- Serum 25(OH)D < 25 nmol/l found in 2-30% of adults
- 75% or more in older persons in institutions
- Northern Europe:
  - high consumption of fatty fish and cod liver oil (= 400IU Vitamin D/day)
Nutritional Status

- **Australia Institute of Sport (AIS)**
- 18 female gymnasts 10-17
- 15 were below 75 nmol/L
- 6 were below 50 nmol/L
- 13 also had dietary Ca intakes below recommended for age


Vitamin K

- Recently – osteocalcin found to be Vitamin K dependent (needed for carboxylation) – hydroxyapatite binding capacity can be improved with adequate Vitamin K
- Prospective studies linking Vitamin K and bone health:
  - Nurses' Health Study cohort
  - Framingham Heart Study

Vitamin K1 (phylloquinone)
- Green leafy vegetables

Vitamin K2 (menaquinones)
- Fermented products (soybeans)

**Recommended:**
- 90 mcg/day for women
- 120 mcg/day for men
- Vitamin K1 (phylloquinone)
- Green leafy vegetables
- Vitamin K2 (menaquinones)
- Fermented products (soybeans)
Bone-Morphogenic Proteins

- **BMPs stimulate bone formation**
- **BMP2 gene linked to osteoporosis**
- **Dietary sources:**
  - Statins – via ↑ BMP? 27%
  - Flavonoids (phytoestrogens):
    - Ipriflavone
    - Genistein
    - Red Yeast rice (Monasus purpureus Went)
- **Variety of effects on bone formation/resorption**

Treatment Strategies

- **Restore normal menstrual cycling**
- **Increase energy availability, increase 200 to 300 kcal/day**
- **Decrease or limit training?**
  - Use of a contract
  - Hospitalize if severe
Treatment Strategies

- Replacement hormones
  - Oral contraceptives?
    AAP Committee on Sports Medicine, 1988 (If >16)
    Liu & Lebrun BJSM 2006
- Calcitomin
  Drinkwater et al., J Bone Min Res 8:S264, 1993
- Bisphosponates not recommended
- Leptin?
  Welt et al., NEJM 351:10,2004

...another double blind study

Education

Research

www.ncaa.org
**ACSM Initiatives**

- Female Athlete Triad Position Stand (1993) 1997 Otis et al., MSSE
- (revised 2007, EBM guidelines)
- Nattiv, Loucks, Manore, Sanborn, Sundgot-Borgen, Warren
- Female Athlete Triad slide series (2000)
- ACSM-CASM Joint initiative: CD-ROM on Female Athlete Triad
- Being revised 2010 by ACSM SHI

[www.acsm.org](http://www.acsm.org)

**CASM Initiatives**

- Position Stand on Body Composition

**Female Athlete Triad Coalition**

- “To promote the health and well-being of female athletes by education, advocacy, public policy, global leadership, and research”

[www.FemaleAthleteTriad.org](http://www.FemaleAthleteTriad.org)

**Female Athlete Triad Coalition**

- Strategies:
  - Public Health
  - Sports Organizations
  - Scientific Foundations
  - Administrative
  - Internet

- Plans:
  - Public Education
  - Professional Education
  - Advocacy/Political Strategies

[www.FemaleAthleteTriad.org](http://www.FemaleAthleteTriad.org)
IOC Medical Commission

- Position Stand on the Female Athlete Triad
  IOC Medical Commission's Working Group:

- Consensus Statement on the Female Athlete Triad
  Drs. M. Mountjoy, N. Constantini et al., November 2005
  “Athletes with anorexia nervosa or bulimia nervosa should be excluded from competition”.

Exercise is Medicine

Thank you for your attention!