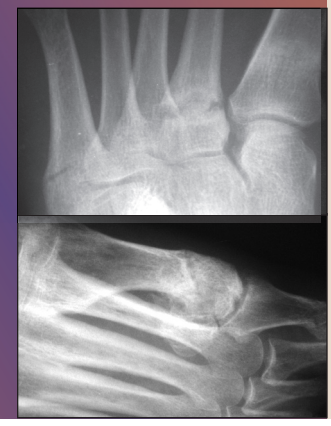
Continuing Medical Education

Osteoporosis—The Fall that Causes the Fracture

Here's a look at the causes and treatment for this condition.



Objectives

1) To demonstrate the complications that result from the disease of osteoporosis, such as low bone density, minimal peak bone mass, stress fractures, and adult bone loss.

2) To demonstrate the components of the female triad, osteoporosis, amenorrhea, and anorexia nervosa.

3) To demonstrate the means of diagnosing osteoporosis via bone mineral density studies, and how to interpret them to diagnose osteopenia vs. osteoporosis.

4) To demonstrate the various means of treatment with bisphosphonate medication, calcium supplementation, and exercise.

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*Following this article, an answer sheet and full set of instructions are provided (p. 202).—**Editor***

By Jeffrey A. Ross, DPM, MD

Osteoporosis or porous bone is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility. It is the most common type of metabolic bone disease. Osteoporosis is a major public health threat that affects 44 million Americans, 68 percent of whom are women. Despite the increased awareness of poor bone health, advances in technology for screening and diagnosis, and the variety of treatments, there continues to be significant morbidity, mortality, and economic burden. In the United States today, 20 million individuals have osteoporosis and 34 million have low bone mass, placing them at increased risk for the disease. One out of every two women and one in four men over 50 will have an osteoporosis-related fracture in their lifetime. More than two million American

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men suffer from osteoporosis, and millions more are at risk.

Osteoporosis is responsible for 1.5 million fractures annually including 300,000 hip fractures, and approximately 700,000 vertebral fractures. The direct and indirect cost of osteoporosis is estimated between $14-18 billion per year.[1] As a result of this disease, 50,000 deaths occur each year. It is a culmination of a process that begins in the third and fourth decades of life. For the female athlete triad, osteoporosis also refers to the premature loss of bone or inadequate bone formation in the younger female athlete, which also results in a greater risk for fracture.[2]

The World Health Organization (WHO) defines that women are osteoporotic if they have bone densities more than 2.5 standard deviations (SD) below the mean density for young adults.[3] This amounts to a loss of 25 to 30 percent from normal peak bone mass. Osteopenia is defined as a lesser degree of bone loss, in which the measured density is between 1.0 and 2.5 standard deviations below normal peak bone mass. This amounts to a loss of 10 to 25 percent from normal peak bone mass.

Bone Health

Bone is a living tissue where changes occur regularly in a continued process of bone resorption and bone formation known as remodeling. The remodeling process involves the bone growth, changes in bone density, and the regulation of calcium levels in the body. The process of remodeling occurs throughout the life span, and once peak bone mass has been achieved, bone formation generally equals bone resorption; thus, the density of the bone remains unchanged.[4]

We can define peak bone density, also referred to as peak bone mass, as the highest amount of bone mass achieved during a lifetime. When that peak bone density is attained continues to remain unclear.[5] Some research studies has have shown that peak bone mass occurs in the 20's or 30's;[6] however, other research studies suggest that the peak bone density may occur as early as 18 years of age.[7] It can be deduced that after bone growth has peaked and no longer continues, the resorption process exceeds small extent bone formation; consequentially, bone mass will be lost during the aging process.

Maximizing Peak Bone Mass

Peak bone mass, along with age-related bone loss, are the two principal factors determining bone mass late in life.[7] Due to this fact, fragility fractures are related to bone density.[8] Maximizing peak bone mass could assist in protecting individuals against osteoporosis.[7] Various experts differ on the age that peak bone mineral content (BMC) is attained; however, the important time period seems to be between ages 9 and 20 years of age.[9] Before the time of puberty, there are few, if any, gender differences.[10]

Increasing peak bone mass during skeletal maturation is important, but the mechanism remains unknown. In a review of ethnic and genetic differences in bone mass, it was concluded that the amount of peak bone mass that can be attained depends on a strong hereditary contribution that can be modulated through diet, physical activity and hormonal factors.[11] By the conclusion of adolescence, 90 percent or more of adult bone mineral content (BMC) has been deposited.[7,10,12]

Research shows the importance of exercise in establishing optimal levels of bone mineral during those years in which bone modeling accompanies growth.[13] Exercise in youngsters has been shown to have an integral relationship with achieving peak bone mineral density. Retrospective studies of children commonly report an affirmative association between bone mineral density (BMD) and weight-bearing, but not non-weight-bearing activities (swimming, bicycling, etc.).[12,14,15]

Prevention

To reach optimal peak bone mass and continue building new bone tissue as you age, there are several factors that need to be considered. An inadequate supply of calcium over a lifetime contributes to the development of osteoporosis. Research has shown that dietary calcium has an important role in attaining peak bone mass.[16]

National nutrition surveys show that many people consume less than half the amount of calcium recommended each day. Calcium intake needs alter during the course of one's lifetime. The body's demand for calcium is greater during childhood and adolescence, when the skeleton is growing. Postmenopausal women and older men also need to consume more calcium. Also, as you age, your body becomes less efficient at absorbing calcium, resulting in chronic medical problems and the use of medications that may impair calcium absorption.

Diminishing Adult Bone Loss

Peak bone mass is achieved during the first two decades of life. As a result, one's bone mineral density is at risk for a multitude of factors which can develop into bone loss. Efforts have been concentrated on postmenopausal women due to estrogen deficiency, which results in an increased bone loss rate. Studies have examined the effects of combining exercise, calcium supplementation, and hormone replacement in postmenopausal women.[17-19] Estrogen therapy has been proven to be enhanced by the addition of weight-bearing exercises,[17] resistance training,[19] and exercise plus calcium supplementation.[18] Calcium supplementation unaccompanied does not appear to protect against the accelerated bone loss during early menopause.[20,21]

Exercise is an important component of an osteoporosis prevention and treatment program. Exercise not only improves bone health, but also leads to better overall health.

There is no perfect exercise training program to enhance skeletal integrity. However, it has been established in research studies that load-bearing exercise at high magnitude with few repetitions creates adaptable strain distributions all through the bone structure, while being long-term and progressive.[22,23] Resistance training or weight lifting exercise meets that requirement, and can easily be performed.

Exercise has been recognized as an integral part of maintaining physical function in older adults. In addition, participation in athletics can be a valuable asset for increasing bone mineral density. Studies have revealed the positive effects of sports participation and resistance training

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on maintaining good bone health.[24,25] Sports participation that involves impact-loading (gymnastics or volleyball) seems to have a greater benefit for improving bone mineral density than those sports without impact loading (cycling and swimming).[23-25]

Female Triad

Female athletes are particularly at risk even though they may participate in mechanical-loading athletic training. These athletes are at a higher risk for developing the female triad, namely, osteoporosis, amenorrhea and eating disorders (anorexia nervosa or bulimia). The time frame for development of anorexia nervosa and bulimia nervosa is usually during late adolescence or early adulthood. The occurrence of eating disorders has risen significantly in recent decades among the general population.[26] In regard to the female triad, the term osteoporosis refers to a premature bone loss or inadequate bone formation or both, resulting in low bone mass, micro-architectural deterioration, increased skeletal fragility, and an increased risk of fracture.[27]

There should be great concern for these athletes, since these women have lowered bone mass at a time when they should be forming bone mineral. With reduced bone mineral mass, the targeted levels may not be achieved, placing them at risk for developing premature osteoporosis. The question is whether the reduction in bone mineral density in the amenorrheic athlete is a premature, permanent loss. Many of the studies examining amenorrheic athletes report a 10 to 25% lower bone mineral density at the lumbar spine in the amenorrheic athlete compared to the controlled eumenorrheic athlete.[28-30]

Osteoporosis

For the older postmenopausal white female, osteoporosis is a major concern. Osteoporotic fractures in this older female group are associated, to a great degree, with the woman's bone mineral density.[5] For the young amennorrheic athlete with low bone mineral density, the risk for developing osteoporosis and developing fractures later in life has tremendous implications. Early screening and detection with effective intervention can have a major impact in the prevention of this disease.

Stress Fractures

It has been estimated that if a Caucasian woman lives to be 90 years of age, she has a 32% chance of sustaining a hip fracture. About one million bone fractures occur in women over 45 years of age, of which 150,000 are hip fractures. The death rate within three months of developing a hip fracture is 12 to 20%. These facts should be alarming. For instance, in 2000, approximately 30 million women were known to be at risk annually in the United States for suffering an osteoporotic fracture. It has become a major contributor to morbidity and mortality in postmenopausal women.

The rate of bone mineral loss is greater in women (1% per year) than in men. At the time of menopause, an accelerated rate of demineralization (2 to 5% per year) occurs in these women. It has been estimated that during the first five years after menopause, calcium loss is primarily from trabecular bone (vertebrae). Later, calcium loss occurs nearly equally from trabecular and cortical bone (hip and long bones). Due to this bone mineral loss, crush fractures of the vertebral bodies will predominate. As a result, back pain, loss of height and a stooped posture (dowager's hump) will develop.

If there is any suspicion that the patient may have osteoporosis, order a DXA scan before initiating any surgery.

There are many other risk factors for developing fractures. Some include: the person's balance, leg strength, physical agility, and eyesight. Older age is a risk factor for fracture, independent of bone density. Those osteoporosis patients who have suffered a previous fragility fracture are considered to have severe osteoporosis, and have a high risk for future fractures.

Hip Fractures

Hip fractures have the greatest impact from osteoporosis. It is estimated that osteoporosis causes more than 250,000 hip fractures in the United States annually. It is estimated that 50-year old Caucasian women have a 17.5% lifetime risk of fracture of the proximal femur. The incidence of hip fractures increases for both men and women from the sixth through the ninth decade of life. The greatest incidence occurs in men and women 80 years of age or older.

It is estimated that between 35-50% of all women over 50 will suffer from at least one vertebral fracture. In the United States, 700,000 vertebral fractures a year occur, but only a third of them are documented.

Risk Factors for Osteoporotic Fracture

Risk factors for the development of an osteoporotic fracture include the following: Personal history of fracture as an adult, history of fracture in a first-degree relative, Caucasian or Asian race (although African Americans and Hispanics are at significant risk as well), advanced age, being female, dementia, poor health, frailty, current cigarette smoking, low body weight, anorexia nervosa, estrogen deficiency (past menopause, menopause before age 45), low testosterone levels in men, use of certain medications such as corticosteroids and anticonvulsants, lifelong low calcium intake, excessive alcohol intake, recurrent falls, and inadequate physical activity.

When anticipating osseous surgery, particularly involving osteotomies, the surgeon should take an accurate history to determine if the patient has a history of osteopenia or osteoporosis. It would also be advantageous to know if the patient in her younger years suffered from anorexia nervosa, predisposing her to low bone mineral density. When reviewing the x-rays, evaluate whether the bone appears normal or osteoporotic. If there is any suspi-

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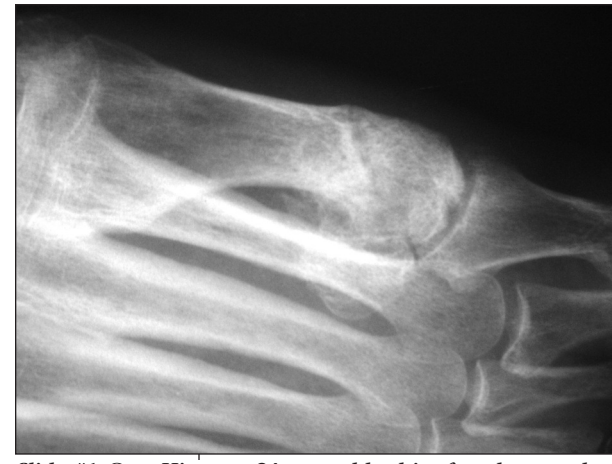
cion that the patient may have osteoporosis, order a DXA scan before initiating any surgery. This will help predict the viability of the bone, and help predict how the patient will heal post-operatively.

Estrogen Deficiency

Evidence suggests that estrogen deficiency may increase skeletal production of bone resorbing cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor. Estrogen deficiency may also reduce skeletal production of growth factors and stimulate bone formation, such as insulin-like growth factor-1, and transforming growth factor-B. Estrogen deficiency increases the skeleton's sensitivity to the resorptive effects of parathyroid hormone, which leads to a small increase in serum calcium levels. The theory is that this will limit intestinal calcium absorption. Estrogen receptors on osteoblasts propose that estrogen deficiency may also alter bone formation directly.

Osteoporosis is often called the "silent disease" because bone loss occurs without symptoms. Often people may not know that they suffer a fracture of the hip or a vertebra collapse. Collapsed vertebrae may initially be felt in the form of severe back pain, loss of height, or spinal deformities. Later in the course of the disease, fractures of the hip and forearm may occur. Clinically, significant fractures are five to eight times more common in women than in men. The incidence of fractures is greater in Caucasian than in African-American women due to greater peak bone mass at maturity in African Americans.

Osteoporosis can also affect the male population. One study found that men with the highest homocysteine levels were four times as likely to develop hip fractures as men with the lowest levels. A second study found that men and women with the highest levels of homocysteine had twice the risk of suffering a fracture compared with those with the lowest levels. Homocysteine (an amino acid) has been linked to a greater risk of heart disease. Elevated homocysteine is typically treated with folic acid and B-vitamin supplements.



Slide #1 Case History—24 year old white female marathon runner with recently diagnosed osteopenia (pre-osteoporosis). Stress fractures of the 1st, 2nd, 3rd, 4th, and 5th metatarsals.

In a recent study reported in the journal Cell, Karsentry, et al. showed that gut serotonin can directly control bone formation. This serotonin is released into the blood, and the more serotonin that reaches the bone, the greater the bone loss. The less serotonin, the stronger the bones.

In another study, it was reported that SSRI users had an increased rate of hip bone loss when compared to nonusers. The rate of loss was 1.6 fold higher than in nonusers. Similar rates of hip bone loss were seen when tricyclic antidepreassant users were compared to non-users.[32]

A bone mineral density (BMD) test is the best way to determine bone health.

Bone Mineral Density Tests

A bone mineral density (BMD) test is the best way to determine bone health. BMD tests can identify osteoporosis, and determine the risk for fracture. The most widely recognized bone mineral density test is called the dual-energy x-ray absorptiometry or DXA test, and is considered the gold standard for the diagnosis of osteoporosis. They are extremely precise, with precision in the range of 1% to 2% being reported. DXA can be used as a precise method to monitor changes in bone density, particularly in patients undergoing treatment.

Measurement of bone mineral density by quantitative computerized tomography (QCT) can be performed with most standard CT scanners. QCT is unique since it provides for true three-dimensional imaging and reports BMD as true volume density measurements. The advantage of QCT is the ability to isolate an area of interest from surrounding tissues. The radiation dose with QCT is about ten times that of DXA, and the QCT test may be more expensive than DXA.

Single-photon absorptiometry (SPA) method works when a single-energy photon beam is passed through bone and soft tissue to a detector. The amount of mineral is quantified. The distal radius is typically used as the site of measurement, SPA is accurate, and the test takes about 10 minutes.

Dual-photon absorptiometry (DPA) uses a photon beam that has two distinct energy peaks. One energy peak is absorbed more by the soft tissue. The other peak is absorbed more by bone. The soft-tissue component is subtracted to determine the bone mineral density.

Radiographic measurement is also used; however, because bone density is not apparent on a plain x-ray until 40% of the bone is lost, different methods of bone mineral density measurement have been developed. The Singh index describes the trabecular patterns in the bone at the top of the femur. X-rays are graded 1 through 6 according to the disappearance of the normal trabecular pattern. The studies correlate a Singh index of less than 3 for fractures of the hip, wrist, and spine. Radiographic absorptiometry

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is another simple way to determine bone mineral density with plain x-ray. Incorporating an aluminum reference wedge, the x-ray is analyzed, and the density of the bone is compared to the density of the reference wedge.

Interpreting a Bone Density Report

The primary reason for ordering a bone density test is to determine the risk for developing a fracture. Bone mineral density correlates closely with the risk of fracture. It is a very close predictor for development of fractures in osteoporosis.

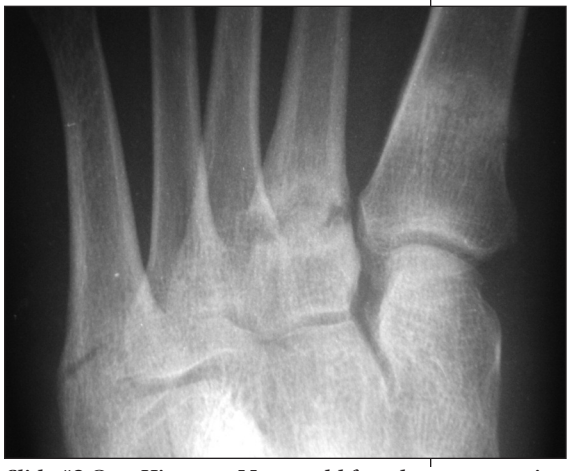
The T-score is the number of standard deviations (SD) above or below the young adult mean. The young adult mean is the expected normal value for the patient compared to others of the same sex and ethnicity. It is approximately what the patient should have been at his/her peak bone density at about age 20 years. As a general rule, for every standard deviation below normal, the fracture risk doubles. For example, a patient with a bone mineral density (BMD) of 1 standard deviation (SD) below normal (a T-score of -1) has twice the risk of fracture as a person with a normal BMD. If the T-score is -2, the risk of fracture is four times normal. A T-score of -3 is eight times the normal fracture risk. Patients with high fracture risk can be treated to prevent future fractures.

The Z-score is the number of standard deviation (SD) the bone density measurement is above or below the value expected for the patient's age. Primary osteoporosis is age-related osteoporosis, with no secondary causes. Secondary osteoporosis occurs when underlying conditions induce bone loss. Some of the causes of secondary osteoporosis include mal-absorption, alcoholism, smoking, thyroid or parathyroid abnormalities, and the use of corticosteroids.

A Z-score lower than -1.5 is suggestive of secondary osteoporosis. When suspected, laboratory tests should be performed to determine the underlying cause of the osteoporosis. By treating the underlying condition, the low bone density may be able to be corrected.

Biochemical Markers of Bone Turnover

Recently, tests for biochemical markers of bone formation (serum osteocalcin, bone specific alkaline phosphatase, or type-1 procollagen carboxyl-terminal propeptide) and bone resorption (urine hydroxyproline, urine pyridinium cross-links) have drawn interest in predicting rates of bone loss. The theory is that a simple blood or urine test could predict rates of bone resorption, or serve as an indication of the response to therapy.



Slide #2 Case History—55 year old female post-operative Austin bunionectomy, with history of osteopenia. Active exerciser, takes calcium and Boniva

Treatment—Medications

Bisphosphonates are the main pharmacological measures for treatment. They are a class of drugs that inhibit osteoclast action and resorption of bone. Its uses include the prevention and treatment of osteoporosis, osteitis deformans ("Paget's disease of bone"), bone metastasis (with or without hypercalcaemia) multiple myeloma, and other conditions that feature bone fragility. Drugs such as teriparatid and strontium ranelate appeared in the 1990's as an early means of treatment.

When osteoporosis is confirmed, bisphosphonate drugs are the first-line treatment. The most frequently prescribed bisphosphonates are presently alendronate (Fosamax) 10 mg. a day, or 70 mg. once a week. Others such as risedronate (Actonel) 5 mg. a day or 35 mg. once a week, ibandronate (Boniva) once a month, and a newer drug zoledronic acid (Reclast) 5 mg. which is given once yearly.

Oral bisphosphonates are relatively poorly absorbed, and as a result need to be taken on an empty stomach, with no food or drink for 30 minutes.

A study in 2007 suggested that in patients who had suffered a low-impact hip fracture, annual infusion of 5 mg zoledronic acid reduced risk of any fracture by 35% (from 13.9 to 8.6%), vertebral fracture risk went from 3.8% to 1.7%, and non-vertebral fracture risk from 10.7% to 7.6%. This study also revealed a mortality benefit: after 1.9 years, 9.6% of the study group (compared to 13.3% of the control group) had died of any cause, showing a significant mortality benefit of 28%.[33]

Oral bisphosphonates are relatively poorly absorbed, and as a result need to be taken on an empty stomach, with no food or drink for 30 minutes. Esophagitis is a common side-effect; therefore, weekly or monthly administration has become the standard.

Calcium is essential to support bone growth, bone healing and the maintenance of good bone health, and is therefore regarded as a treatment for osteoporosis. The body's demand for calcium is greater during childhood and adolescence, when skeletal growth is occurring. For postmenopausal women, calcium is even more important, since as we age the body becomes less efficient in absorbing calcium. The daily recommendation for women over 50 is 1,200 mg of calcium per day, and 200 to 800 IUs vitamin D. For women between 19 to 50 years

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of age, the recommendation is 1,000 mg. a day of calcium and 200 IUs a day of vitamin D.

Conclusions

Good bone health is essential to everyone, regardless of age. Osteoporosis is a preventable disease; however, steps must be taken to increase bone mass at an early age. To increase bone mass, the best time for early intervention with calcium supplementation and exercise is in the pre-pubertal years. In the older athletic female, bone mineral density is typically well above normal; however, the young amenorrheic athletes can have bone density values equal to that of an elderly osteoporotic woman. Treatment options are available for patients with low bone mass, but prevention is a much preferable option. ■

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EXAMINATION

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See answer sheet on page 203.

1) What is the most common metabolic bone disease?
- A) hypocalcemia
- B) Paget's disease
- C) hyperpituitary
- D) osteoporosis

2) How many Americans suffer from osteoporosis?
- A) 1 million
- B) 10 million
- C) 20 million
- D) 50 million

3) Osteoporosis is responsible for how many fractures per year?
- A) 10,000
- B) 1 million
- C) 1.5 million
- D) 5 million

4) The World Health Organization definition for women with osteoporosis is that they demonstrate a bone mineral density of how much greater than the standard deviation?
- A) 1.0
- B) 2.0
- C) 2.5
- D) 3.0

5) Osteopenia is defined as a lesser degree of bone loss. The density measure is between what standard deviations below normal peak bone mass?
- A) 0-1.5
- B) 1.0-2.0
- C) 1.5-2.0
- D) 1.0-2.5

6) Peak bone mass occurs during what period of life?
- A) birth to 10 years
- B) teenage years
- C) teenage though 20's
- D) 20's and 30's

7) What component has been shown to be integral in achieving peak bone mineral density?
- A) calcium intake
- B) impact exercise
- C) resistance training
- D) vitamin D

8) In the female triad, the time frame for anorexia nervosa or bulimia is?
- A) early childhood
- B) early adolescence
- C) late adolescence
- D) late adolescence or early adulthood

9) Three months after a 45 year or older female develops a hip fracture, the death rate is estimated to be?
- A) 12-20%
- B) 10-15%
- C) 20-30%
- D) 30-40%

10) In the year 2000, how many women in the U.S. were at risk for developing an osteoporotic fracture?
- A) 10 million
- B) 20 million
- C) 30 million
- D) 50 million

11) It has been estimated that after the first five years of menopause, the bone loss is primarily from?
- A) cortical bone
- B) cortical and trabecular bone
- C) trabecular vertebrae bone
- D) hip trabecular bone

12) It is estimated that a 50 year old Caucasian woman will have what percentage risk of developing a fracture of the proximal femur?
- A) 10%
- B) 15%
- C) 17.5%
- D) 20%

13) Osteoporosis affects women more than men. Woman will suffer fractures to what greater degree than men?
- A) 3-5 times
- B) 5 to 8 times
- C) 10 times
- D) 15 times

14) What medications have been shown to cause a 1.6 fold increase in hip fractures?
- A) tricyclic antidepressants
- B) SSRI's
- C) tricyclic antidepressants and SSRI's
- D) SSRI's

Continued on page 202

Continuing Medical Education

EXAMINATION

(cont'd)

15) Which test is regarded as the gold standard for the diagnosis of osteoporosis?

A) single-photon absorptiometry (SPA)
B) dual-photon absorptiometry (DPA)
C) quantitative computerized tomography (QCT)
D) dual-energy x-ray absorptiometry (DXA)

16) If the T-score is -1.0, the patient will have what higher risk factor of developing a fracture?

A) 2 times
B) 3 times
C) 4 times
D) 8 times

17) A Z-score lower than what figure is suggestive of secondary osteoporosis?

A) -1.0
B) -1.5
C) -2.0
D) -2.5

18) On plain x-ray, bone mineral density (BMD) loss is not detected until what percentage is lost?

A) 10%
B) 20%
C) 30%
D) 40%

19) Bisphosphonates have been shown to be effective in the prevention of bone mineral loss. What new drug is given only once a year?

A) alendronate (Fosomax)
B) risedronate (Actonel)
C) ibandronate (Boniva)
D) zoledronic acid (Reclast)

20) After 50 years of age, what is the recommended daily requirement of calcium?:

A) 500 mg
B) 1000 mg
C) 1200 mg
D) 1500 mg

See answer sheet on page 203.

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ENROLLMENT FORM & ANSWER SHEET (cont'd)

EXAM #5/09
Osteoporosis—The Fall that Causes the Fracture (Ross)

Circle:

1.	A	B	C	D	11.	A	B	C	D
2.	A	B	C	D	12.	A	B	C	D
3.	A	B	C	D	13.	A	B	C	D
4.	A	B	C	D	14.	A	B	C	D
5.	A	B	C	D	15.	A	B	C	D
6.	A	B	C	D	16.	A	B	C	D
7.	A	B	C	D	17.	A	B	C	D
8.	A	B	C	D	18.	A	B	C	D
9.	A	B	C	D	19.	A	B	C	D
10.	A	B	C	D	20.	A	B	C	D

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