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PURPOSE AND OBJECTIVES

Osteoporosis is a major health problem associated with significant mortality and morbidity risks. With awareness, screening, and proper treatment, it can be prevented. Physicians in all specialties, especially those in primary care, have a crucial role to play in the prevention, recognition, and treatment of osteoporosis. After reading the following section, physicians should be able to recognize the risk factors for the disease and implement appropriate preventive measures; as well as treat active disease so as to ameliorate the likelihood of further bone loss. In addition, they should be aware of ongoing clinical trials, publications, and other useful resources.

DISCLOSURE

In publishing this section in *Southern Medical Journal*, the Southern Medical Association recognizes educational needs of physicians in all specialties, especially those in primary care, for current information regarding the diagnosis and treatment of osteoporosis. In this section, authors may have included discussions about drug interventions, whether Food and Drug Administration approved or unapproved. Therefore, it is incumbent on physicians reading this section to be aware of these factors in interpreting the contents and evaluating recommendations. Moreover, views of authors do not necessarily reflect the opinions of the Southern Medical Association. Every effort has been made to encourage the author to disclose any commercial relationships or personal benefit that may be associated with this section. If the author disclosed a relationship, it is indicated below. This disclosure in no way implies that the information presented is biased or of lesser quality.

Ronald C. Hamdy, MD, FRCP, FACP

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DISCLAIMER

The primary purpose of this section in the *Journal* is education. Information presented and techniques discussed are intended to inform physicians of medical knowledge, clinical procedures, and experiences of physicians willing to share such information with colleagues. It is recognized that a diversity of professional opinions exists in the contemporary practice of medicine that influences the selection of methods and procedures. The views and approaches of authors are offered solely for educational purposes. The Southern Medical Association disclaims any and all liability for injury or other damages to any individual reading this section and for all claims that may result from the use of techniques and procedures presented in it.

Highlights of the Fourth Annual Conference on Osteoporosis, Amelia Island, Florida, February 22-24, 2001

The SMA's Fourth Annual Conference on Osteoporosis was held in conjunction with the International Society of Clinical Densitometry in Amelia Island, Florida, February 22 to 24. The Conference was jointly chaired by Ronald Hamdy, MD (East Tennessee State University, Johnson City, TN) and Leon Lenchik, MD (Wake Forest University, Winston-Salem, NC). The Conference Faculty included: Marjorie Gass (University of Cincinnati College of Medicine, Cincinnati, OH), Michael Holick, PhD, MD (Boston University School of Medicine, Boston, MA), Hartmut Malluche, MD (University of Kentucky, Lexington, KY), Veronica Piziak MD, PhD (Texas A&M College of Medicine, Temple, TX), Anthony Saway MD, (St Vincent's Hospital, Birmingham, AL), Andrew Shields MD (University of Washington Medical Center, Seattle, WA) and Nelson Watts MD (Emory Clinic, Atlanta, GA). Dr Watts was installed 3 weeks after the Conference as President of the International Society of Clinical Densitometry. There were over 150 participants at this Conference; many elected to also get the ISCD certification and became Certified Clinical Densitometrists.

This year most of the formal presentations were in the form of "Point/Counter Point" and were very well received by the participants. In addition to the formal presentations, there were a number of DXA and Exercise workshops that enabled participants to get a hands-on experience with DXA scanners and Exercise programs. The GE/Lunar Corporation made a DXA scanner available to be used during the workshops. Instructors included Judy Beamer (DXA and Exercise Workshops) and Heather Campbell (DXA Workshops). There were also a number of exhibitors attending this conference. Unrestricted educational grants were provided by The Alliance for Better Bone Health, Aventis Pharmaceuticals and Proctor Gamble Pharmaceuticals, Eli Lilly & Company, GE Lunar, Merck U.S. Human Health, Novartis Pharmaceuticals, Pfizer Pharmaceuticals, SMA Services, Inc, and SmithKline Beecham.

The main objectives of the Conference were to enable participants to:

- Diagnose osteoporosis with confidence and understand the usefulness and limitations of various laboratory investigations, as well as bone mass measurement techniques.
- Appreciate the indications, effectiveness, and potential adverse effects of various medications used in the treatment and prevention of osteoporosis.
- Develop a treatment strategy tailored to individual patients.
- Diagnose and manage secondary osteoporosis and related causes of bone loss.
- Manage acute vertebral fractures and apply current clinical pathways to treatment.

DIAGNOSING OSTEOPOROSIS

The **main goals of the diagnostic process** in osteoporosis are to establish the diagnosis,

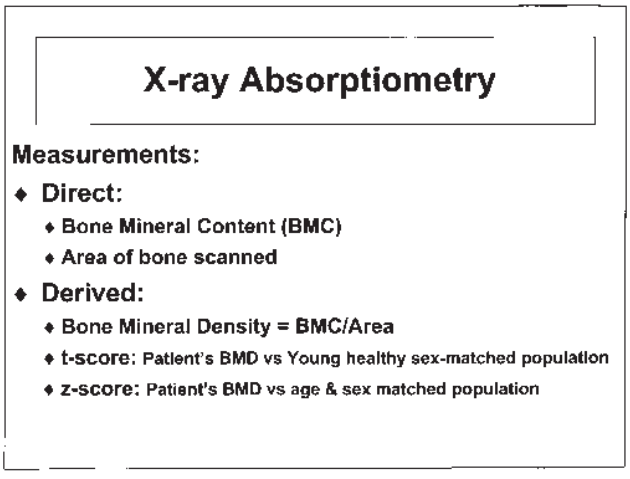

FIGURE 1.

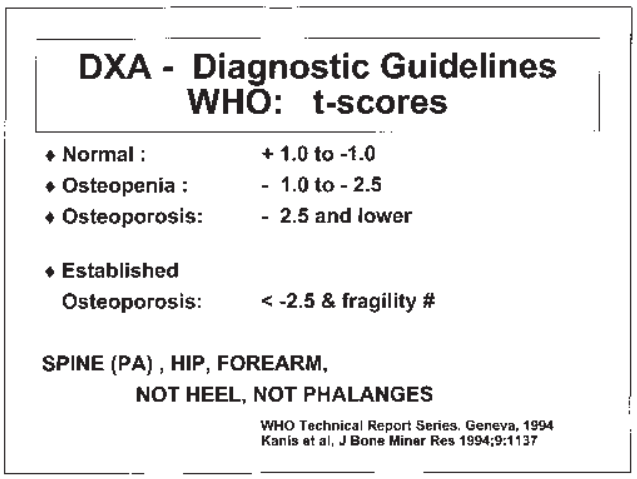

FIGURE 2.

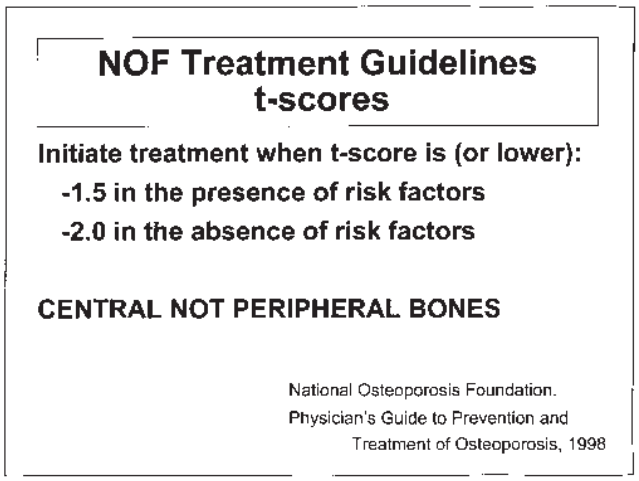

FIGURE 3.

identify the presence of secondary causes of bone demineralization and quantify the severity of the disease to establish the patient's prognosis and to monitor the patient's progress and response to therapy.

The gold standard for the non-invasive diagnosis of osteoporosis is **Dual X-ray Absorptiometry (DXA).** During this procedure two different energy beams (soft x-rays) are directed at the patient. The x-ray beams could be directed at the patient in a narrow collimated manner (pencil beam) or as an array (fan beam). The latter is a much faster procedure than the former, but otherwise offers little advantage in terms of accuracy. Detector crystals across the patient's body record the amount of energy that has not been absorbed by the patient's body. The difference in rate of absorption of the two energy beams by the patient's body allows the system to estimate the mineral content in the bone. The bone surface scanned is also measured.

The **bone mineral density (BMD)** is calculated by dividing the bone mineral content by the surface area of the bone scanned. The patient's BMD is then compared to that of reference populations of the same gender and, in some models, ethnic group. The **t-score** represents the number of standard deviations when the patient's BMD is compared to that of young, healthy reference population. The z-score represents the number of standard deviations when the patient's BMD is compared to the age matched population.

The t-score, rather than the absolute BMD is used to diagnose osteoporosis because different DXA models use different technologies to produce the 2 beams of x-rays. The absolute BMD value is therefore different when a patient is scanned with different densitometers. Different manufacturers also have different reference populations. Furthermore, different manufacturers estimate the BMD in different parts of the femoral neck, although they still label it as the "Femoral Neck." For all these reasons, comparing the absolute BMD values obtained from different manufacturers is not meaningful.

The World Health Organization has issued **diagnostic guidelines** to help define the degree of bone demineralization by using the t-score. The normal range is above –1.0. A diagnosis of osteopenia is made when the t-score is between –1.0 and –2.5 and the diagnosis of osteoporosis is made when the t-score is –2.5 or lower. This classification applies only to the lumbar vertebrae, proximal femurs and distal radius and ulna and only to postmenopausal white women. It applies to neither the calcaneus, nor the phalanges. It also applies to neither non-Caucasian women, nor premenopausal women, nor men. In the absence of any other guidelines, however, most clinicians use this definition also for non-Caucasian women and for men. In premenopausal women, however, the consensus is to use the term "Low Bone Mass" as opposed to osteopenia or osteoporosis.

The t-score can also be used to develop a treatment strategy. The National Osteoporosis Foundation has issued **treatment guidelines** based on the t-score. Treatment is recom-

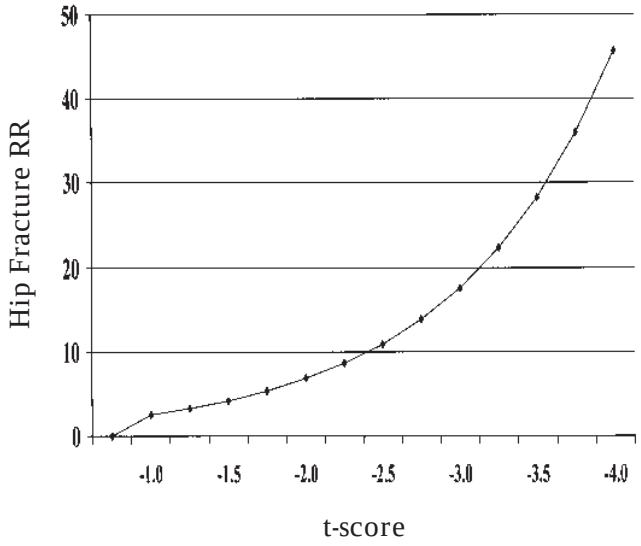

FIGURE 4. T-Scores and Relative Risk Hip Fracture. (Adapted from Marshall D, et al: Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. *BMJ* 1996; 312:1254-1259.)

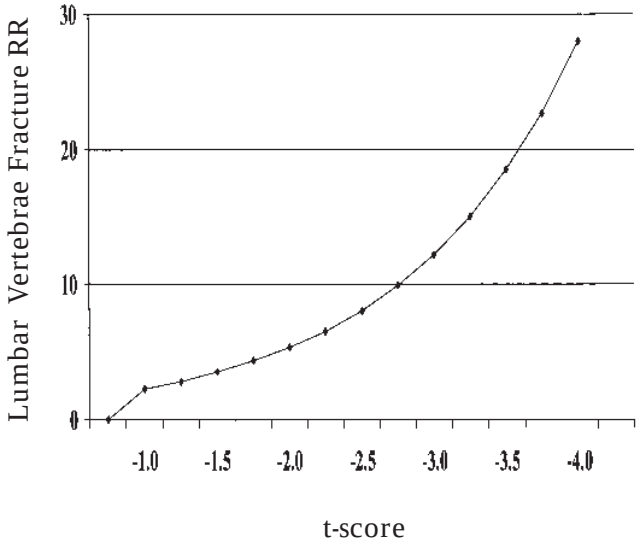

FIGURE 5. T-Scores and Relative Risk Lumbar Vertebrae Fracture. (Adapted from Marshall D, et al: Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. *BMJ* 1996; 312:1254-1259.)

mended if the t-score is –2.0 or lower if the patient does not have any risk factor for osteoporosis and when the t-score is –1.5 or lower if the patient has risk factors for osteoporosis. These recommendations also apply only to white postmenopausal women, although most clinicians use them also for non-Caucasian women and for men.

A good correlation exists between the BMD and the **fracture risk,** especially in the untreated patient. The t-score is also used to predict the fracture risk. Several formulas have been put forward. A frequently used one is that developed by Marshall et al (*BMJ* 1996; 312:1254-1259). The fracture risk at the hip is calculated by raising 2.6 to the power of the t-score. The fracture risk of the lumbar vertebrae is calculated by raising 2.3 to the power of the t-score. As can be seen from the accompanying charts, the risk of fracture increases exponentially and inversely with the t-score and is a gradient, not a threshold. It must be remembered that this represents the Relative Risk of fracture and not the Absolute Risk of fracture, and that this estimated fracture risk is site-specific and not global.

DXA scans should not be performed in women who are pregnant even though the exposure to x-rays is minimal. These scans also should not be performed if the patient had a recent radiological GI study using a contrast medium or had a nuclear medicine scan. Radiopaque or metallic objects in the path of the beams interfere with the accuracy of the results. Obesity also interferes with the accuracy of the scans. Most densitometers have an upper weight limit above which the scans are not reliable and the scan table can be mechanically damaged.

The BMD can also be calculated by using **Computerized Tomography** technology. The main advantage of this technique is that it measures selectively the bone mineral density of trabecular bone only and excludes all other extra-osseous calcium deposits as may occur in osteophytes and in calcifications in the aorta. Another main difference between DXA and CT BMD measurements is that the former measures the BMD in a surface area, whereas the latter measures the BMD by volume. The main limitations of this procedure include its inability to measure the BMD of the proximal femur and the relatively high dose of exposure to radiation, when compared to DXA scans. There is also a better correlation between the BMD as measured by DXA and the risk of fractures than the BMD as measured by CT.

Over the past few years **peripheral bone scanners** that measure the BMD of peripheral bones such as the calcaneus and phalanges have become popular as they are smaller (and therefore portable), cheaper and require less expertise to perform and interpret. Their main disadvantage, however, is that normative

DXA - LUMBAR VERTEBRAE

Region	BMD	t-score	%	Area
L1	0.686	-2.17	74	10.38
L2	0.723	-2.77	70	11.76
L3	0.762	-2.93	70	13.37
L4	0.786	-3.00	70	15.90
L1-L4	0.745	-2.74	71	51.41

NO EVIDENCE OF VERTEBRAL COMPRESSION: gradual increase in area and BMD of vertebrae.

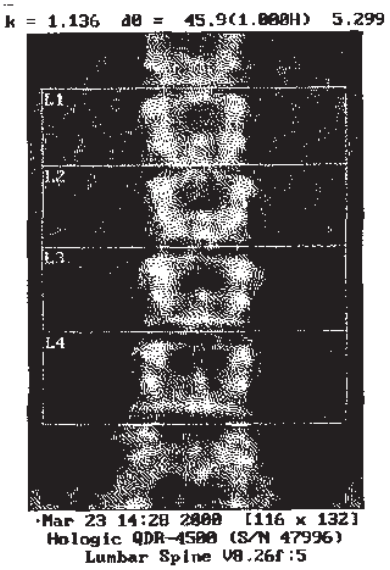

FIGURE 6.

data and diagnostic and therapeutic guidelines have not yet been established. There is also a significant degree of discordance in the BMD of various bones, which casts a great deal of doubt on determining a "normal" bone mass based on the assessment of the BMD in a single bone, especially a peripheral one. More work is presently under way to establish the normative data and hopefully to develop diagnostic and therapeutic guidelines based on these peripheral bone mass measurements.

Some peripheral bone scanners use bone absorptiometry techniques to estimate the BMD of the peripheral bones. Other peripheral scanners use ultrasound technology to measure the speed of sound transmission across the bone examined and the degree of attenuation of the sound wave as it passes across the bone examined. Both the speed of sound transmission and the attenuation of the sound waves are functions of the bone density. Unfortunately, there is much less standardization with ultrasound than with bone absorptiometry techniques. Although most ultrasound scanners are site specific, some can be used for more than one site.

Laboratory tests cannot be used to diagnose osteoporosis. Their main use is to identify secondary causes of osteoporosis. Bone markers can be used to monitor the patient's response to therapy.

Evidence of osteoporosis on **plain x-ray films** includes bone demineralization, and the presence of Schmorl's nodules, wedge deformities and compression fractures of the vertebrae. Stress fractures may also be observed. Unfortunately by the time these signs are manifest, the disease is well advanced.

Clinical features suggestive of osteoporosis include loss of height, kyphosis and atraumatic or low impact fractures. As with plain x-rays, by the time these signs are manifest, the disease is well advanced.

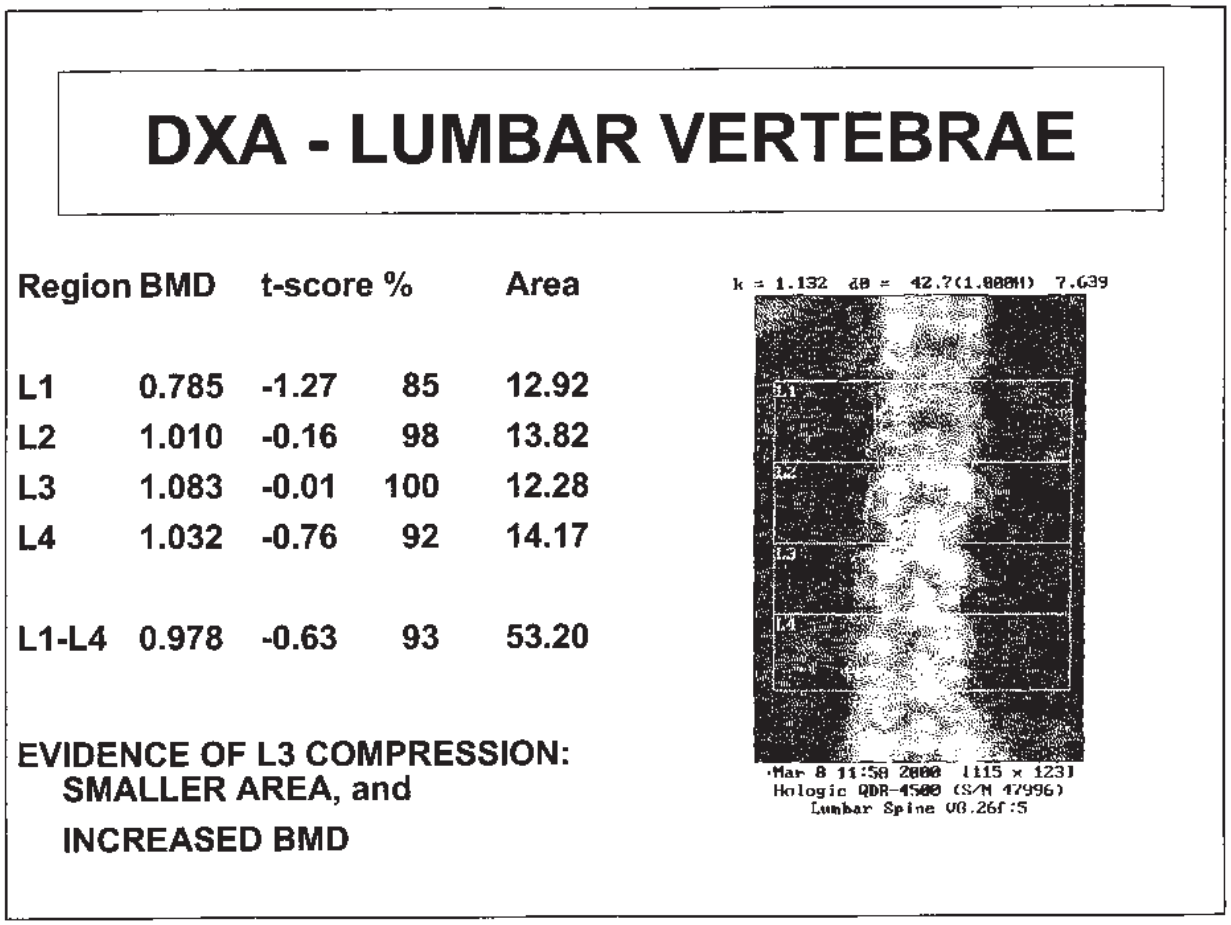

FIGURE 7.

Of all the diagnostic modalities available, DXA is the best non-invasive reproducible method of diagnosing osteoporosis. It can also be used to motivate patients to adhere to their prescribed treatment.

SELECTED RISK FACTORS FOR OSTEOPOROSIS

Non-modifiable risk factors:

- Gender: women are more susceptible than men.
- Race, ethnic group: Caucasians are more susceptible than non-Caucasians.
- Age: Older people are more susceptible than younger people.
- Body frame: People with a small body frame are more susceptible.
- Menopause: The earlier the menopause, the more susceptible is the person.
- Family history: A positive family history, especially of a non-traumatic fracture increases the risk of osteoporosis.

Modifiable Risk Factors:

- Low daily calcium and vitamin D intake.
- Cigarette smoking
- Alcohol abuse
- Excessive caffeine
- Excessive salt intake
- Sedentary life-styles

Disease states predisposing to osteoporosis:

- Ovarian dysfunction
- Hypogonadism
- Rheumatoid arthritis
- Cushing's disease
- Hyperparathyroidism
- Thyrotoxicosis
- Diabetes mellitus
- Strokes
- Malabsorption
- Anorexia nervosa

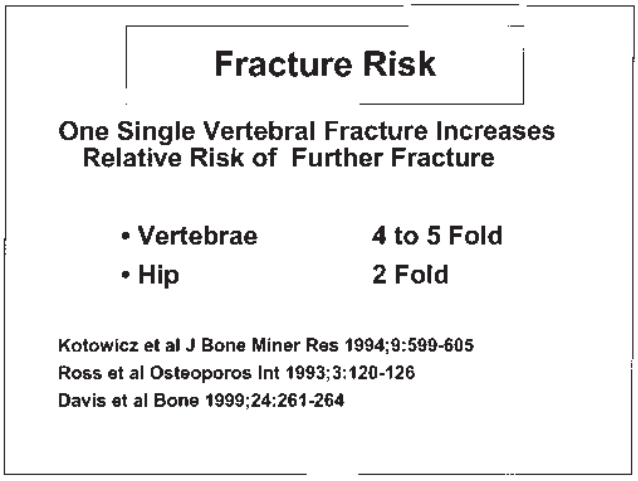

FIGURE 8.

FOODS RICH IN CALCIUM

Approximate elemental calcium content per serving:

FOOD	SERVING SIZE	ELEMENTAL CALCIUM
Milk	1 glass (8 oz)	300 mg
Yogurt	1 cup (8 oz)	400 mg
Ice cream	1 cup (8 oz)	400 mg
Cheese	1 oz	200 mg
Sardines with bones	3 oz	370 mg
Collards	1 cup	200 mg
Broccoli	1 cup	130 mg
Calcium-fortified Orange juice	1 glass (8 oz)	300 mg

ELEMENTAL CALCIUM CONTENT OF SELECTED CALCIUM SUPPLEMENTS

Name Brand	Strength (total)	Elemental calcium
Alka Mints	850 mg	340 mg
Caltrate	1,500 mg	600 mg
OsCal	625 mg	250 mg
Rolaids	550 mg	220 mg
Tums	500 mg	200 mg

Medications:

- Corticosteroids
- Loop diuretics
- Immunosuppressants
- Chemotherapy
- Others

MONITORING PATIENTS WITH LOW BONE MASS

The main goals of monitoring patients with low bone mass include quantifying the rate of change, and motivating patients to comply with the intake of their prescribed medication. In order to do so, two conditions must be met.

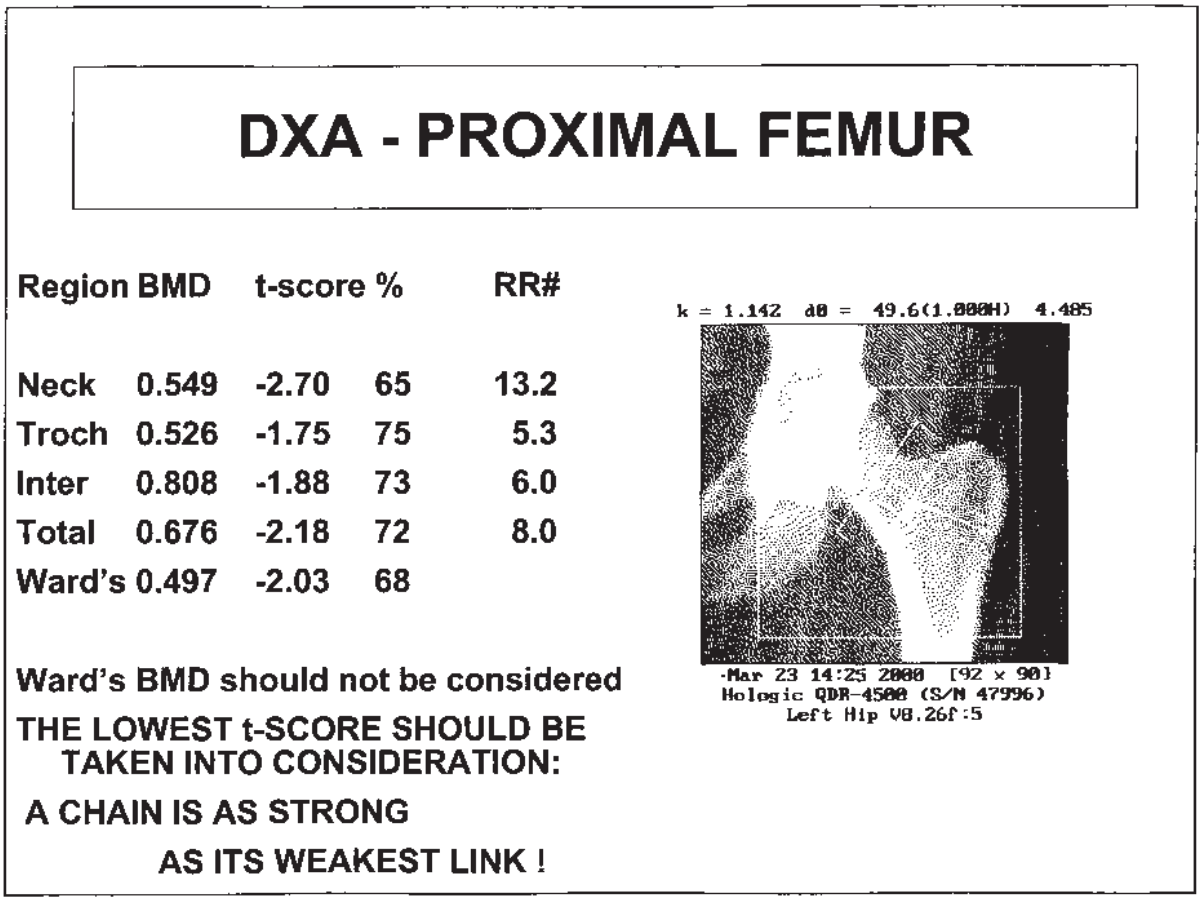

FIGURE 9.

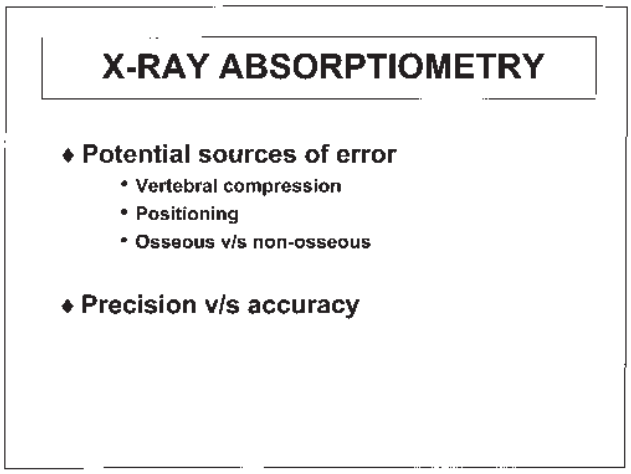

FIGURE 10.

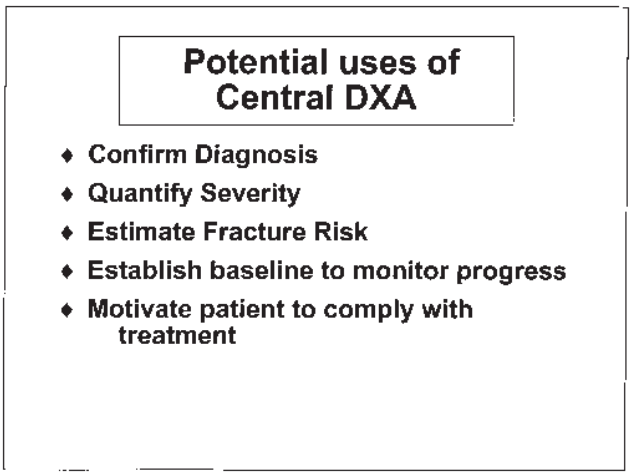

FIGURE 11.

First, one needs to know the expected changes in the patient's bone mineral density or other parameter used to quantify the degree of bone demineralization. Second, one should know the precision and accuracy of the method used to assess that particular parameter.

Bone densitometry (DXA) is often used to monitor the patient's progress and response to treatment. Unfortunately, as different manufacturers use different reference populations and use different technologies to produce the two beams of energy required for the DXA scan, their results are not comparable. It is therefore important to ensure that the patient is scanned with the same densitometer or densitometers produced by the same manufacturer in order to evaluate the changes in BMD.

Also, before giving any credence to observed changes, one should know the precision of the center where the DXA scans are done. Precision is different from accuracy. **Accuracy** is a function of the densitometer and is a comparison between the true value and the measured value. **Precision,** on the other hand is a comparison between serial measurements of the same object or patient. It is dependent on the operator's skills at repositioning the patient in the same position before the scans are performed and is expressed as a percentage error between measurements. Guidelines for calculating the precision of a center are available (Gluer et al, *Osteoporosis International* 1995; 5:262).

Laboratory tests can also be used to monitor the patient's response to therapy: a reduction of more than 40% in urine bone markers, such as the urinary N-telopeptides, over an 8 to 12 week period after initiating treatment is suggestive that the bone turnover rate has been reduced and that the patient is responding to treatment.

TREATMENT OF OSTEOPOROSIS

The FDA has approved 5 medications for the management of osteoporosis:

- Alendronate (Fosamax)
- Calcitonin (Miacalcin)
- Raloxifene (Evista)
- Risedronate (Actonel)
- Estrogen

The profile of these medications is outlined in the Medication Update Section.

GOALS OF THERAPY

It is important to bear in mind that the main goal of treating osteoporosis is to reduce the fracture risk. The BMD, bone markers and "quality of bone" are important surrogate measures of the efficacy of the administered medication, but do not replace the main goal of treating osteoporosis: to **reduce the fracture risk.**

Fortunately, with most of the medications approved by the FDA, results of clinical trials assessing the reduction in fracture risk are available. Unfortunately, with the exception of the FOCUS and IN-FOCUS studies, which have compared the effects of alendronate and calcitonin on the bone mineral density, there has been no head-to-head comparison among

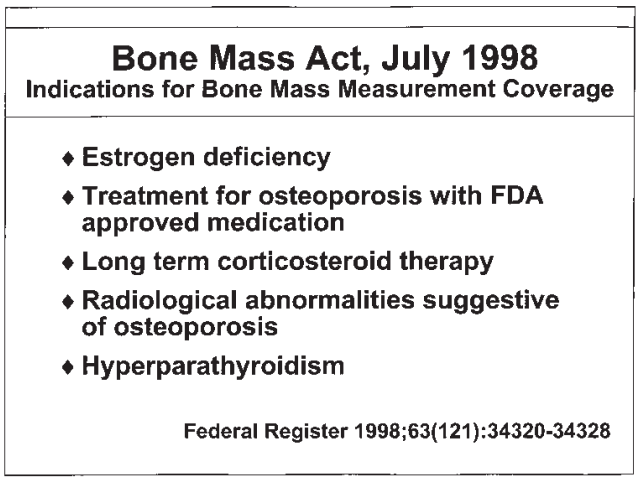

FIGURE 12.

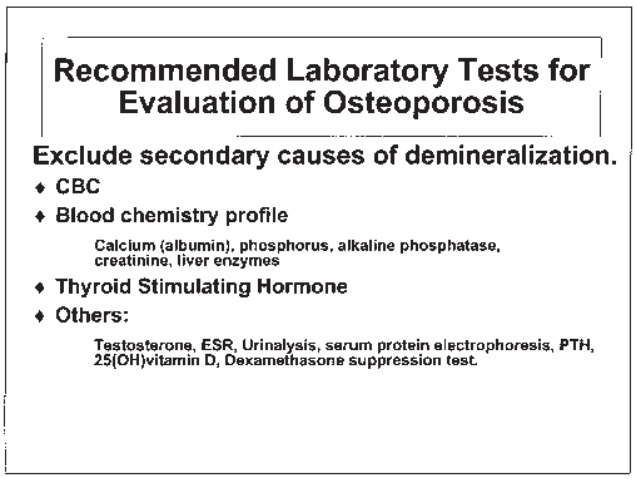

FIGURE 13.

these various medications either on BMD or fracture risk reduction. An accurate comparison between the various medications is therefore not possible. Interested readers are encouraged to review the key papers listed with the references at the end of the Medication Update section.

It must be emphasized that, whichever medication is prescribed, it is important to ensure that the patients get an adequate amount of calcium and vitamin D. The recommended daily intake of elemental calcium for postmenopausal women on hormonal replacement therapy is 1,000 mg. For those not on hormonal replacement therapy it is 1,500 mg.

The recommended daily vitamin D intake is 400 to 600 units.

Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture.

Consensus Development Conference, 1993,
American Journal of Medicine 1993; 94:646-650