FALL 2008

JOURNAL OF THE SPINAL RESEARCH FOUNDATION

Volume 3, Number 2

THE JOURNAL OF THE SPINAL RESEARCH FOUNDATION
A multidisciplinary journal for patients and spine specialists

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THE JOURNAL OF THE SPINAL RESEARCH FOUNDATION

Volume 3, Number 2
"The Crisis of Osteoporosis"

From the Editor

Brian R. Subach, M.D., F.A.C.S.

Osteoporosis is a term which is frequently discussed, however public knowledge regarding the breadth and seriousness of the disease is relatively limited. Osteoporosis is medically defined as a condition in which bones of the skeleton lose calcium resulting in decreased strength and ability to resist injury. The combined loss of bone mineralization and weakening of the intrinsic structure of bone leads to an increasing risk of fracture in an individual. The overall scope and impact of osteoporosis in the United States and the world in general, may be underscored when we consider the fact that one in two women (50%) and one in four men (25%) age fifty and older will experience an osteoporosis-related fracture during their lifetime.

The Spinal Research Foundation, often referred to as SRF, is one of the few non-profit health organizations focused entirely upon spinal health care. Intrinsic to spinal health care is bone health and normal bone density. The National Osteoporosis Foundation (NOF) estimated in 2002, that over 43 million American men and women over the age of fifty were at risk for osteoporosis or low bone mass (formerly known as osteopenia). It is projected that this number will rise to over 52 million in 2010 and more than 61 million in 2020. Clearly, this country faces a major public health threat with a growing population of aged adults. It is currently estimated that there are nearly 12 million individuals with the diagnosis of osteoporosis in this country.

Nearly 80% of those people affected by the disease are women, men are less likely to have osteoporosis and more likely to have the diagnosis of low bone mass. The number of men affected by this disease process is expected to increase to over 17 million by 2010.

Aside from the shear numbers of people affected by osteoporosis, there are a number of problems which arise as a direct result of the disease. For example, in 1991 approximately 300,000 Americans age 45 and over were admitted to hospitals with hip fractures related to osteoporosis. An average of 24% of the hip fracture patients age 50 and older will die in the year following their fracture. Fully one fourth of those who are ambulatory before their hip fracture require some degree of long term care afterward. At six months following hip fracture surgery, only 15% of hip fracture patients can actually walk across the room without some type of support or aide. Numerous studies indicate that physicians are missing critical opportunities to diagnose and treat osteoporosis at younger ages.

In addition to the obvious physical effects of osteoporosis, the disease may have a psychiatric impact as well. It is common for patients to express concerns over the possibility of falling down and fracturing a hip or wrist. There may be fears about the pain of a fracture or the need for surgery to stabilize an injury. Loss or limitation of mobility can have a profound effect upon one's sense of independence and confidence. Depression can also be a serious side effect of osteoporosis. The patient's quality of life can be impacted by diminished self-esteem and self-image as a result of living with osteoporosis. Imagine what it would be like for a woman who can no longer easily stand from a chair or place groceries on her kitchen shelves. She becomes quickly isolated from her daily activities and the community in general. Think about a grandfather who is afraid to receive a big hug from a grandchild for fear of a fracture occurring. These fears may seem unrealistic to you and I, but to an individual afflicted by osteoporosis, fear can dominate their daily lives.

The National Osteoporosis Foundation (NOF) has championed

efforts to diagnose and treat osteoporosis and low bone mass at all ages. On both a national and local level, the NOF works with patients and families through support groups to help those who are living with osteoporosis develop mechanisms to cope with the disease.

We have entitled this edition of the Journal of the Spinal Research Foundation "The Crisis of Osteoporosis" for a specific reason. There are vast numbers of people who are going through the aging process suffering from low bone mass and osteoporosis. It has affected both their lives and the lives of their families. There is a huge cost to society in general, in terms of financial, physical and emotional liabilities. Given the severity of the consequences of osteoporosis, this disease should be discussed, diagnosed and treated aggressively as soon as it is discovered.

Given the breadth of the disease process, any solution to the crisis of osteoporosis must encompass all medical specialties. All of us must be aware of the risks associated with low bone mass and osteoporosis to educate our patients, to refer them for appropriate diagnostic testing and when that diagnostic testing identifies a bone mass deficit, to initiate treatment. Perhaps the most valuable function of medicine is to raise awareness in the public that this is not simply a disease of the elderly, it is a disease of both adulthood and youth alike.

At the Spinal Research Foundation, we view osteoporosis as a major threat to spinal health care and will do our best to assist the National Osteoporosis Foundation in carrying the torch in this worthy effort. ■

From the President
Thomas C. Schuler, M.D., F.A.C.S.

Dear Friends of The Spinal Research Foundation:

It is my pleasure to inform you of the dramatic success of the inaugural Spinal Research Foundation (SRF) "We've Got Your Back" race and fun walk held on May 31, 2008. Over a thousand runners and walkers showed up in support of this most worthy cause. The mission of the Spinal Research Foundation (SRF) has been defined as "Improving spinal health care through research and education". The goal of the race and the associated health fair paralleled this mission in attempting to increase public knowledge of ongoing research in the field of spinal disorders and to educate participants regarding advances in spinal health care and the newest technologies available to treat ailing spines. The massive success of this event far surpassed our original expectations, with benefits appreciated by contributors, participants, and health care providers alike.

Perhaps the greatest success was the sense of accomplishment that many patients experienced upon successfully completing the four-mile run or two-mile walk. Many of these participants were overwhelmed with emotion upon crossing the finish line for several reasons. First and foremost, they were able to accomplish a feat which would never have been possible prior to their treatment. Second, as they crossed the finish line, they saw the faces of many of the physicians, therapists and health care providers who had helped engineer their successful recovery. Finally, the joy and confidence they felt in regaining an active and functional lifestyle brought out both smiles and tears.

It was fitting that the honorary chairs of the event were both patients with spine issues. Washington Redskins NFL stars Shawn Springs and Reed Doughty were able to share with the

From the President

public and the media their personal success stories, each having received recent treatment for spinal problems. They also discussed the significant impact that spinal disorders may have on simple activities of daily life in addition to interfering with job-related duties, particularly when those job-related duties involve sprinting and tackling. Both the avid runners and the recreational athletes appreciated the message shared by these two gentlemen and took advantage of the opportunity to ask for autographs and photos with the football stars.

Many elite runners from throughout the mid-Atlantic region participated in the race. The winning time in the four-mile run was 19 minutes and 22 seconds, truly a remarkable pace, and one which had even the professional athletes amazed.

The contributors and benefactors who formed teams to support and compete in the event said that it served as a wonderful team-building experience for their organizations. Working together, training together and participating as a team in an event representing such an amazing cause fostered a great sense of camaraderie. They also teamed up to raise funds for the Spinal Research Foundation and its noble mission of improving spinal health through research and education.

Michael Howland, CEO of Executive Technologies Group, stated that his employees embraced the opportunity to pursue this athletic challenge while benefiting health care and society. He and his group were extremely appreciative of the opportunity presented by this race/walk and eagerly look forward to providing continued support and participation in the future.

I can speak on behalf of my own practice, The Virginia Spine Institute, in saying that this was a magnificent team-building experience for our company as well, and a wonderful opportunity to see the true level of professionalism exemplified by our employees while working cooperatively to achieve great success for this national organization.

Given the outstanding success of the inaugural race/walk, it is not surprising that the Spinal Research Foundation has already begun planning for the 2009 event. To further spread the word about the importance of spinal health and the great work that is being conducted by SRF, we have encouraged our Regional Research Partners around the country to sponsor identical events in their own cities.

I would like to offer my sincere appreciation to all who worked so hard to make this event such a tremendous success and to further the mission of our distinguished foundation. ■

Dr. Brian Subach, Reed Doughty, Shawn Springs and Dr. Thomas Schuler

Ask the Expert

Questions answered by Mark McLaughlin, M.D., F.A.C.S., Neurosurgeon at Princeton Brain and Spine Care.

Dr. McLaughlin is the Scientific Program Chairman of the AANS/CNS joint spine section and an editor of spineuniverse.com. He has published many articles on neurosurgery and spine surgery and two textbooks about spine surgery. He teaches complex spine surgery nationally and internationally. He initiated the first ever Russian-American Spine Symposium in St. Petersburg.

What does the DXA scan T-score mean to the patient?

In a DXA scan, the amount of mineralized tissue within a section of spine or hip is measured and expressed as grams per cm^2 (square centimeter). Values are often compared to others of the same age and gender (called a Z score) or to healthy 35-year-olds of the same gender who are felt to have attained peak bone mass (T score). These scores are then expressed as measurements of deviation from the average indicating how far above or below normal one's bone quality lies.

How do you evaluate your patients for osteoporosis prior to spinal surgery?

I use x-rays of the spine to look for evidence of prior compression fractures and to get a rough estimate of bone density. In patients requiring surgery using instrumentation, I usually order a DXA (pronounced DEXA) scan, which stands for Dual-Energy X-ray Absorptiometry. It is a low-level x-ray examination measuring the density of three important bone sites and it is probably the most common technique used to assess bone density. It is completely painless, non-invasive and takes only minutes to complete.

What type of calcium supplement do you recommend for your patients?

The two types of calcium which are available over the counter are calcium carbonate and calcium citrate. Either type of calcium is an acceptable supplement for patients with normal bone density or patients attempting to increase mineralization of their bones. There is some thought that the calcium citrate is better absorbed from the gastrointestinal system. It can be taken either with food or on an empty stomach. Calcium carbonate is better absorbed with meals because it requires the presence of stomach acid to be absorbed. In either case, I ask my patients to adhere to the recommended daily dosing table and to take no more than 600mg of calcium supplement at one time.

How are most spinal fractures associated with osteoporosis currently treated?

Most people simply need a protective brace for osteoporotic compression fractures. It generally takes 3 months for such fractures to heal. In other cases of severe pain or development of kyphosis (forward bending of the fractured spine) rapid hardening bone cement may be injected into the fractured spine. Vertebroplasty involves injecting cement directly into fractured vertebral bodies. This has been shown to decrease pain, increase mobility and improve spine stability.

What numbers do you consider diagnostic of osteoporosis?

In our practice, we utilize the established World Health Organization (WHO) criteria to determine osteopenia and osteoporosis in our patients.

- *Individuals within one standard* deviation of peak bone mass (T score 0 to -1.0) are considered to have normal bone density.

- *If bone mass is between one and* 2.5 standard deviations below peak bone mass (T score -1.1 to -2.5), osteopenia is diagnosed.

- *If bone mass is 2.5 standard* deviations below peak bone mass (T score less than -2.5), osteoporosis is diagnosed. ■

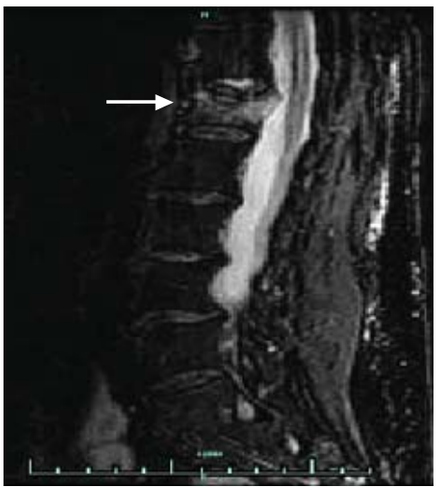
Spine Tale

Irma Greenberg is our Spine Tale for this issue dealing with osteoporosis and the crisis which faces us as spinal health care providers.

Irma is a seventy-six year old retired woman who was living at Manor Care, an assisted living facility. She had been very highly functioning, suffering only from hypothyroidism, a very common condition. She was able to essentially do most activities of daily living, cook for herself and clean, although her stamina was not what it used to be. She had had no previous surgery on her skeletal system but had been previously diagnosed as having a history of osteopenia or bone loss.

She was doing quite well up until May 2, 2008. She fell backwards in her kitchen, landing on her lower back and buttocks region. She noted the immediate onset of low back pain but believed that she had simply bruised and strained her low back. She did not seek immediate medical attention and tried to deal with the discomfort.

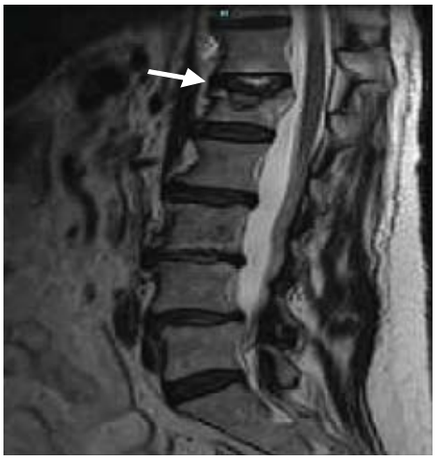
Irma Greenberg



Fat suppression sagittal MRI of lumbar spine. Arrow points to L1 vertebral burst fracture.

She thought that like most bruises it would simply go away. She noted increasing pain when she was in the seated position. Her low back pain was really quite severe, particularly with movement. Walking was very difficult secondary to the severity of the pain. She did find some relief when she was lying on one side or lying flat on her back. The severe pain failed to improve over the next few days and, unfortunately, she began developing nausea, vomiting and diarrhea. She had to be admitted to the hospital. She was essentially admitted for a severe bout of gastroenteritis and the doctors at Virginia Spine Institute were asked to see her for her severe low back pain.

In discussion with the patient, the doctors identified that not only did she have a history of hypothyroidism but she also had a history of hypercholesterolemia and tobacco use. She had x-rays obtained across the lower spine; she had a CT scan through this area and eventually had an MRI scan performed. The doctors were able to identify a fracture of the first lumbar vertebral body with evidence of osteoporosis throughout her skeleton. The L1 fracture was biomechanically described as a burst fracture, meaning there was compression of the front part of the vertebral body as well as the back part of the vertebral body. The back of the vertebral body is adjacent to the spinal cord at this region and a burst fracture may compress the spinal cord. The reason for the MRI scan was to assess the degree of compression



T_2 weighted sagittal MRI of lumbar spine. Arrow points to L1 vertebral burst fracture.

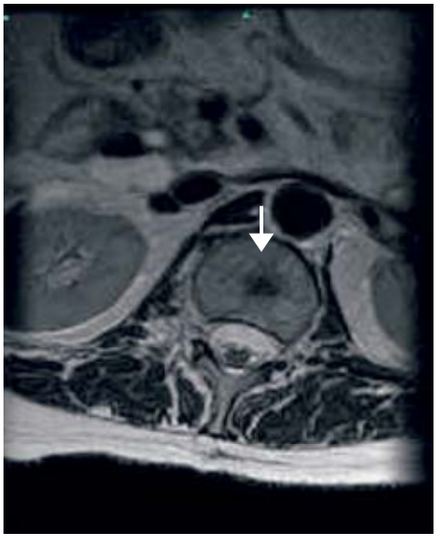
of the spinal cord and the extent of injury in that region. The MRI scan showed that there was some bone residing in the spinal canal as a result of the fracture. This broken bone did indent the spinal fluid space surrounding the spinal cord; however, the bone did not appear to be compressing the spinal cord

TLSO back brace
(picture courtesy AMI Industry Co.)

itself. Most importantly, there was neither evidence of damage to her spinal cord nor signs of spinal cord injury on her examination. She had intense pain due to pressure overlying the area of the fracture. When asked to stand she would stand in a bent forward position, called kyphosis. Due to the severity of her pain, her surgeons considered the possibility of reconstructing her back with stabilizing rods and screws. Unfortunately, given her other medical issues, any surgical procedure could threaten her life.

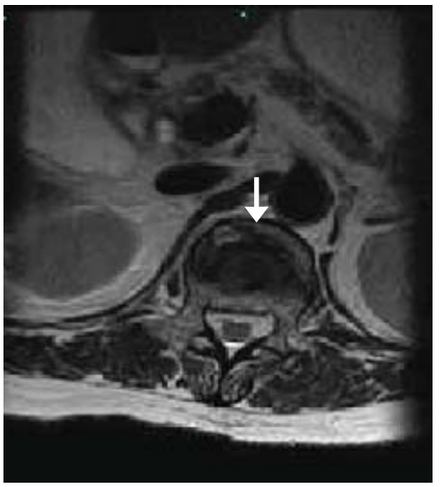
She worked with the physical therapists and was placed in a brace which went from her chest down to her lower back. The brace essentially attempted to hold her in a supported upright posture to alleviate her symptoms until the broken bone could heal. She was also prescribed Miacalcin (calcitonin) nasal spray which seemed to reduce the pain associated with her acute spinal fracture and is also known to promote mineralization of osteoporotic bone.

In essence, her pain was controlled; she was mobilized with physical therapy and placed in a brace. By late July, when Irma was seen back in the doctor's office, she was no longer having any back pain whatsoever. She was walking much better, her pain had decreased and she had returned to her normal activities. She was still wearing the supporting brace across the thoracic and lumbar spine, which is usually kept in place for a total of three months after such a fracture. She was maintained on the same Miacalcin (calcitonin) nasal spray which promoted mineralization and healing of the fractured area. She had essentially avoided surgery. She had fallen, broken her osteoporotic lumbar spine and avoided surgery.



T_2 weighted axial MRI of lumbar spine. Arrow shows normal vertebral body.

Irma has been chosen as the Spine Tale because she is a true success story. She has dealt with osteoporosis as a disease in one of its most terrible manifestations, that of a lumbar burst fracture. Approximately 50% of the people with lumbar burst fractures will develop symptoms from compression on the spinal cord or nerve endings, leading to weakness in the legs or bladder dysfunction.



T_2 weighted axial MRI of lumbar spine. Arrow shows narrowing of spinal canal caused by bone fragment of L1 burst fracture.

This compression syndrome typically requires some surgical reconstruction for postural reasons such as kyphosis (bent forward) and decompression of the spinal canal.

We attribute her success to her motivation to return to her former lifestyle, as well as her dedication to following the orders of her physicians. We have chosen to tell the story of Irma Greenberg in this issue of the Journal of The Spinal Research Foundation because she has fought the disease of osteoporosis and won. ■

"We've Got Your Back" Race Review

By Ashley Holmberg

The first annual Spinal Research Foundation "We've Got Your Back" event was a great success thanks to all the support from the community and sponsors. Over 400 runners and walkers participated in the 4-mile run and 2-mile fun walk. The spinal health fair provided information to those wishing to improve their own spinal health.

Washington Redskin's players Shawn Springs and Reed Doughty were the honorary chairs for the event and gave the official start to the race and walk. We were delighted to have Youth Sports FX competitive jump rope team perform several routines highlighting their athletic skills.

This event would not have been as successful without the help of presenting sponsors, Virginia Spine Institute and Medtronic. Many patients of Drs. Schuler, Subach and Hasz were able to participate in the race thanks to the successful treatment they received from the surgeons. It was amazing to see the outpouring of emotion from patients previously suffering from spinal disorders, who were now able to run and walk. Based upon the level of interest and participation in the race, our goal of raising awareness for spinal disorders and their impact on society was clearly reached.

Thank you to all the volunteers, sponsors and participants for your overwhelming support. We hope to see you again next year on race day.


MARATHON
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WE'VE GOT
ACK
Awareness

J Spine Res Found 3(2):9-18

Osteoporosis and Spine Health

By Anne G. Copay, Ph.D. and Marcus M. Martin, Ph.D.

Osteoporosis rates have increased steadily in recent years and are projected to increase even further. Several strategies are known to prevent and treat osteoporosis. Dissemination of complete and accurate information could contribute to the improvement of bone health in the United States population. The current review describes aspects of bone physiology pertinent to osteoporosis. A general overview of the process, diagnosis, prevention, and treatment of osteoporosis is then presented.

Bone

Living bone is composed mainly of collagen (which provides a soft framework) and minerals (calcium, magnesium, sodium, and potassium). Minerals cause bone to be so durable that, even after death, bone resists decomposition. The combination of collagen and minerals provides both flexibility and strength, allowing bone to withstand stress. Bone performs several vital functions, such as formation of red blood cells, mineral storage, and support of the musculature to allow for locomotion.

Throughout the life of a human, old bone is removed by resorption and new bone added by formation. Bone is deposited by osteoblast cells and resorbed by osteoclast cells. From childhood through the teenage years new bone formation exceeds bone resorption. As a result, bones become larger and increase in mineral density. Peak bone mass is usually reached by age 30. Bone mass is maintained for a few years, following which bone resorption gradually begins to exceed bone formation. Bone loss occurs at a rate of 0.5% -1.0% per year. In women, bone loss accelerates to 1.0%-2.0% per year for 5-10 years following menopause.

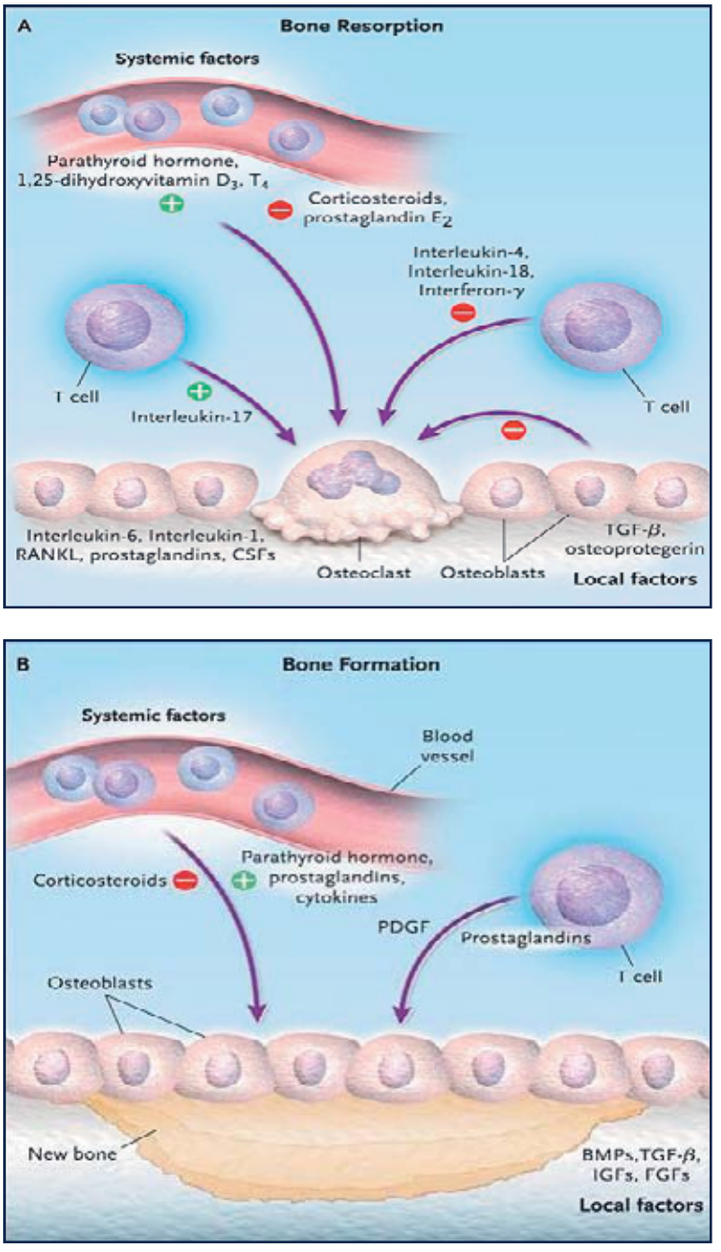


Figure 1. Regulation of Bone Formation
(pictures courtesy Mechanisms of Bone Metastasis G. David Roodman, M.D., Ph.D.)

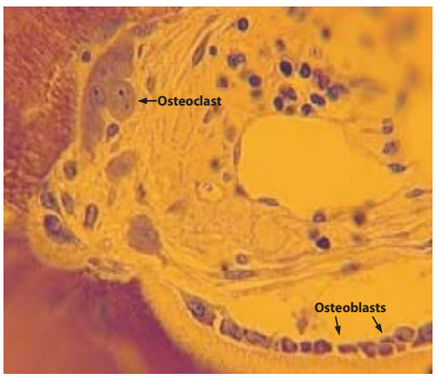


Figure 2. Osteoclasts and osteoblasts in normal bone
(picture courtesy Mechanisms of Bone Metastasis G. David Roodman, M.D., Ph.D.)

There are two types of bone tissues:
Cortical bone (also called compact or dense bone) is a strong type of bone and forms the outer layer of bones.
Cancellous bone (also called trabecular or spongy bone) is more fragile than cortical bone and is found at the center of bones.

The distribution of cortical and cancellous bone varies across the skeleton: some bones and part of bones have less cortical bony tissue and are therefore more fragile.

Bones with a thick layer of compact bony tissue will be strong (such as the long bones in the leg and arms). Bones with a thinner layer of compact bony tissue will be more fragile. This is the case of spine, wrist, hip bones, and the ends of the long bones.

Osteoporosis

Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture. Bone strength may be compromised by a reduction in bone mineral density (BMD) and disruption of the bone microarchitecture.

Cancellous bone is composed of a network of rods (trabeculae) and has a lattice-like appearance with openings for blood vessels and bone marrow. Bone loss decreases the strength of cancellous bone in two ways: the trabeculae get thinner and they lose some connecting parts. The loss of connections in the trabeculae greatly decreases bone strength. For the same decline in bone mass, the loss of trabecular elements decreases bone strength two to five times more than the thinning of the trabeculae[2].

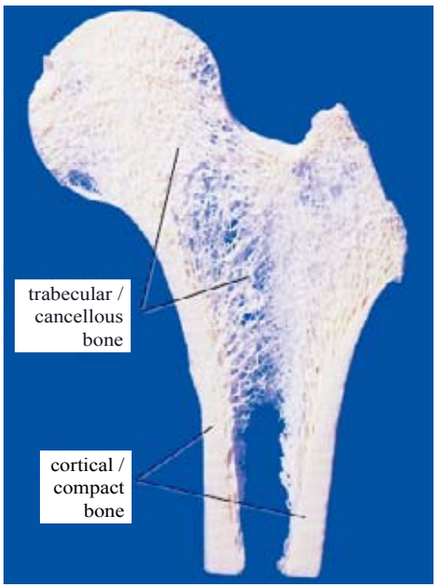


Figure 3. Cancellous bone and cortical bone in the femur
(picture courtesy Lutz Slomianka)

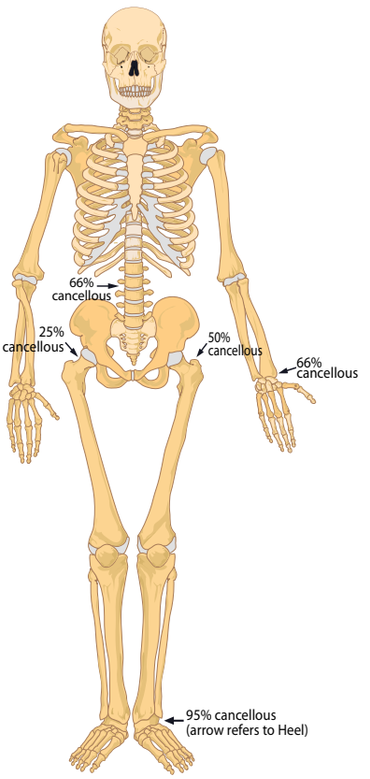


Figure 4. Distribution of cancellous bone in the skeleton

Osteoporosis may occur when bone resorption occurs too quickly or bone formation occurs too slowly. The hormonal balance of individuals directly affects the rate of bone turnover. The reduction in the amount of estrogen which occurs after menopause increases bone turnover. However, osteoporosis is more prone to develop if optimal bone mass was not reached during the bone building years. It is most prevalent among older individuals and non-Hispanic Caucasian women, but can occur at any age in both genders and in all ethnic groups. Though women are at higher risk of developing osteoporosis, men are the most under diagnosed group.

Measurement of Bone Mineral Density (BMD)

Dual X-ray Absorptiometry (DXA) is the current standard for BMD measurement. BMD is typically measured in the spine and the hip. Spine and hip fractures are the most frequent fragility fractures and are the most debilitating. Measurement at one site is better at predicting fracture for that specific site, that is, spine BMD is better at predicting spine fracture than hip fracture and, conversely, hip BMD is better at predicting hip fracture than spine fracture. Recently, it has been recommended to measure BMD at the hip (femoral neck) because hip BMD might be more predictive of fractures at other sites than spine BMD. This might be due to the fact that arthritic changes in the spine of older patients alter spine BMD measurements. The choice of skeletal site for BMD measurement may be influenced by the age of the patients: spine fractures and deformities are likely to occur before hip fracture.

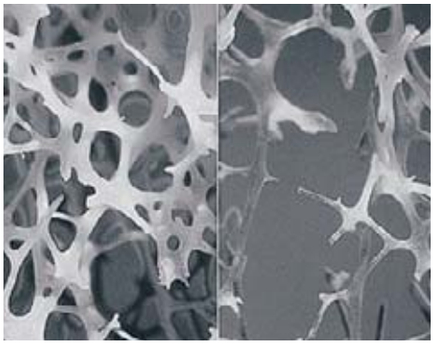


Figure 5. Microarchitecture of cancellous bone in a healthy person (left) and an older person with osteoporosis (right).
(picture courtesy IOF)

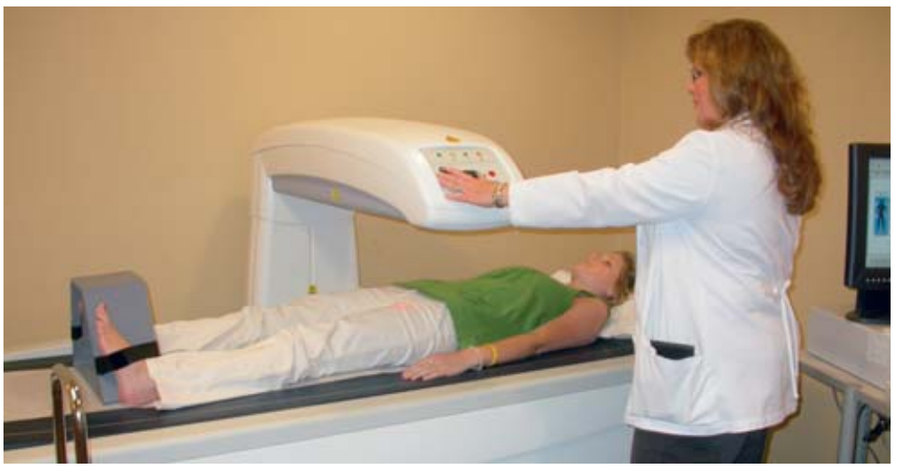


Figure 6. DXA machine

Diagnosis of osteoporosis

An individual's bone mineral density (BMD) is measured and compared to the BMD of young adults. The difference between a person's BMD and the young adults' BMD is expressed as a T-score. Osteoporosis corresponds to a T-score of -2.5 and smaller, low bone mass to a T-score between -1.0 and -2.5.

BMD and fracture risk

A decrease in BMD clearly presents great risk of fracture. For each 1-point T-score decrease, the risk of fracture doubles.

Age and fracture risk

BMD is a major determinant of fracture risk. However, advancing age increases the risk of fractures regardless of BMD. Individuals over 64 years old had twice as many fractures as individuals between 50 and 64 years old (Table 14). This is probably due to age-related factors such as impaired balance and gait.

BMD, age, and type of fractures

Cancellous and cortical bone loss occurs at different rates. At menopause, the loss of cancellous bone accelerates and the incidence of wrist fractures increases.

Table 1. Meaning of T-Scores

	T-score	BMD value is lower than
Osteoporosis	-2.5	99% of young adult* BMD
Low bone mass	-1.0	84% of young adult* BMD

*Because osteoporosis was considered a women's disease, women of 20-29 years old are the young adult reference group. And because the early BMD studies were conducted with white Caucasian women, the young adult reference group is made of white Caucasian women (from the third National Health and Nutrition Examination Survey). It is now recognized that osteoporosis also occurs in both genders, at all ages, and in all ethnic groups. No general agreement exits yet concerning the BMD thresholds for different ages and ethnic groups. T-scores are used to compare BMD of women and men over 50 to the BMD of 20-29 year old Caucasian women. T-scores are called Z-scores when a BMD score is compared to the BMD of any other group. However, there are no standard comparison groups for age, gender, and ethnicity.

After menopause, the loss of cancellous bone continues at a slower pace and the risk of vertebral fractures increase due to the cumulative bone loss. Cortical bone is lost more gradually throughout the lifespan. The risk of hip fractures appears at a later year as a result of the loss of both cancellous and cortical bone.

Consequences of fractures

Hip fractures are considered more devastating than any other type of osteoporotic fractures. One in five persons die during the first year after a hip fracture, nearly one third require nursing home placement after hospital discharge, and less than one third regain their pre-fracture level of physical functioning. Vertebral fractures can lead to back pain, height loss, deformity, disability, and death. Multiple fractures can result in restrictive lung disease, abdominal pain, abdominal distention, constipation, reduced appetite, and premature satiety. Psychological distress and depression often accompany the pain and physical changes of osteoporosis[5].

Risk factors for osteoporosis

(according to The National Institute of Arthritis and Musculoskeletal Diseases)

Several risk factors have been linked to the development of osteoporosis. Some risk factors are impossible to change while others can be directly addressed.

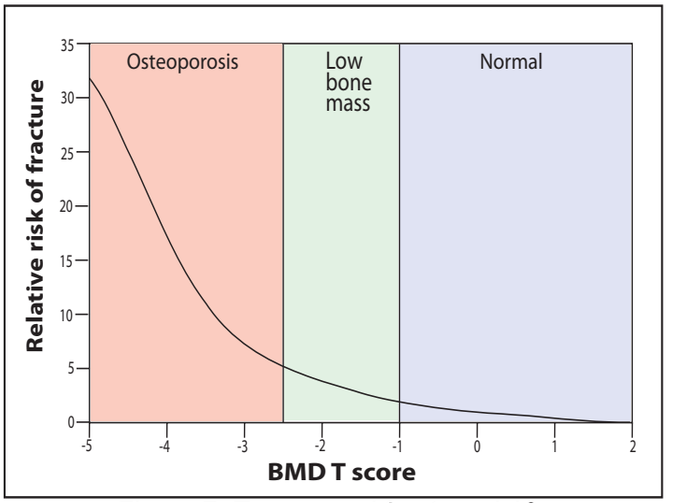


Figure 7. T-score and fracture risk[3]

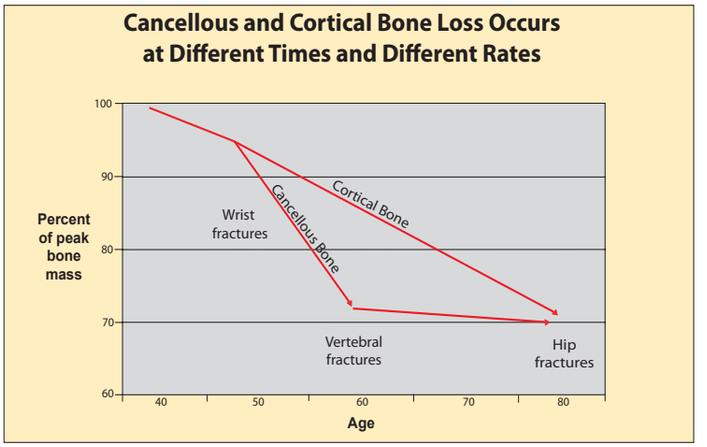


Figure 8. Pattern of bone loss and occurrence of fractures[1]

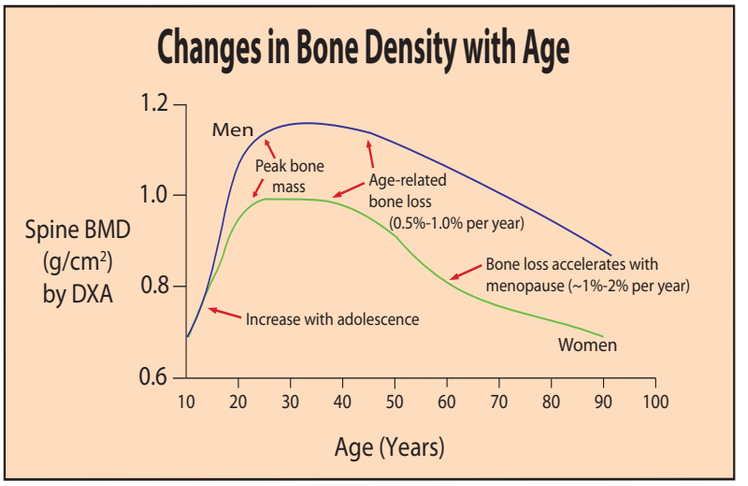


Figure 9. Changes in Bone Density with age[1]

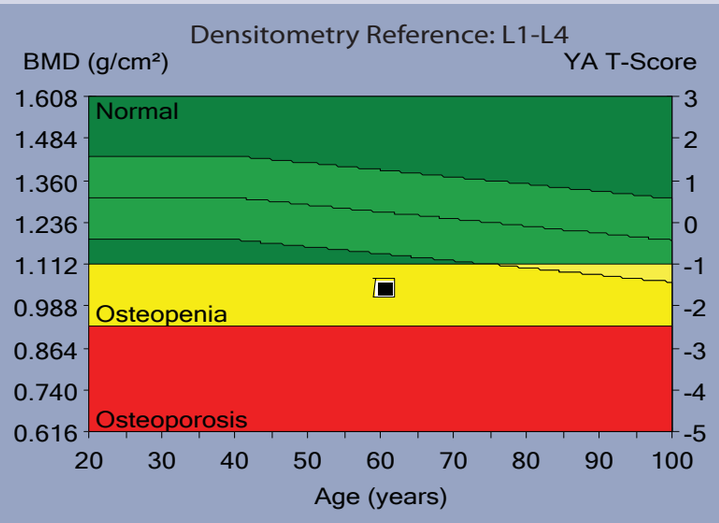
Understanding Your DXA Print-Out

Region	1 BMD (g/cm²)	2 Young-Adult (%)	2 Young-Adult T-Score	3 Age Matched (%)	3 Age Matched Z-Score
L1	0.914	78	-2.1	75	-2.5
L2	0.998	80	-2.1	77	-2.5
L3	1.075	86	-1.5	83	-1.8
L4	1.141	91	-0.9	88	-1.3
L1-L4	1.040	84	-1.6	81	-2.0

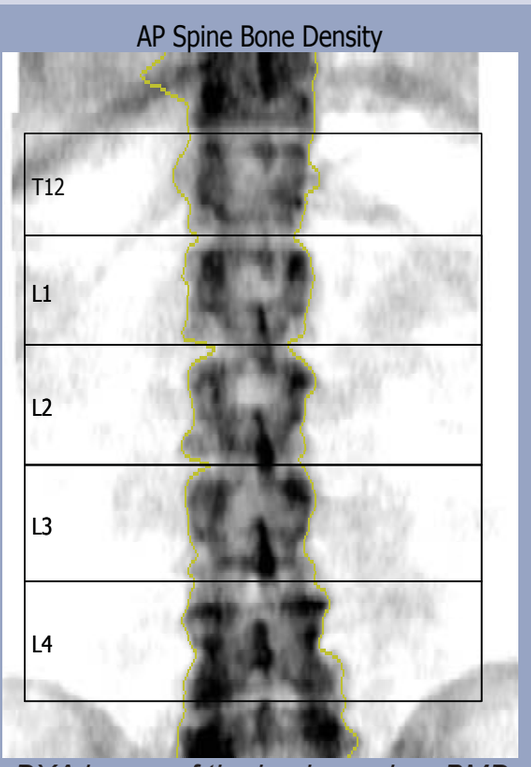
BMD: *bone mineral density of each individual vertebrae and the mean of the 4 vertebrae.*

T-score (comparison to women 20-29 years old): *low bone mass at the 1st, 2nd and 3rd vertebra and the average of the 4 vertebrae.*

Z-score (comparison to individuals of the same age group and gender): *osteoporosis of the 1st and 2nd vertebrae, and low bone mass at the 3rd and 4th vertebrae and for the average of the 4 vertebrae.*



The dot represents the average BMD for the 4 vertebrae. The average lumbar spine BMD of this patient falls within the osteopenia (low bone mass) zone.



DXA image of the lumbar spine: BMD is typically assessed at four lumbar vertebrae: L1, L2, L3 and L4.

How is osteoporosis diagnosed?

The medical team uses a complete history and physical examination, x-rays of the skeleton, bone densitometry (DXA) scan and specialized laboratory tests to diagnose osteoporosis. If low bone mass is identified, additional testing may be ordered to detect other diseases associated with bone loss. These diseases can include osteomalacia (Vitamin D deficiency) or hyperparathyroidism (over activity of these glands).

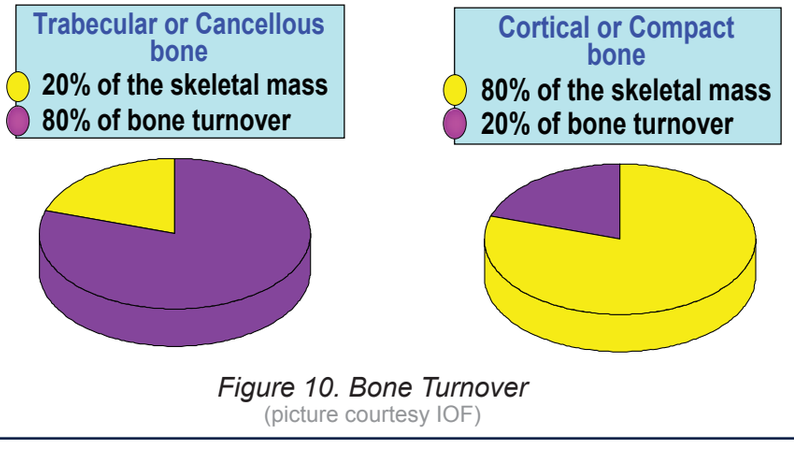


Figure 10. Bone Turnover
(picture courtesy IOF)

Non-modifiable risk factors:

Gender- Women have an increased risk of developing osteoporosis than men. They tend to have less bone tissue and lose bone faster than men due to menopause associated changes.

Age- Older persons are at greater risk of osteoporosis. Their bones become thinner and weaker with age.

Body size- Small, thin-boned women are at greater osteoporosis risk.

Ethnicity- Caucasian and Asian women are at highest risk compared to African American and Hispanic women who have a lower but significant osteoporosis risk.

Family history- Fracture risk may be partly due to heredity. People with parents who have a history of fractures seem to also have reduced bone mass and may be at risk for fractures.

Modifiable risk factors:

Sex hormones- The abnormal absence of menstrual periods (amenorrhea), low estrogen level (menopause), and low testosterone levels in men can contribute to the onset of osteoporosis.

Anorexia nervosa- This eating disorder increases the risk for osteoporosis.

Calcium and vitamin D intake- A diet low in calcium and vitamin D promotes bone loss.

Medication use- Long-term use of glucocorticoids and some anticonvulsants may lead to loss of bone density and fractures.

Lifestyle- An inactive lifestyle or extended bed rest causes bones to weaken.

Cigarette smoking- Smoking has a negative effect on bones as well as the heart and lungs.

Alcohol intake- Excessive alcohol intake increases the incidence of bone loss and fractures.

Symptoms of osteoporosis

Osteoporosis is often referred to as a 'silent disease', because it usually progresses with little or no symptoms. Often, a fracture is the first sign of osteoporosis. Bones may have become so weak that they collapse or break after an otherwise benign bump, fall, or strain. These fragility fractures usually occur in the wrist, hip, rib, and spine. Other symptoms of osteoporosis may include back pain, leg cramps, bone pain, loss of height and spinal deformities such as kyphosis (hunch back) due to vertebral collapse, and chronic pain with a reduction in mobility.

Table 2. Age as a risk factor

Fracture per 1000 patient-years[4]				
	Total Hip		Lumbar Spine	
WHO category	Age 50-64	Age >64	Age 50-64	Age >64
Normal	5.3	9.4	5.6	12.9
Osteopenia	11.4	19.6	9.9	19.4
Osteoporosis	22.4	46.6	14.7	32.3

Treatments and prevention of osteoporosis

The best method of addressing osteoporosis is prevention, particularly the maximal accumulation of bone minerals in the growing years. A comprehensive prevention and treatment program would address nutrition (smoking cessation, limited alcohol use), exercise, fall prevention, and medication (to slow or totally arrest bone loss, increase bone density)[7,8].

Nutrition

The consumption of a balanced diet fortified with sufficient *vitamin D* and *calcium* acts to reduce the likelihood of bone loss due to osteoporosis. Bones serve as the reservoir for the body's calcium. Calcium is important to the development of bone and is also necessary for the maintenance of normal function in the muscles, nerves, blood, and heart. Calcium is lost daily through nail and hair growth, skin, sweat, feces and urine. Other nutrients indirectly affect bone health by influencing the resorption and absorption of calcium. Vitamin D is essential for the development of bone microarchitecture. It increases the absorption of calcium in the small intestine. The daily recommended intake for calcium is 1000 to 1500 mg of calcium and 400 IU of vitamin D (600 IU for persons over 70 years old). The benefit of combining vitamin D and calcium has been demonstrated in several research studies. *Phosphorus*, though necessary for bone formation, may cause a reduction in calcium if present at excessive levels. Excessive *sodium* may cause urinary calcium excretion[9]. *Caffeine* produces a small increase in urinary calcium excretion and a small decrease in calcium absorption. However, the body balances this out by reducing calcium excretion later in the day. As long as calcium intake is within the recommended range, moderate caffeine consumption will have little effect on bone metabolism[10].

Precautions to avoid falls

A comprehensive plan to reduce fracture risk may be helpful in reducing the risk of osteoporotic fractures.

Safety checklist for household hazard elimination:

Floors. Remove all cords, loose wires, unanchored rugs and clutter. Anchor and smooth rugs and keep furniture in its accustomed place.

Bathrooms. Install non-skid tape and grab bars in the tub or shower.

Lighting. Ensure that stairways, entrances, halls etc. are well lit. Avoid navigating your home in the dark.

Kitchen. Clean spills immediately. Install skid resistant surfacing.

Stairs. Ensure rugs and rails are secure.

Other precautions. Wear skid resistant shoes. Minimize alcohol consumption. Ask your doctor whether any of your current medications might increase your fall risk. Use a cane or walker for added stability. Avoid walking on slippery surfaces.

(courtesy National Institute of Arthritis and Musculoskeletal and Skin Disorders)

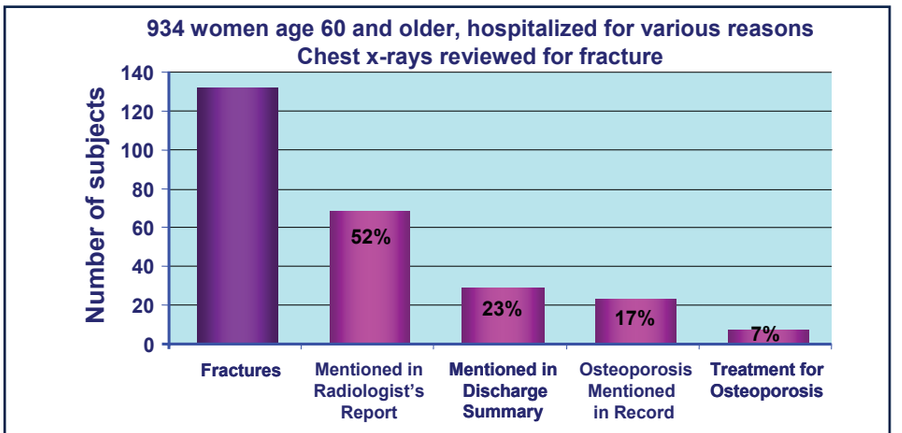


Figure 11. Unrecognized vertebral fractures on x-ray[6]
(picture courtesy IOF)

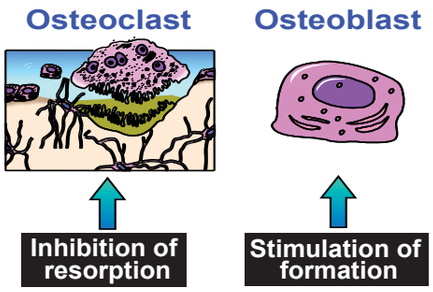


Figure 12. Osteoporosis treatment objectives
(picture courtesy IOF)

Exercise[11]

Similarly to muscles, bones get weaker when they are not used. Normal daily activities, such as walking or climbing stairs, are necessary to maintain bone strength. To increase their strength, bones need to be subjected to greater loads (exercise). Physical activity indirectly helps bone health by increasing muscle strength, improving posture, balance and coordination which all helps reduce the likelihood of falls. Physical activity directly improves bone health by increasing bone strength. The strength increase is specific to the site where the loads are applied, for example, the bone density of the racket arm of tennis players is greater than the bone density of their non-playing arm. The improvement in BMD will vary at specific body sites according to the type of physical activity. However, cycling may not improve BMD and may even contribute to a decrease in BMD.

Medication

The therapeutic medication treatment strategy for osteoporosis usually falls into 2 main categories. First, is the use of anti-resorptive drugs, which inhibit the bone resorption process. The anti-resorptive approach usually fails to restore normal bone density. A second option is the direct stimulation of bone formation by anabolic therapy.

Anti-resorptive Medications

Bisphosphonates are drugs which accelerate apoptosis and inhibit the activity and maturation of osteoclasts. These drugs have been shown to decrease the fracture risk in the lumbar spine and hip. Alendronate (Fosamax), ibandronate (Boniva), Zoledronic Acid (Reclast), and risedronate (Actonel) are used for the prevention and treatment of postmenopausal osteoporosis[12].

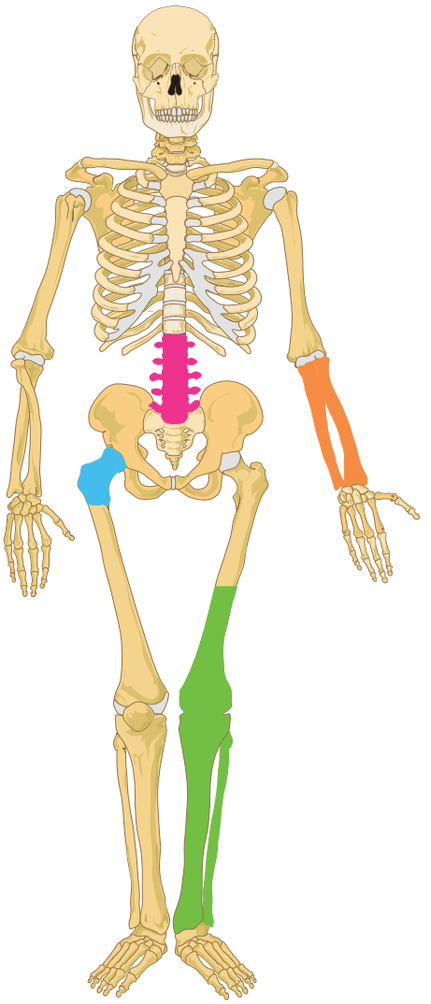


Table 3. Approximate increase in BMD compared to non-exercisers

	Spine	Hip	Arm	Leg
Gymnastics	12% higher	24% higher	7% higher	10% higher
Soccer	7% higher	20% higher	14% higher	16% higher
Weight Lifting	12% higher	6% higher	20% higher	11% higher
Volleyball	12% higher	17% higher	6% higher	12% higher
Hockey	4% higher	7% higher	10% higher	6% higher
Running	5% higher	15% higher	No difference	11% higher
Swimming	3% higher	3% higher	6% higher	2% higher

(modified from the American Society for Bone and Mineral Research http://depts.washington.edu/bonebio/ASBMRed/exercise.html)

Calcitonin (Fortical and Miacalcin) is used to treat osteoporosis in postmenopausal women at least 5 years following menopause. Calcitonin inhibits osteoclast function and has been shown to decrease bone-related pain following injury and to reduce the fracture risk[13,14].

Selective Estrogen Receptor Modulators (SERMs)
bind to estrogen receptors and act as either agonists or antagonists depending on the tissue type. They are often used in the treatment of patients at risk of breast or uterine cancer and unsuitable for hormone replacement therapy. Raloxifene (Evista) is a SERM approved for the prevention and treatment of postmenopausal osteoporosis. It reduces the risk of vertebral fractures while increasing bone turnover and bone mass. The effects and mechanism of these drugs are still being actively studied[15]. Combination therapy using SERMs and bisphosphonates has demonstrated a positive additive effect on BMD.

Estrogen inhibits osteoclast function while progesterone stimulates osteoblast activity. Hormone replacement therapy can augment bone mineral density. However, this method of treatment may result in several potentially fatal side effects, such as, increased risk of breast and ovarian cancer, stroke, cardiovascular disease and thromboses[16, 17].

Table 4. FDA approved pharmaceutical treatments of osteoporosis

Drug	Indication	Dosage
Dietary		
Calcium	Most men and women <50 years old	1000 to 1500 mg/day
Vitamin D	Recommended for men and woman <50 taking calcium	51-70 years old 400 IU/day and >70 years old 600 IU/day
Bisphosphonates		
Alendronate	Prevention and treatment of postmenopausal osteoporosis	
Ibandronate	Prevention and treatment of postmenopausal osteoporosis	Prevention and treatment 150 mg/month
Risedronate	Prevention and treatment of postmenopausal osteoporosis, Paget's disease, glucocorticoid induced osteoporosis	Prevention and treatment 5 mg/day and 35 mg/week
Raloxifene	Prevention and treatment of postmenopausal osteoporosis	60 mg/day
Teriparatide	Treatment of postmenopausal osteoporosis with high fracture risk	20 mg/day SQ injection
Calcitonin	Treatment of postmenopausal osteoporosis in women	<5 years 200 IU/ day intranasally alternating nostrils daily

(Osteoporosis: Pathogenesis, New Therapies and Surgical Implications
Jonathan M. Labovitz, DPM, FACFAS, Kate Revilld)

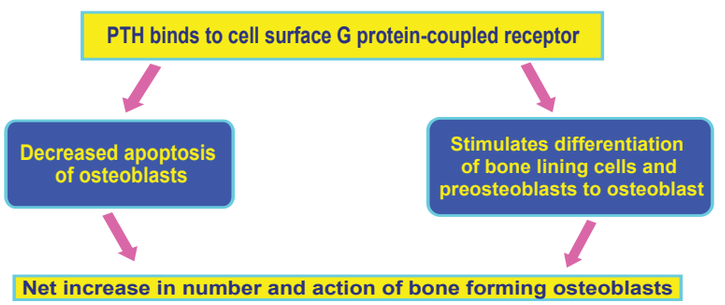


Figure 13. Parathyroid Hormone mechanism of action
(picture courtesy IOF)

Anabolic Medications

Parathyroid Hormone (PTH, Forteo) increases bone turnover through resorption and formation. This increases BMD bone micro-architecture and overall bone strength. These treatments are recommended for persons with very low bone density or those at a high risk of fracture[18]. It is recommended that this drug be taken for no more than 2 years.

Osteoporosis and spine health

Osteoporosis impacts spine health in two ways. Osteoporosis itself may be the source of spine morbidity, as is the case with vertebral fractures. Osteoporosis also impacts the treatments of other spinal conditions such as intervertebral disc degeneration. Spinal surgery typically uses metal implants to support the spinal column. Metal implants are anchored into the bones of the spinal column. Bones weakened by osteoporosis are likely to break under the pressure of the metal implants. Since a greater number of individuals without known risks factors are found to have low bone density, it may become necessary to routinely measure BMD prior to spinal surgery. Patients found to have low bone mass or osteoporosis will need to undergo treatment for their bone health and delay spinal surgery until their bones are strong enough to withstand the surgery. ■

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Dr. Martin's research interests include HIV/FIV vaccinology, immunology and neuroimmunology. He is engaged in collaborative research through SRF, with the Medical University of South Carolina Children's Hospital, geared toward the development of neuroprotective and neuroregenerative compounds for the treatment of nerve pathology.

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J Spine Res Found 3(2):19-24

Contemporary Review of Juvenile Osteoporosis

By Rimon Youssef, M.D., Elizabeth Walsh, M.D., and L. Lyndon Key, M.D.

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Dr. Key is engaged in research involving growth hormone use for short stature, Turner Syndrome, Renal Disease, growth hormone deficiency, calcium physiology, precocious puberty, diabetes care, osteopetrosis and idiopathic juvenile osteoporosis.

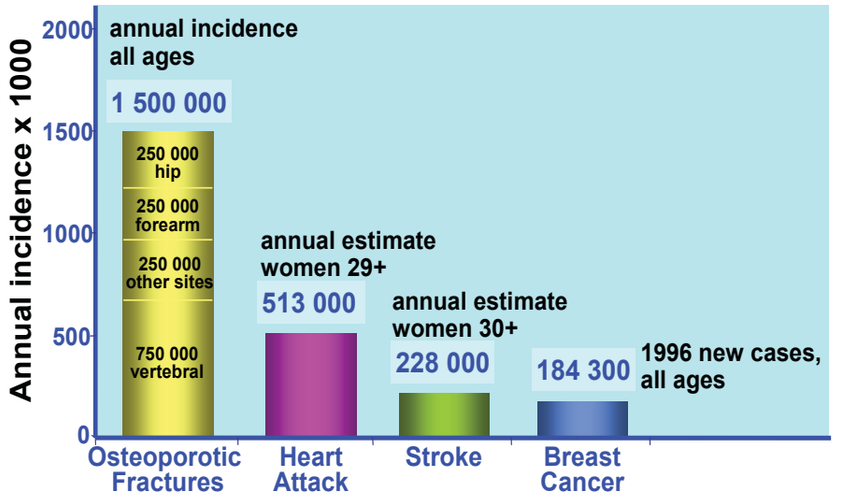

Figure 2. Frequency of osteoporotic fracture compared with other diseases
(picture courtesy IOF)

Osteoporosis is a skeletal disorder of compromised bone strength, which predisposes to increased risk of fractures. It is characterized by a combination of decreased bone mineral mass and deteriorated micro-architecture of the bone. Bone mass is normally maintained through a delicate balance of bone mineral deposition and bone resorption. Tipping the balance in favor of more resorption can result in osteoporosis. This negative balance between bone deposition (mediated through the osteoblasts) and bone resorption (mediated via the osteoclasts) is central to the pathogenesis of osteoporosis. RANKL (RANK-Ligand), which is expressed on the surface of the osteoblasts, binds to the RANK (Receptor Activator of Nuclear Factor Kappa B) on the surface of the osteoclasts and stimulates its differentiation, activation and survival. The osteoblasts also produce osteoprotegerin (OPG), a natural decoy receptor for the RANKL, which blocks its effects and helps in regulating the activation of osteoclasts[1]. Thus, osteoblasts have a vital role in controlling the activity of the osteoclasts.

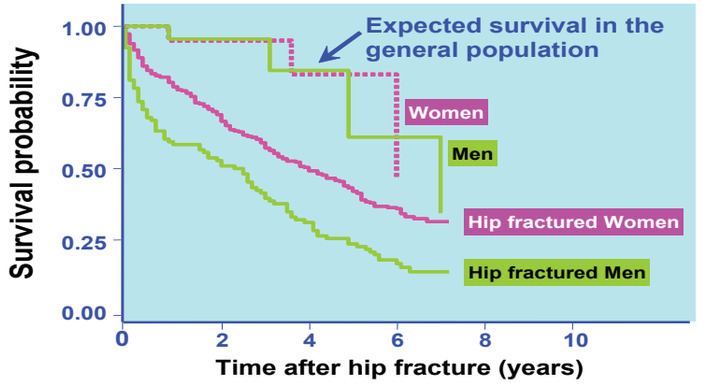

Figure 1. Survival rates after hip fracture
(picture courtesy IOF)

Osteoporosis is the most common human metabolic bone disease and the most common cause of fractures. Because of the incidence of osteoporotic fractures, the number of joint replacement procedures appears to be increasing so as to increase longevity. Osteoporosis is a significant health concern among the elderly population and causes a substantial health care financial burden[2,3]. However, the onset of osteoporosis can be traced back

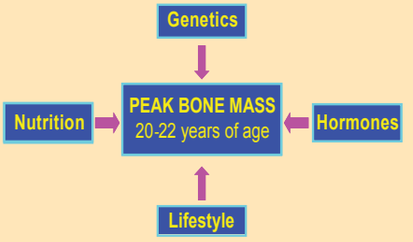

Figure 3. Determinants of Peak Bone Mass
(picture courtesy IOF)

to the prime years of growth and development. Most bone mass is accrued during the period of rapid growth in childhood. Bone mineral density later in life depends on the peak bone mass achieved during the adolescent years[4]. Osteoporosis is associated with increased risk for morbidity and mortality as a result of sustaining serious fractures. In particular, spinal and hip fractures cause severe pain, debilitating deformities, and loss of the ability to walk unassisted. These fractures almost invariably require hospitalization and major surgeries, which poses a substantial risk in the elderly population. The effect of juvenile osteoporosis is highlighted if a child progresses into adulthood with suboptimal bone mass and continues to live with a high risk for fractures.

Symptoms of Ehler Danlos Syndrome

Skin problems:
- soft velvet skin
- fragile skin that bruises or tears easily
- stretchy rubber band-like skin
- easy or severe bruising
- poor and slow wound healing
- small harmless bumps under skin

Joint problems:
- loose or unstable joints
- double jointedness
- joint pain from frequent dislocations

Eye problems:
- nearsightedness

Primary osteoporosis is a rather uncommon disorder; however, secondary osteoporosis is on the rise and its short and long term effects are detrimental[5]. Poor bone health during childhood leads to increased risk of serious fractures with associated pain, decreased activity and hours lost from education and social development[6,7]. Pediatric osteoporosis also has far reaching ramifications on adult bone health. Over the past few decades, the perception that osteoporosis is a disease of the elderly has been gradually changing. This concept started in the last century when professor Dent labeled senile osteoporosis "a pediatric disease". Treating osteoporosis has become an integral part of preventive care, as general pediatricians take an investment in their patients' bone health[8].

Primary Osteoporosis

Primary osteoporosis is categorized as either a hereditary connective tissue disorder or idiopathic juvenile osteoporosis. The etiology is not clearly defined, but it includes an impaired osteoblastic function that results in reduced bone formation rate and propensity to fractures. Connective tissue disorders, such as osteogenesis imperfecta, Ehler Danlos Syndrome, Bruck Syndrome, Marfan syndrome, and osteoporosis pseudogalioma syndrome, run the spectrum of bone disease from mildly affected to severely affected.

The increase of fractures in otherwise healthy children and adolescents initially was correlated to participation in intense physical

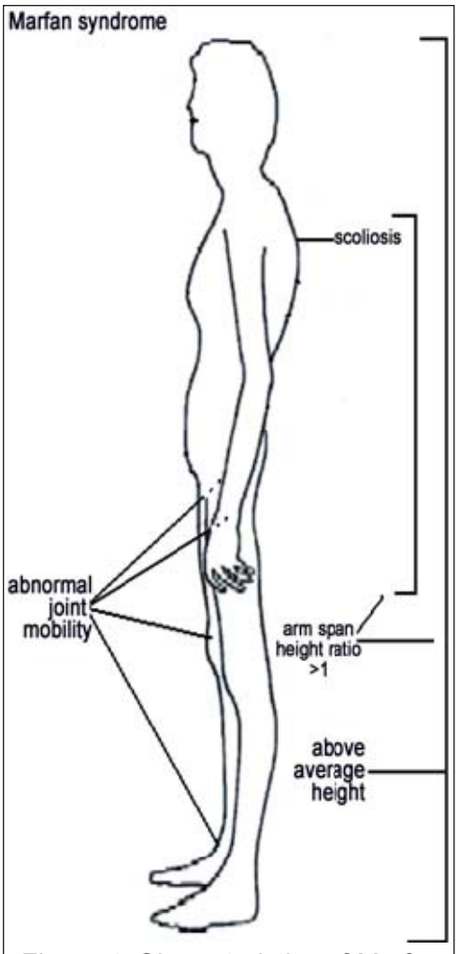

Figure 4. Characteristics of Marfan syndrome
(picture courtesy www.marfan.org)

exercises and sport activities. Recently, it has been shown that the bone mass is 5-10% lower in children with fractures than in age-matched control subjects[9]. The pathogenesis of this decreased bone mass is presumed to be the same as osteoporosis found in adults, with negative balance between bone formation and resorption and new osteoporotic bone forms without callus formation. Idiopathic juvenile osteoporosis is distinguished by onset prior to puberty. Typically, there is a clinical vertebral or metaphyseal fracture, bone pain, or gait disturbance. The clinical manifestations vary in severity and idiopathic juvenile osteoporosis affects males and females equally.

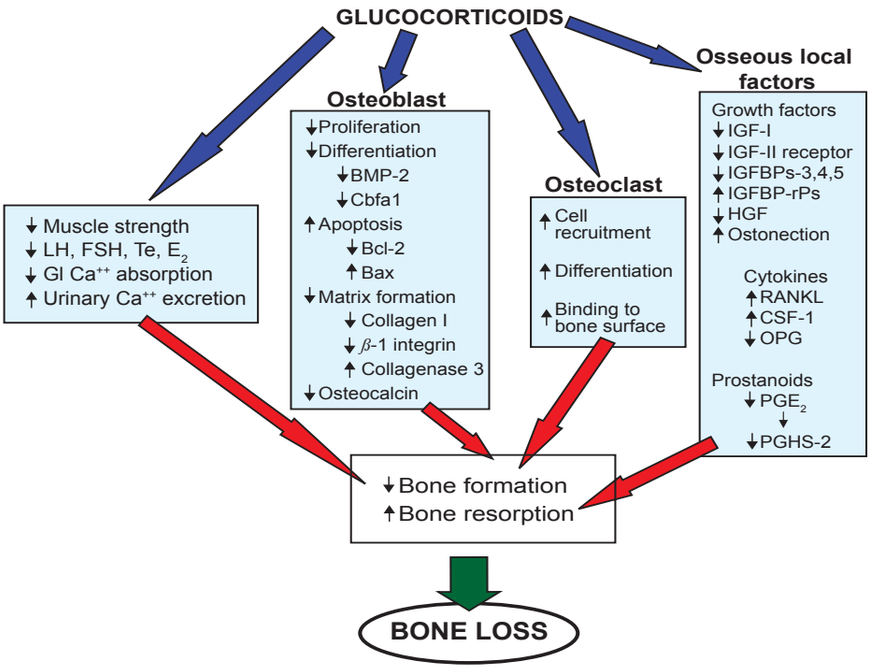

Figure 6.

Secondary Juvenile Osteoporosis

Modern medicine has had a dramatic impact on the decline in childhood mortality rates[10]. These advancements increase the number of children living with chronic medical conditions. These children risk poor bone health and development of secondary osteoporosis. Secondary osteoporosis stems from the underlying pathophysiology of their medical condition and the prolonged administration of medications which adversely affect bone health. It is also compounded by a low level of physical activity and poor nutrition[11].

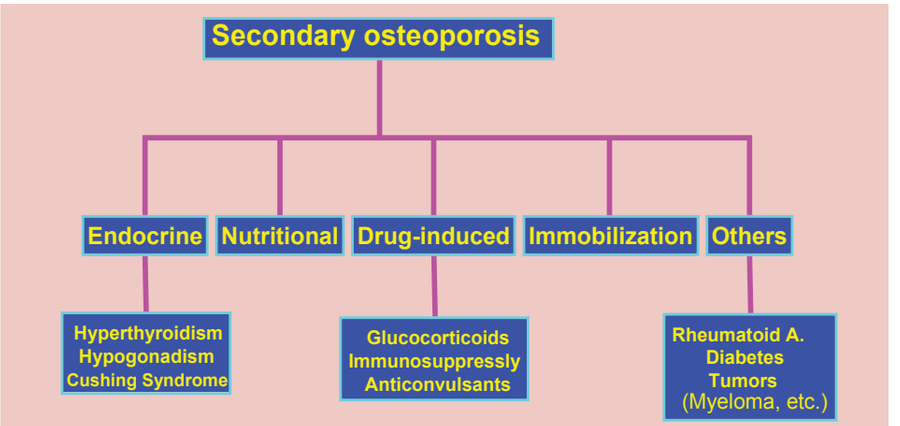

Figure 5. Causes of Secondary Osteoporosis
(picture courtesy IOF)

There are multiple chronic medical conditions which predispose children to secondary osteoporosis. Gastrointestinal malabsorptive disorders, such as celiac disease, cystic fibrosis, and inflammatory bowel diseases[12], can create a chronic negative balance in absorption of calcium and vitamin D. Children with hematological malignancies, including leukemia and lymphoma, are at increased risk for both osteopenia and osteoporosis[13, 14]. The mechanisms involved include leukemic infiltration of bone marrow, secretion of parathyroid hormone related peptide and tumor-related cytokines, (as well as a complication of their treatment). Various chemotherapeutic agents, including cysplatin, methotrexate, cyclosporine, ifosfamide, bleomycin and 6-mercaptopurine,

are hypothesized to increase bone resorption and reduce bone formation. Radiotherapy causes inhibition and impairment of bone growth by direct cytotoxic damage to the bone modeling cells and indirectly through decreased blood supply resulting in avascular necrosis. Physical inactivity and muscle-bone atrophy may be contributing factors[15, 16].

Prolonged glucocorticoid treatment, whether systemic or inhaled, has detrimental effects on bone formation[17]. They inhibit the genes for type 1 collagen synthesis (osteocalcin), transforming growth factor B (TGF-B) and RANKL. Glucocorticoids reduce the replication, differentiation, and life-span of the osteoblasts. They also inhibit bone matrix deposition. Prolonged glucocorticoid treatment predisposes the patient to secondary hyperparathyroidism. This elevation of parathyroid hormone triggers osteoclast activation, leading to increased bone resorption. Glucocorticoids exert a negative feedback inhibition on the pituitary gland, thus decreasing secretion of gonadotrophic hormones (follicular stimulating hormone and luteinizing hormone). This process results in decreased ovarian and testicular secretion of the sex hormones (estrogen and testosterone, respectively). Glucocorticoids do exert an effect on bone resorption although it is modest in comparison with the effect on bone formation. Even though the use of glucocorticoids is a well known risk factor for juvenile osteoporosis, it is an integral part of many chemotherapeutic regimens. Glucocorticoids play an essential role in transplant medicine, a well-established therapy for many end-stage diseases. The post-transplant pediatric patient receives high dose glucocorticoids. These are administered either as part of their pre-transplant preparation protocol, or more frequently to treat episodes of graft rejection. In cases of bone marrow transplant, glucocorticoids are used to treat episodes of graft versus host reactions.

Table 1.

		Z-Score
Normal	»	BMD -1 and above
Osteopenia	»	BMD -1 to -2
Osteoporosis	»	>2 SD below mean for age and gender

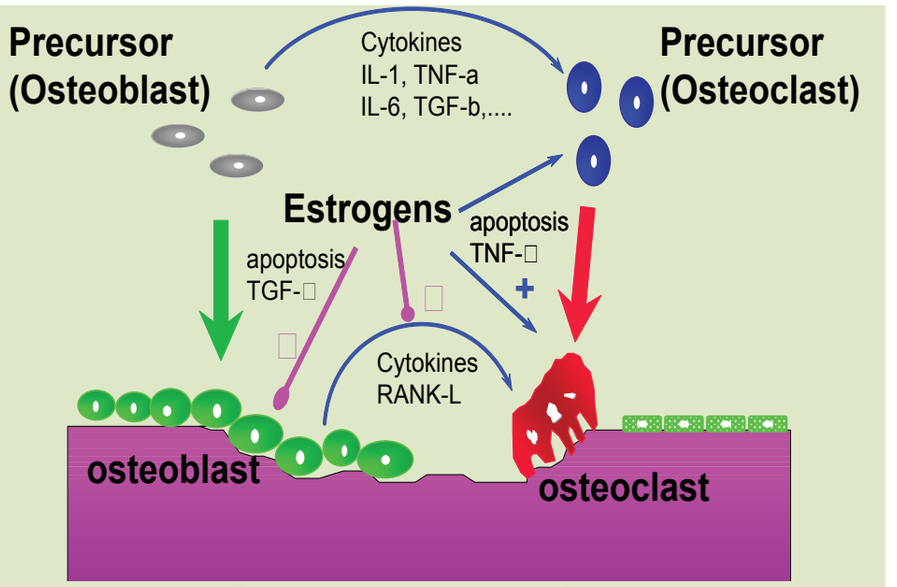

Figure 7. Estrogens mechanism of action in bone
(picture courtesy IOF)

Diagnostic Methods

Decreased bone strength can be suspected clinically after sustaining a low impact fracture (fall from a standing height or lower)[18] and confirmed by radiographic methods. Radiographic studies are also used as a method of screening and diagnosis as most patients are clinically silent. Radiographic methods to measure bone mineral density include dual-energy x-ray absorptiometry (DXA), quantitative CT, and quantitative ultrasound. In pediatrics, the assessment of bone densitometry is challenging, secondary only to growing bones[19]. DXA scans are the most widespread method currently used to assess bone mineral density. DXA measures bone mineral

content by bone area (g/cm^2). The WHO set diagnostic criteria for osteoporosis in postmenopausal women by the use of a T-score, an assigned value reflecting the standard deviation from the mean adult value. However, in pediatrics, the Z-scores are used instead, to match the child with healthy controls of the same age and gender. In pediatrics, osteoporosis is diagnosed with a Z-score of two or more SD below the mean value for the age and gender. Likewise, juvenile osteopenia can be defined radiographically with a bone mineral density Z-score between -2 and -1. DXA scans are limited by being a two-dimensional measurement, thus they do not adjust for bone thickness. In addition, BMD results should be interpreted with consideration for bone age and pubertal progression. Nevertheless, DXA scans remain the gold standard as their results have good reproducibility, high precision and accuracy, low radiation exposure, and the short duration of the scan limits the discomfort of the patient.

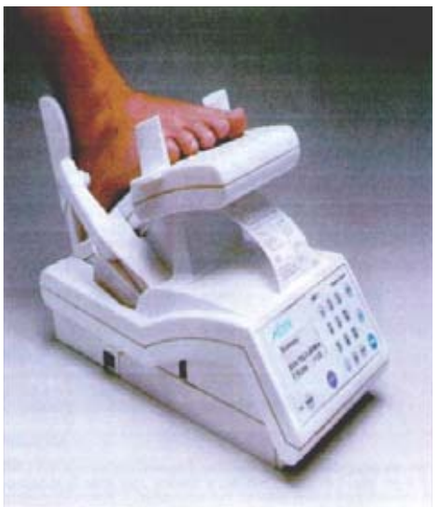

Figure 8. Quantitative ultrasound device
(picture courtesy IOF)

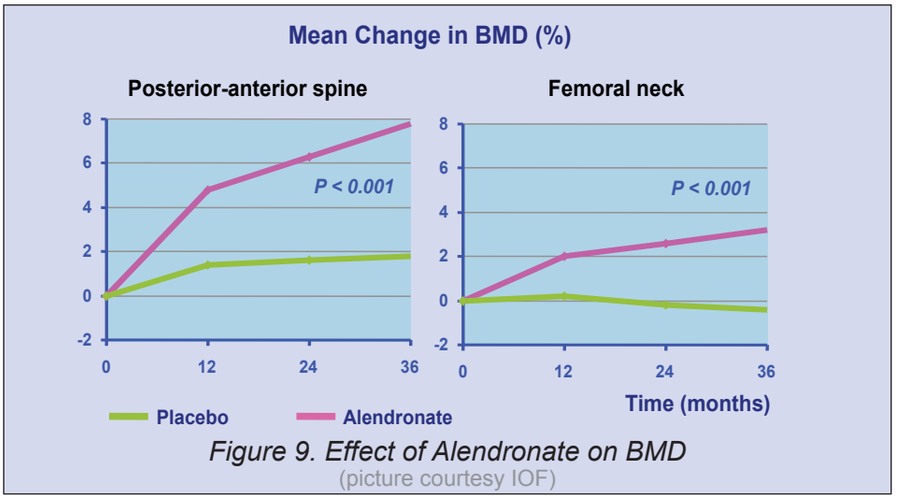

Figure 9. Effect of Alendronate on BMD
(picture courtesy IOF)

Quantitative CT directly measures bone density (g/cm^3) at any skeletal site. This procedure has not had widespread use, as it does involve a significant radiation exposure and prohibitive cost; and this cost renders it less suitable for follow-up on treatment efficacy. Quantitative ultrasound is the most investigated newer method of evaluating bone strength. It uses sound velocity and broad band attenuation as an alternative for measuring bone mineral density. It is the most promising, as it may offer more information regarding bone micro-architecture and elasticity. It is a radiation free, noninvasive and mobile alternative. However, quantitative ultrasound has not been well investigated clinically among the pediatric population and more controlled studies must be conducted to compare quantitative ultrasound with the standard DXA. The newer DXA scans provide pediatric reference Z-score values to children in early infancy.

Management

Bone is a living tissue undergoing a continuous turn-over and approximately half of the normal adult bone mineral mass is accrued during the adolescent years. Normal bone mass is maintained by a balance of deposition and resorption. Although this balance is tipped in favor of more deposition early in life, it changes to favor slightly more resorption during adulthood. This occurs gradually near the end of the third decade of life. Therefore, treatment of juvenile osteoporosis not only will decrease children's risk for fractures, but also can lead to better bone health when they become elderly. The primary goal among pediatric patients is to ensure adequate supplementation

of calcium and vitamin D, as there is sufficient evidence for the safety and efficacy of vitamin D and calcium supplements among pediatric patients[20].

Drawing from the accumulating experience in treating postmenopausal women with osteoporosis, treatment has become aimed towards decreasing bone resorption by interfering with osteoclast differentiation and activity. Alendronate is approved by the FDA to treat osteoporosis among adults and is broadly used off-label among children to treat patients with severe osteogenesis imperfecta and osteoporosis secondary to prolonged immobilization. Pamidronate is approved to treat hypercalcemia secondary to malignancy in adults and is used off-label in children who cannot tolerate oral alendronate. Clinical studies in pediatrics have shown that alendronate use in patients with osteogenesis imperfecta can increase bone mineral density, relieve pain, increase mobility, and decrease bone fragility[21, 22]. In addition to the occasionally experienced muscle aches and gastrointestinal effects, there have been concerns about the potential long term adverse effects of bisphosphonates. In particular, the potential for damaging skeletal and tetragenic effects is a concern, as bisphosphonates continue to be released from bone tissue for many years after the therapy is completed. However, clinical trials are currently underway and near completion for assessing the safety and efficacy of alendronate in pediatric patients with osteoporosis.

In Summary:

More attention is being focused on recognizing the roots of adult chronic medical disorders, with more emphasis on prevention rather than treatment, as a means to control health care expenditure. Treatment of juvenile osteoporosis is a good example of providing long-term adult health benefits. Vitamin D and calcium supplements have proven efficacious for improvement of bone density. Currently, no drug has been approved for treatment of juvenile osteoporosis. However, both alendronate and pamidronate are used empirically, based on safety and efficacy data accumulating from years of experience in treatment of adult osteoporosis. ■

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SPINAL RESEARCH FOUNDATION

J Spine Res Found 3(2):25-28

Vitamin D and Bone Health

By Marcus M. Martin, Ph.D.

Humans require vitamin D for several biological functions. Historically, vitamin D deficiency was associated with the development of rickets and osteomalacia, two conditions where bones fail to mineralize normally. Recently, vitamin D deficiency has been associated with increased risk of cancer, diabetes, and heart disease. The current review briefly highlights the history and biochemistry of vitamin D. It provides an outline of the risk factors and health consequences of its deficiency as well as the recommended allowances from National Institute of Health.

During the industrial revolution environmental pollution and cramped living conditions forced many people to have very limited sun exposure. This led to the development of vitamin D deficiency and rickets in many children and osteoporosis in many adults. It was estimated that in the early 1900s over 80% of children suffered from rickets in Boston. Children living in the cities had a high incidence of rickets but it was almost non-existent in the countryside.

In the early 1900s, several scientific discoveries were made which led to our current understanding of the synthesis and biological functions of vitamin D. Scientists determined that, when exposed to sunlight (UV-B radiation), 7-dehydrocholesterol in skin was converted to a molecule which prevented lab animals from developing rickets. It was also found that cod liver oil supplementation could prevent rickets. The active molecule was found to be vitamin D. Using this information chemists were able to formulate ways of artificially synthesizing vitamin D and were able to develop protocols for fortifying food products with this vitamin.

Functions

Vitamin D is crucial to the regulation of bone mineralization through its influence on calcium absorption but is also instrumental in the regulation of calcium and polypeptide levels in the blood, control of cell potentiation, cell differentiation and immune modulation.

Biochemistry

Vitamin D is considered a prohormone. Its molecules have no hormonal activity, but rather are converted to active hormones within the body. Several forms of vitamin D exist. Of these, the two major forms which are usable by the human body are vitamins D2 and D3. Both of these prohormones increase the vitamin D hormone level in the circulation.

Exposure to sunlight results in the production of Vitamin D3 in the skin. This form of vitamin D is also known as cholecalciferol and is synthesized when light energy (UV) is absorbed by its precursor molecule, 7-dehydrocholesterol, in the skin of animals. Vitamin D3 enters capillary beds in the skin where it then, binds to vitamin D binding protein.

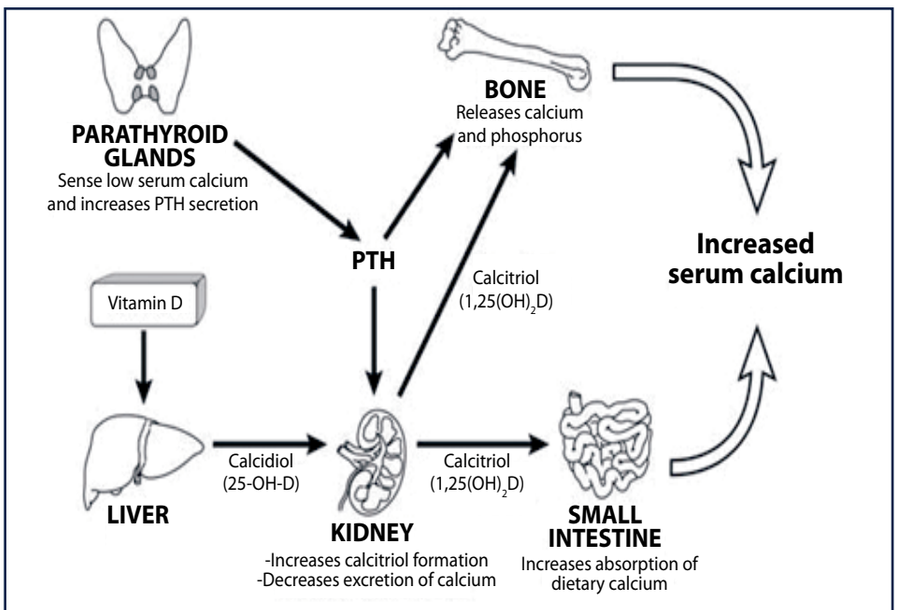

Figure 1. Vitamin D in the endocrine system

(picture courtesy Jane Higdon, copyright 2008 LPI, used with permission)

In plants, the form of vitamin D produced is vitamin D2 or ergosterol. This molecule is formed when the leaves of the synthesizing plants are exposed to UV light. Both vitamin D3 and D2 lack major biological activity. They are metabolized by hepatic and renal processes to a hormonally active form, 1,25-dihydroxycholesterol. First cholecalciferol is hydroxylated to form 25-hydroxycholecalciferol in the liver and is then later converted to 1,25-dihydroxycholesterol.

Safety

Excessive vitamin D intake can lead to vitamin D intoxication. This may be derived from dietary sources of either vitamin D2 or D3. It is impossible, however, to develop vitamin D intoxication from exposure to sunlight. Vitamin D overload can cause excessive absorption of calcium. A possible sequela is the formation of calcium deposits in soft tissues such as the heart and lungs, thereby limiting their functional abilities. Persons with hyperthyroidism or an overactive parathyroid gland have an increased risk of vitamin D toxicosis and should only take vitamin D supplementation following consultation with and monitoring by a physician.

Vitamin D in diet

Most organisms with sufficient sunlight exposure do not require daily vitamin D supplementation. However, due to several factors such as skin pigmentation, age, skin sunlight exposure, air pollution, latitude, and season, many individuals are vitamin D deficient and require dietary sources to fulfill their vitamin D requirements. The only major food sources of vitamin D are fatty fish and their derivatives (e.g. cod liver oil), eggs of chickens fed vitamin D fortified foods and some species of wild mushrooms.

Age	Children	Men	Women	Pregnancy	Lactation
Birth-13	5 µcg (200 IU)				
14-18		5 µcg (200 IU)	5 µcg (200 IU)	5 µcg (200 IU)	5 µcg (200 IU)
19-50		5 µcg (200 IU)	5 µcg (200 IU)	5 µcg (200 IU)	5 µcg (200 IU)
51-70		10 µcg (400 IU)	10 µcg (400 IU)		
71+		15 µcg (600 IU)	15 µcg (600 IU)		

Table 1: Adequate Intakes (AIs) for Vitamin D
(table courtesy NIH Office of Dietary Supplements)

Recommended Daily Allowance

Since vitamin D can be produced through light exposure, it is difficult to establish a Recommended Daily Allowance (RDA). Persons that are exposed to adequate sunlight have no additional requirement for dietary vitamin D. The FDA recommendations are listed in Table 1 above.

Measurement

Vitamin D status can be determined by assessment of the serum 25(OH)D concentration since it reflects both the result of dietary sources and vitamin D produced by the skin. Normal levels are between 25-130 nmol/L dependent on the latitude and season.

Deficiency

Vitamin D and Bone Quality

Vitamin D deficiencies result in the development of abnormal calcium and phosphorus metabolism. Vitamin D is instrumental in the regulation of calcium balance. It promotes calcium absorption in the gut. Sufficient levels facilitate the absorption of roughly 30% of dietary calcium. This value is elevated during pregnancy, lactation or periods of growth to 60%- 80%. It is very important in the maintenance of bodily function that blood calcium concentration remain at normal levels. Therefore, in the absence of sufficient calcium intake due to vitamin D deficiency, the bones are often robbed of calcium. When there is a calcium deficient state

ng/mL**	nmol/L**	Health status
<11	<27.5	Associated with Vitamin D deficiency and rickets in infants and young children.[1]
<10-15	<25-37.5	Generally considered inadequate for bone and overall health in healthy individuals.[1,2]
≥30	≥75	Proposed by some as desirable for overall health and disease prevention, although a recent government-sponsored expert panel concluded that insufficient data are available to support these higher levels.[2,3]
Consistently >200	Consistently >500	Considered potentially toxic, leading to hypercalcemia and hyperphosphatemia, although human data are limited. In an animal model, concentrations ≤400 ng/mol (≤1,000 nmol/L) demonstrated no toxicity.[4,5]

*Table 2. Serum 25-Hydroxyvitamin D[25(OH)D] Concentrations and Health**
(table courtesy NIH Office of Dietary Supplements)

$1,25(OH)_2D$ (the active form of vitamin D) binds to osteoblasts and induces the production of cell signaling molecules which induce preosteoclasts to mature to osteoclasts[6]. Calcium is thus mobilized from the bones in order to maintain the normal range within the blood. This explains why serum calcium levels in children with rickets are often normal. Vitamin D deficiency may lead to secondary hyperparathyroidism, causing phosphorus loss through urine and reduced phosphorus absorption in the gut. The combination of low phosphorus and low calcium causes abnormalities in bone mineralization and the development of degenerative bone conditions, such as rickets, osteomalacia, and osteoporosis.

Other health consequences

Vitamin D is an essential nutrient required for several biological functions. Vitamin D deficiency has been associated with several disease conditions. Currently, research is being conducted to establish if potential links exist between vitamin D deficiency and the risk of diabetes, glucose intolerance, hypertension, multiple sclerosis, and several other medical conditions. Much of this stems from the observation that these conditions tend to occur with greater frequency in regions further away from the equator which receive less UV light. These observations have spurred epidemiological studies and animal studies aimed at understanding the link between these disease conditions and low systemic vitamin D .

Figure 2. Young boy suffering from rickets
(picture courtesy www.mdtext.com)

Another potential effect of vitamin D deficiency is the development of various forms of cancer. For decades, researchers have observed that cancer incidence appears to increase with increasing latitude in the US. Epidemiological data indicate that vitamin D may play a role in the prevention of colon, prostate and breast cancer.

Groups at risk of deficiency

People with limited sun exposure

Geographical and cultural factors influence sun exposure. Generally, areas further away from the equator

receive less UV-B exposure than equatorial areas, and, therefore, residents synthesize vitamin D at a lower rate. Extensive body covering, such as 'purdah', where the entire body is heavily veiled and shielded from the sunlight, limits sun exposure. Fear of skin cancer has caused many to avoid the sun exposure or block UV rays by using high SPF sunscreen whenever sun exposed. This has exacerbated the extent of this vitamin D deficiency problem.

Breast fed infants

Human milk is a poor source of vitamin D. The vitamin content is only about 25 IU/L. It is not possible to satisfy a child's vitamin D requirement by breast milk consumption alone.

People with dark skin

Greater amounts of melanin pigmentation result in darker skin. This increased pigmentation also slows the rate of production of vitamin D from sunlight exposure. Some studies suggest that older women with dark skin pigmentation have a greater incidence of low serum vitamin D levels.

Older adults

In aging adults, the ability of the skin to synthesize vitamin D eventually decreases. The ability of the kidneys to convert vitamin D to its active form also wanes. In fact, approximately half of osteoporotic hip fracture patients in the US have serum 25(OH)D levels <30 nmol/L (<12 ng/mL).

People with fat malabsorption

Vitamin D is fat soluble and requires the presence of dietary fat for normal absorption. In individuals with a reduced ability to absorb fat there is often a reduced ability to absorb vitamin D. These individuals may require vitamin D supplementation.

Obese individuals

As previously mentioned, vitamin D is fat soluble and when synthesized in the skin it is often stored in adipose tissue. Obesity itself does not reduce the ability of the skin to synthesize vitamin D. However, the increased sequestration of the vitamin D produced into the subcutaneous fat alters the rate at which it is released into circulation. It has been observed that persons with a body mass index of ≥30 usually have a low plasma vitamin D concentration.

Conclusion

Vitamin D is essential for overall health. Currently cases of vitamin D deficiency are becoming increasingly prevalent. The health repercussions of this situation are only just being understood. Deficiency has been linked to several disease conditions including cancer, diabetes, and heart disease. Emerging research findings should provide further insight into the role of vitamin D. By reducing the prevalence of this deficiency we may also be able to reduce the incidence of several diseases which are major health concerns. ■

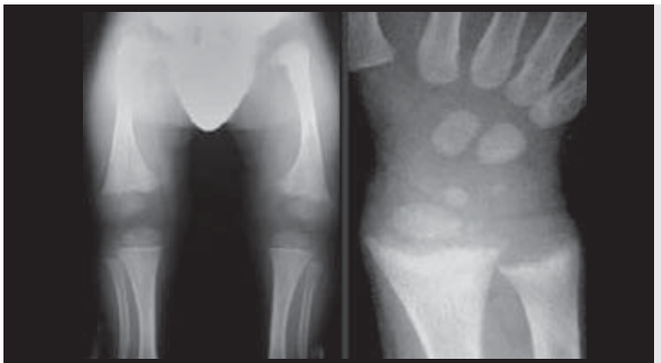

Figure 3. X-ray of child's legs and hand with rickets.
(picture courtesy www.zadeh.co.uk)

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J Spine Res Found 3(2):29-32

Physical Therapy for Osteoporosis

By Carey White, M.S.P.T., D.P.T.

Carey White, M.S.P.T., D.P.T.

Dr. White's interests are bio-mechanics of the body and the study of movement as they relate to injury and prevention.

Osteoporosis is a silent disease affecting 28 million women and men age 50 and over. It is estimated that 80% of reported cases are women. The National Osteoporosis Foundation reports that one out of every two women and one in eight men over 50 years of age has an osteoporosis related fracture. Fracture is one of the leading causes of disability in this population. Increased activity level and resistance training has shown positive effects on slowing bone loss and demineralization and reducing the risk of fracture.

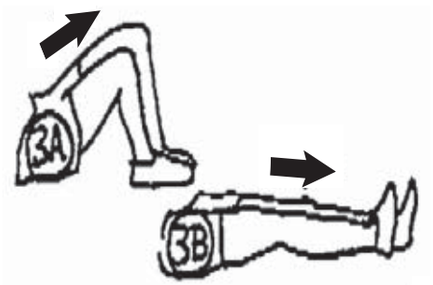

Figure 1. Leg lengtheners exercise
(picture courtesy Richmondspine.com)

Physical therapists can assist patients in addressing many of the issues related to osteoporosis. When it comes to treating osteoporosis, the goal of physical therapy is to properly educate the patient on preventing fracture and to restore function, range of motion (ROM), strength and balance.

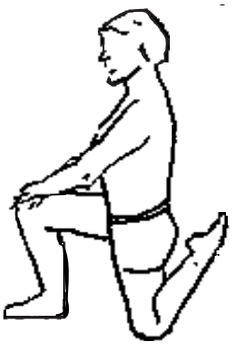

Figure 2. Front hip stretch
(picture courtesy Wettons swimming club)

Evaluation

A physical therapy evaluation will always begin with a detailed medical history. When it comes to osteoporosis, the results of a bone density scan will help the therapist determine risk factors for treatment. A multi-view postural assessment is then performed to look for any spinal deformities, general abnormalities or compensatory postures that may indicate a need for more specific evaluation. Before treatment begins body height should be measured as a starting point to determine improvement at a later time. Range of motion of the spine, upper extremity and lower extremities is assessed, taking care to avoid spinal flexion and lateral bending and rotation in combination, as these positions put the patient at risk for compression fracture. Flexibility is then measured more specifically in areas where range of motion is restricted. Gait is observed to view how the patient carries him or herself and to observe abnormal patterns or compensatory movements that may be putting the patient at risk for injury. Balance may be observed in a variety of ways;

Figure 4. Opposite arm-leg lift
(picture courtesy www.getfit.com)

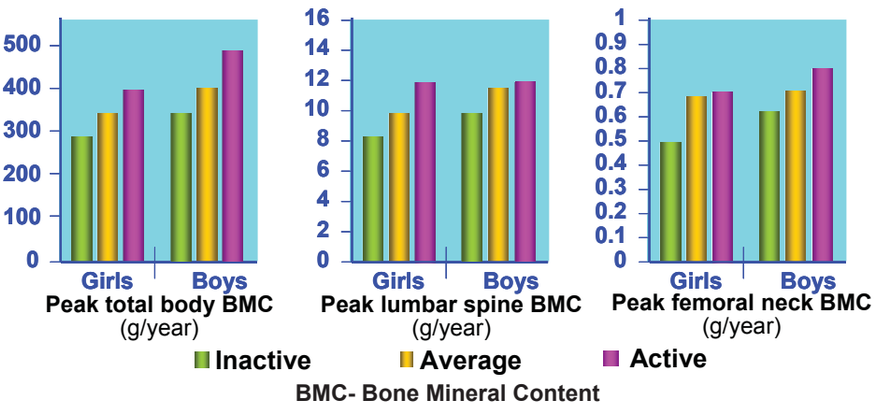

Figure 3. Effects of physical exercise on peak bone mass
(picture courtesy IOF)

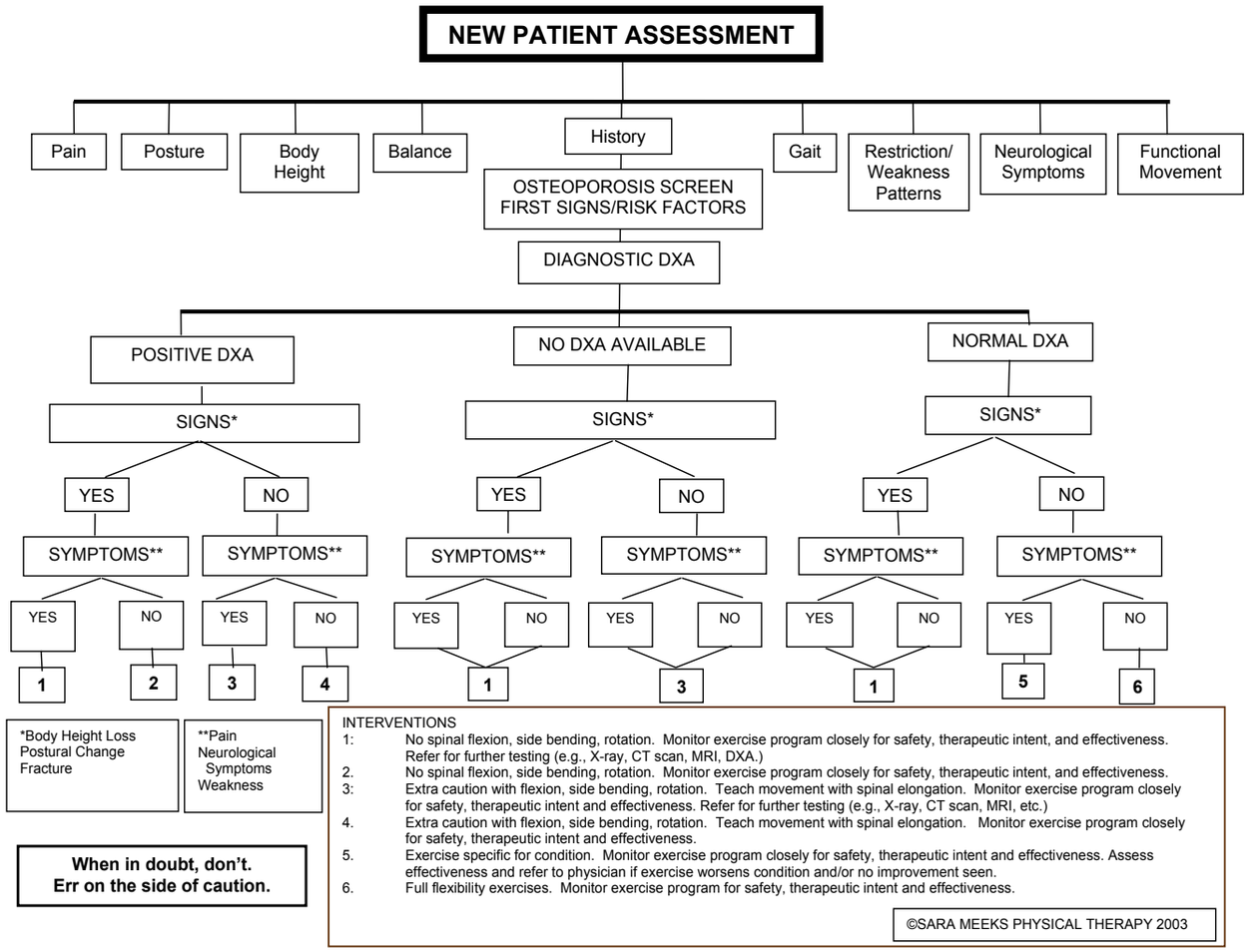

Figure 5. The Decision Tree
(picture courtesy Sara Meek, P.T., M.S., G.C.S.)

simple timed single leg stance, functional balance test such as timed sit to stand, or instrumental balance testing. General strength can be tested through a series of functional tests. Specific manual muscle testing is not always indicated in a patient that is a high fracture risk. Core muscle strength, however, can be tested to see if the patient is simply able to activate key muscles. All this information is then compiled by the physical therapist to design an individualized treatment program for the patient.

Treatment

Physical therapy treatment of osteoporosis focuses on patient education, body and postural awareness, balance, body mechanics, core strengthening, flexibility, weight bearing activities, proper breathing techniques, and resisted exercise training.

Patient education is one of the most important aspects of beginning treatment. Patients should initially be educated about the disease process and their personal risk factors. If the patients have an existing fracture, they will receive education on how to perform activities of daily living, such as getting into and out of bed, retrieving objects, cleaning the house, coughing or sneezing techniques, etc. The presence of fracture may lead to a need for special devices to function safely in the home. Proper usage of such devices may be demonstrated by the physical therapist. Education on fall prevention is appropriate as well, and will help identify safety hazards in the home or office.

Physical Therapy for Osteoporosis

Postural and body awareness is essential to address in treating osteoporosis. Changes in posture generally occur as the disease progresses. Restoring proper spinal alignment can help with reducing pain, improving breathing capacity and to ensure proper loading of the joints in the spine and the hips. Proper joint loading helps maintain better balance and fosters better muscle activation to help strengthen bones. If restoring spinal alignment is difficult, patients may benefit from wearing a brace.

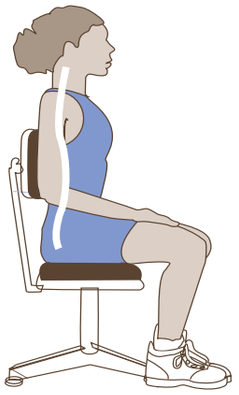

Figure 6. Good sitting posture means keeping your spine and head erect, and maintaining the three natural curves of your back.
(picture courtesy APTA)

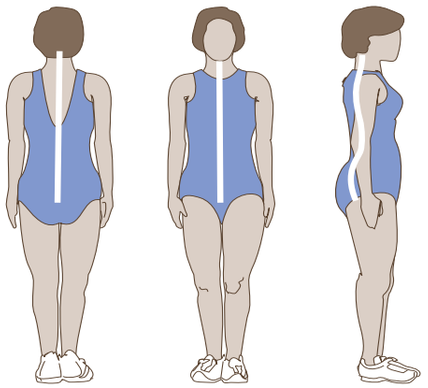

Figure 7. Proper posture is important in preventing the effects of osteoporosis. Here are back, front and side views of good standing posture.
(picture courtesy APTA)

Balance training is another essential part of physical therapy treatment for this disease. A patient with poor balance and osteoporosis is more likely to sustain a fracture if they fall. Balance training will consist of challenging the patient to stand on different types of surfaces, single limb standing and to perform activities while standing on different surfaces. The patient may also be challenged to perform strengthening exercises on different surfaces, an exercise ball or close their eyes. The patient is usually also given exercises to perform in the home once they are deemed safe by the therapist.

Body mechanics training is an integral part of physical therapy treatment. Many patients with osteoporosis put themselves at risk for fracture if they are performing activities of daily living incorrectly. Instruction and practice of the proper way to perform simple activities will reduce their risk of fracture and help to prevent falls.

To provide overall spinal support, core strengthening must be a part of any treatment program. Experts in the field of treating osteoporosis recommend that core strengthening occur before flexibility is addressed. Core strengthening consists of activating the pelvic floor muscles, transverse abdominus and multifidus muscles simultaneously in order to stabilize the spine. Initially these are performed as isometric contractions that are later augmented by dynamic exercises.

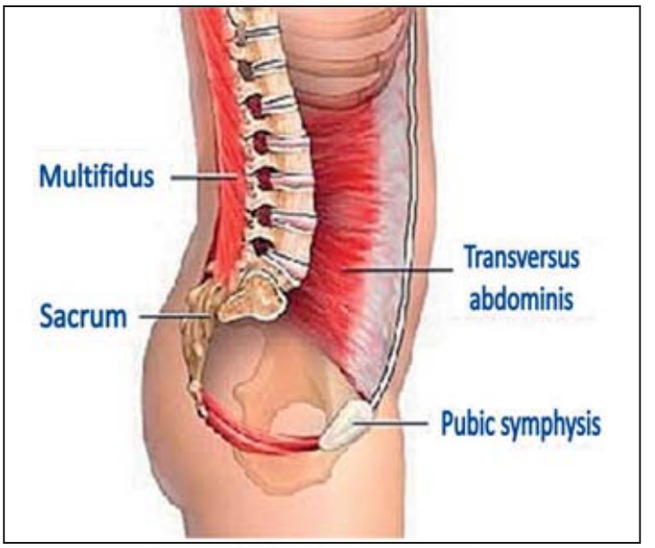

Figure 8. Pelvic floor muscles
(picture courtesy Cenk Chiropractic LLC)

General flexibility must be maintained to manage osteoporosis. Increasing safe spinal and joint mobility will help the patient prevent fracture. More specifically, the shoulders, anterior chest wall, front of the hips and thighs as well as the spine are usually areas found to be restricted. All these areas can be addressed with a customized stretching program to address the areas that need increased mobility.

Much of the research on osteoporosis has demonstrated that weight-bearing activities have a positive impact on bone growth and functional mobility in individuals with osteoporosis. These activities are defined as ones that place compressive forces through the joints. Casual walking is consequently not enough loading to make a substantial difference in bone density. Patients with osteoporosis are instructed on brisk walking, jogging and dancing. Improving walking posture can help align the spine for improved bone and joint health.

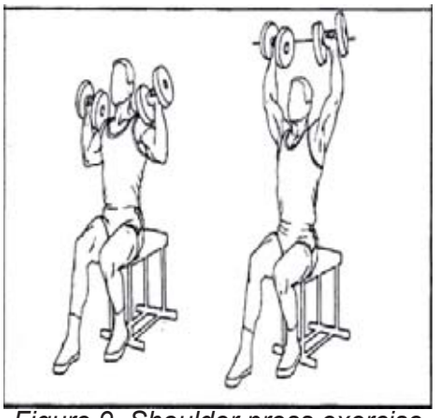

Figure 9. Shoulder press exercise
(picture courtesy Petersborough Rowing Club)

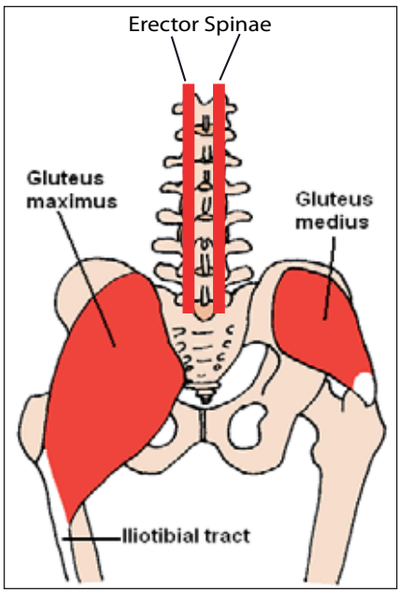

Figure 10. Posterior muscles
(picture courtesy www.wikimedia.com)

Breathing is something that can be compromised in individuals with osteoporosis. As the disease progresses and natural spinal curves become compromised, efficient breathing becomes increasingly difficult. Techniques to improve breathing should be part of standard treatment of this disease. Exercises to utilize the diaphragm and expand the intercostals are performed to increase lung function.

Lastly, resisted exercise training or strength training is one of the most important parts of the treatment program. It has been widely documented that strength training can help improve bone density. It also has been documented that specific exercises are more effective in improving bone mass and preventing falls then general strength training. Specific areas to train include the erector spinae, gluteus maximus and gluteus medius. In addition, strengthening the scapular area is recommended to assist with improved posture. Resisted exercises include use of resistance bands, free weights, weight machines, medicine balls or gravity. Exercises may also be performed in the water if the patient is recovering from a fracture or simply feels more comfortable in this environment.

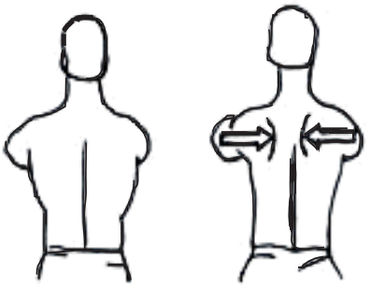

Figure 11. Scapular retraction
(picture courtesy Fitness Advantage)

In conclusion, physical therapy plays a very important role in the treatment of osteoporosis. It is a necessary adjunct to increasing calcium in order to reduce loss of bone mass. With proper evaluation and individualized treatment, one can prevent fracture later in life and maintain a very functional life. ■

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What you need to know about Osteoporosis, A physical therapist's Perspective. American Physical Therapy Association., Alexandria, VA, 1997
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J Spine Res Found 3(2):33-37

Advances in Osteoporosis Treatment

By Marcus M. Martin, Ph.D.

Summary

The number of osteoporosis cases in North America is predicted to spike considerably in the next decade. This will likely increase the strain on an already over extended healthcare system. Significant research efforts have been devoted toward the development of new osteoporosis treatments in order to forestall this crisis. The current review highlights promising new therapies being evaluated for the treatment of osteoporosis. It is hoped that these new approaches will lead to the development of effective therapies for osteoporosis prevention and treatment.

It is estimated that by the year 2020, 14 million Americans will be affected by osteoporosis[1]. As the US population grows older, the strain on the health care system caused by osteoporosis-related health complications is expected to increase. Some possible preventative treatments include vitamin D supplementation, calcium supplementation and exercise. If pharmacological intervention is necessary, available options incorporate the use of selective estrogen receptor modulators (SERMs), bisphosphonates, hormone replacement therapy, strontium ranelate, and teriparatide treatment[2].

Currently the main options for osteoporosis treatment fall into two main categories: 1) Anti-resorptive agents, which slow bone turnover, and 2) Anabolic compounds that directly stimulate bone growth[3]. Both approaches have significant limitations. Anti-resorptive therapy only stops bone loss, it does not directly increase bone density[4]. Whereas anabolic therapy can directly stimulate bone growth but may cause several side effects[5]. To avert a potential osteoporosis crisis, there is an urgent need for novel approaches to treatment. Current research has yielded several new advances in treatment which may prove useful in staving off an osteoporosis epidemic. Statins, nitrates, low intensity pulsed ultrasound stimulation (LIPUS), cathepsin K inhibitors, beta blockers, vitamin B supplementation, RANK- inhibitors and monoclonal antibodies, all offer possible options for the future treatment of osteoporosis.

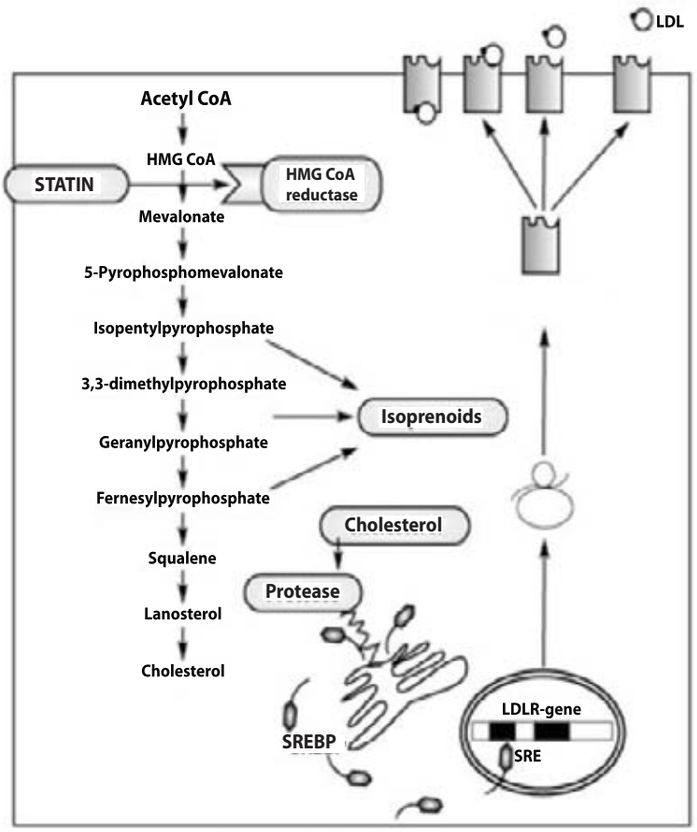

Figure 1. Statin Action

(picture courtesy the American College of Cardiology. Vaughan, CJ, Gotta, AM, Basson, CT. *J. AM Coll Cardiol* 2000;35: 1)

Statins

Statins are a class of drugs routinely prescribed for the treatment of high cholesterol. These drugs act through inhibition of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. Statins may have several other

peripheral pleotrophic applications[6]. Studies performed in both animals and humans have demonstrated that in addition to reducing cholesterol levels, statins may also reduce the risk of developing osteoporosis. In one study, rats injected with simvastatin in the subcutaneous tissue surrounding fractures demonstrated faster progression through the stages of fracture repair[7]. These studies demonstrate that statin treatment facilitates faster bone healing by increasing the formation and differentiation of osteoprogenitor cells more rapidly than that of the control group[7, 8].

Studies performed in rats indicate that statins may also enhance the alkaline phosphatase activity and mineralization of bone[9]. It was also demonstrated that statin therapy may regulate osteoblast function through upregulation of bone sialoprotein (BSP), type I collagen and osteocalecin (OCN), and through the suppression of collagenase gene expression. Statins have also been shown to stimulate the expression of BMP-2, promoting osteoblast differentiation and bone formation[10]. The use of statins for osteoporosis prevention is currently being studied. The results of these investigations will determine if osteoporosis treatment will be added to the expanding list of applications for statin drugs.

Nitrates

Organic nitrates have long been clinically used in the treatment of ischemic heart disease. These molecules may also have a positive effect on bone density[11]. Nitrates have demonstrated inhibition of bone resorption in in-vitro studies[12]. Recent studies have verified that organic nitrates increase Bone Mineral Density (BMD)[13]. Clinical trials using isosorbide mononitrate caused a decrease in bone resorption and an increase in bone formation[14]. In a cross-sectional analysis of osteoporotic fractures of 6,201 post menopausal women, nitrate use was associated with higher BMD[14,15]. The beneficial effects of estrogen on the skeleton are attenuated following menopause[16]. This attenuation can be countered by the use of nitric oxide inhibitors, indicating that some estrogenic effects may utilize the nitric oxide/cyclic guanosine monophosphate (NO/cGMP) pathway[17]. Direct stimulation of this pathway may have a beneficial effect on BMD. Current NIH funded research is aimed at determining if topical administration of nitroglycerin is effective in preventing bone loss[17]. If these results are positive, there could be a new category of osteoporosis treatments which stimulate increased bone density by using the NO/cGMP pathway.

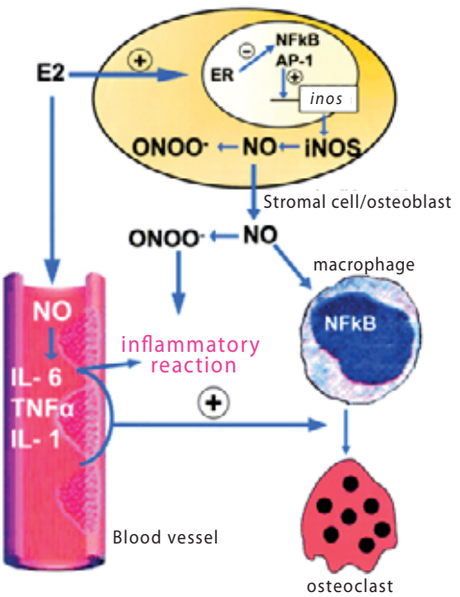

Figure 2. Proposed model for the estrogen depletion and Nitric Oxide action
(picture courtesy Dr. Salvator Cuzzocrea)

Lipus

As early as 1949, it was recognized that ultrasound waves might have the capacity to stimulate osteogenesis[18]. However, recently there has been a resurgence in interest in this treatment method. The result has been the production of commercially available units which use ultrasound therapy to stimulate growth of connective tissue.

Figure 3. Lipus device
(picture courtesy www.bremed.co.uk)

Low intensity pulsed ultrasound stimulation (LIPUS) represents a new technology which may have the potential to improve bone healing. Studies show that LIPUS may enhance bone regeneration during fracture healing[19]. This treatment facilitates enhancement of the callous area of bone[19].

More research needs to be done to determine if this technology may be used to improve bone density as a preventative method to osteoporosis. However, LIPUS does appear to have potential efficacy in expediting the bone healing process and may have an application in the treatment of osteoporosis related fractures[20]. These fractures have a very high mortality rate[21, 22]. Though the amount of energy used in LIPUS treatment is low, there is still an effect on cells both in-vivo and in-vitro[19]. The exact mechanism of activity has not yet been confirmed.

Cathepsin K Inhibitors

Cathepsin K is a cysteine protease necessary for bone collagen degeneration. The action of this molecule exposes the bone matrix to degeneration by proteases[23]. By inhibiting Cathepsin K, bone resorption is reduced and osteoblast activity is enabled[24]. In both preclinical and clinical studies Cathepsin K inhibitors have been shown to decrease bone resorption[25]. In a 12 month phase 2-b study involving 339 postmenopausal women performed at the Oregon Osteoporosis Center, the use of Cathepsin K inhibitors showed favorable results in reduction of bone degeneration[26]. Odanacatib, a Cathepsin K inhibitor, showed bone mineralization similar or superior to that derived from the use of bisphosphonates[26]. Cathepsin K inhibitors could therefore represent a new class of osteoporosis drugs which stimulate bone growth.

Beta Blockers

Animal studies indicate that bone turnover is under B-adrenergic control through the sympathetic nervous system[27]. Use of beta blockers appears to lower the fracture risk in postmenopausal women[22]. One clinical study showed a 30% reduction in fracture rates in women older than 50 years of age who use beta blockers[28]. These results are believed to be mediated by effects on BMD, trabecular bone micro-architecture and cortical bone geometry. In another study, performed in Germany, beta blockers were associated with reduced risk of fractures in middle-aged and older subjects[29]. The beta blocker group showed a statistically significant reduction in the fracture risk compared to the control group from the same general population[29].

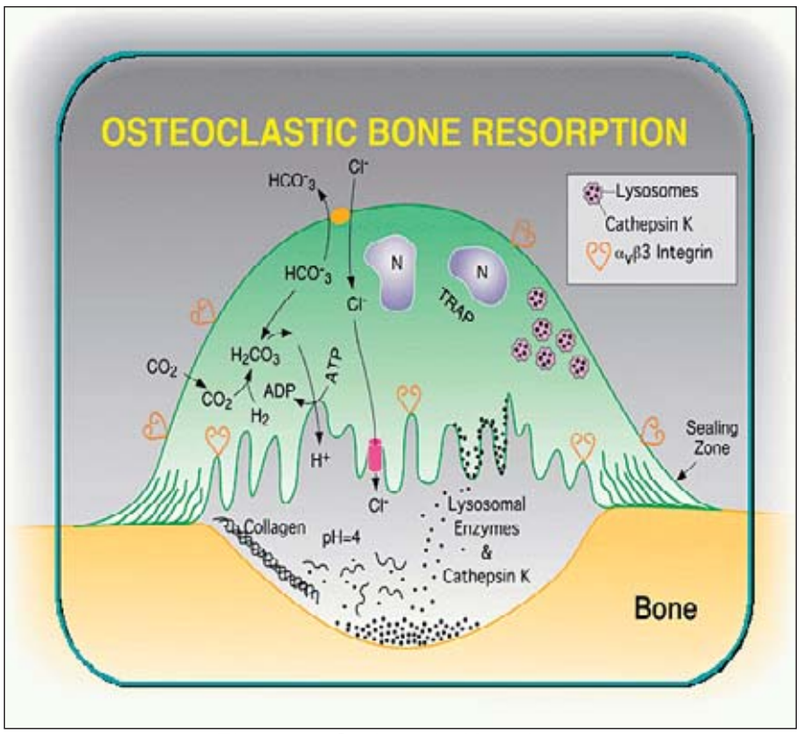

Figure 4. Cathepsin K pathway
(picture courtesy of www.merckfrosst.ca)

Vitamin B

Supplementation research has demonstrated that elderly patients with high levels of homocysteine are at an increased fracture risk[30]. Combined vitamin B12 and folate therapy has been considered as a therapeutic option since these reduce homocysteine levels[31]. It is hoped that this will lead to a reduction in the fracture risk. Vitamin B12 promotes osteoblast activity. Recent studies performed at Harvard Medical School demonstrated that high B-vitamin concentrations may directly correlate with good bone health[30]. A recent population-based cohort of 1,869 peri-menopausal women enrolled in the Danish Osteoporosis Prevention Study, demonstrated that high dietary folate intake but not vitamin B2 or B12 positively influenced BMD[32]. However, more research must be performed to confirm this association.

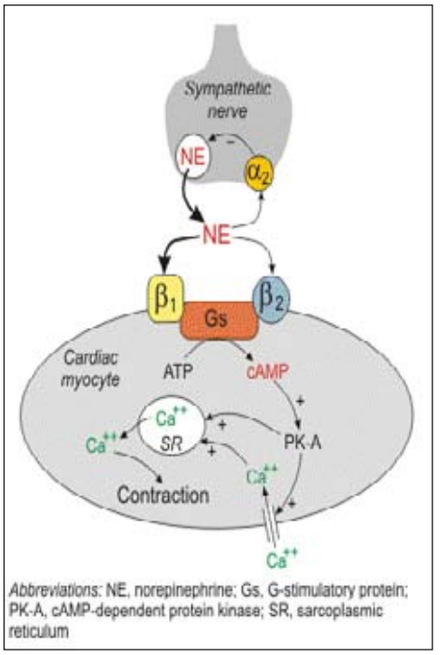

Figure 5. Beta Blocker pathway
(picture courtesy Richard Klabunde, Ph.D.)

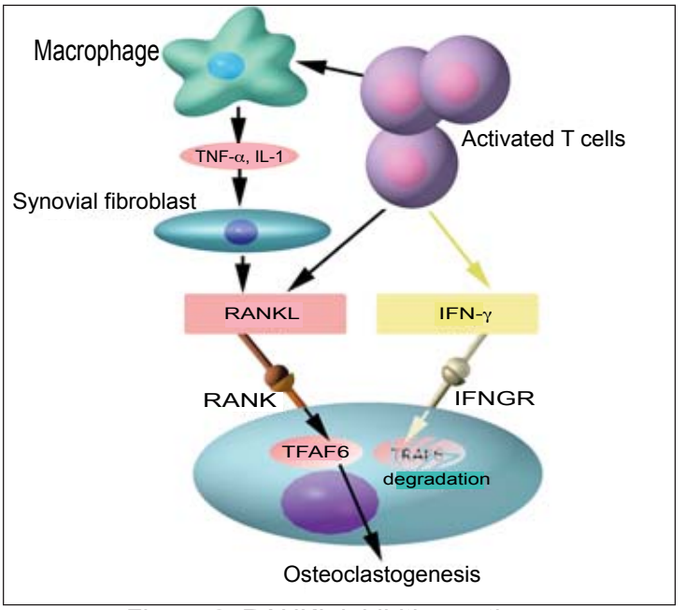

Figure 6. RANKL inhibition pathway
(picture courtesy Professor H. Takayanagi. Tokyo Medical and Dental University. reprinted with permission from AAAS.)

RANKL inhibition

Receptor activator of nuclear factor ***k*** B (RANK) is expressed by osteoclasts and their precursors[33]. The binding of RANK to RANK-ligand (RANKL) is a common pathway regulating bone resorption[34]. This pathway controls the proliferation, differentiation and survival of osteoclasts[34]. The natural inhibitor of RANKL is osteoprotegrin (OPG)[35]. The RANKL pathway provides a molecular target for potential osteoporosis therapies[36]. One option of pathway inhibition is the use of monoclonal antibodies directed against RANKL. Denosumab (AMG 162) is a specific anti-RANKL monoclonal antibody which binds with higher affinity than the natural inhibitor of OPG[37]. It also has a longer half-life, which permits less frequent dosing[36]. A human clinical trial involving 412 women demonstrated that Denosumab treatment may facilitate increased lumbar bone density in postmenopausal women[38]. Anti-RANKL antibody therapy appears to be a very promising target for the treatment of osteoporosis. This should afford a viable treatment option, provided there are no harmful side effects.

With an aging world population, it is projected that the number of age-related health conditions will also increase significantly. The challenge falls upon the current health care systems and medical researchers to create methods of addressing these challenges. In order to effectively address the

increase in osteoporosis, the strategy may require a combination of established treatment approaches as well as new therapies. Increased vigilance by patients and health-care providers may facilitate the detection of low bone density before the development of osteoporosis and new treatments could potentially help remedy the problem both before and after disease onset. ■

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Research Notes

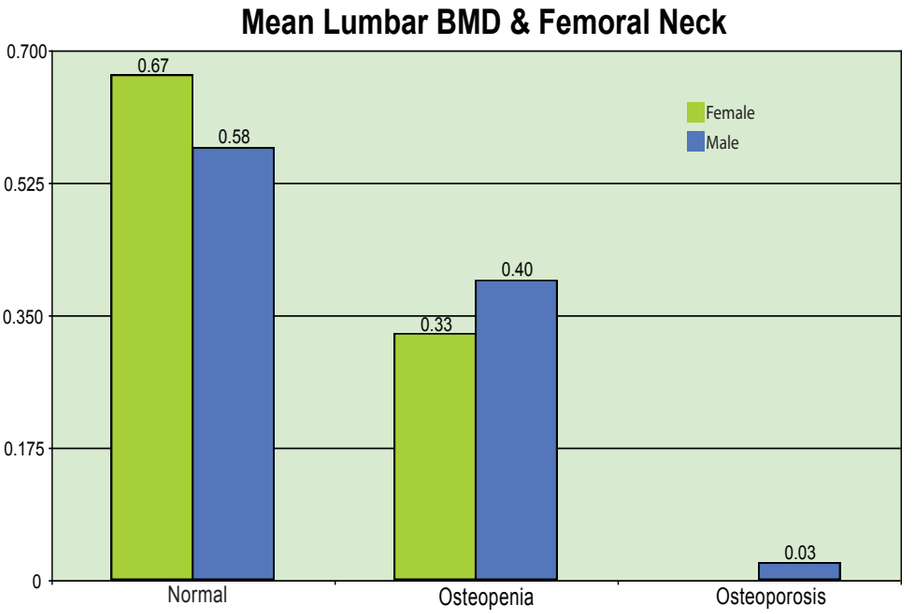
Bone Mineral Density of Spine Patients

By Anne G. Copay, Ph.D.

Osteoporosis is a disease of the bone which presents in the form of a reduced BMD and disruption of the bone architecture. There is an alteration of the amount of many non-collagenous proteins and an increased risk of fracture. This condition is most prevalent in post menopausal women. However, men also experience age-related bone loss and the degeneration of bone micro-architecture. The test to determine the bone density is called the DXA scan. The Z-score is the number of standard deviations a patient's BMD differ from the average BMD of their age, sex, and ethnicity. This value is used in premenopausal women, men under the age of 50, and in children.

Osteoporosis has been a concern for individuals over fifty years old. More recently, poor bone health has been reported in younger individuals. The reasons for this observation are not certain. Some experts believe that individuals in the western world are at increased risk of osteoporosis due to the higher consumption of carbonated beverages and lower consumption of milk. Others believe that the increasingly sedentary nature of the modern lifestyle is to blame.

In our area, bone mineral density (BMD) was measured in a group of 113 patients (73 women and 40 men) less than 50 years old. These individuals were seeking treatment for back pain and their DXA scans revealed an alarming rate of low bone mass and osteoporosis. Based on the average BMD of their lumbar spine and femoral neck, 35.4 % had osteopenia and 1% osteoporosis. Based on the BMD of individual vertebrae and femoral neck, 46.9% had osteopenia and 8.0% had osteoporosis.



Rarely, do we worry about osteoporosis in young individuals. Osteoporosis studies typically examine the BMD of individuals over 50. This study discovered an unexpectedly high prevalence of low bone mass and osteoporosis in spine patients less than 50 years old. Low bone mass and osteoporosis are likely to compound the spine pathology of these patients and will cause a delay of necessary surgical treatment. Our discovery may be just the tip of the iceberg. Further studies must be performed to understand the true magnitude of this disturbing trend. ■

What is osteoporosis?

Osteoporosis is a disease of progressive bone loss and skeletal deterioration in which bones become fragile and more likely to fracture. This disease develops slowly and may be unnoticed for years due to lack of symptoms or discomfort.

Often the first indication of osteoporosis is a fracture. The wrist, hip and spine tend to fracture more easily, although any bone may be affected. Many times fractures can lead to acute or chronic pain resulting in decreased activity or disability.

Research Notes

Role of Sex Steroids in the Pathogenesis of Osteoporosis in Men

By Sundeep Khosla, M.D.

With the aging of the population, osteoporosis is a growing medical problem in men. Men are estimated to lose bone mineral density (BMD) at a rate of up to 1% per year with advancing age, and one in eight men over age 50 years will experience an osteoporosis-related fracture in their lifetime. A major goal of my research program has been to understand the mechanisms of bone loss in men.

Since estrogen deficiency following menopause is the single most important factor leading to osteoporosis in women, it had long been recognized that estrogen was a major regulator of bone metabolism in women. Because testosterone is the predominant sex steroid in men, it was generally assumed that, similar to estrogen in women, testosterone was the major regulator of bone metabolism in men. However, in a study of elderly men in whom we suppressed endogenous sex steroid levels and replaced them selectively with testosterone alone, estrogen alone, both, or neither, we unequivocally demonstrated that, even in men, estrogen was the dominant sex steroid regulating bone metabolism. This study showed that the conversion of testosterone to the estrogen, estradiol, in men is critical for suppression of bone resorption and maintenance of bone formation.

In further work, we extended our findings to population studies and showed that in normal aging men, serum estradiol levels (particularly the fraction of estradiol not bound to sex hormone binding globulin, or "bioavailable" estradiol) correlated better with bone mineral density and with rates of bone loss in men as compared to serum testosterone levels. We also found that there may be a "threshold" bioavailable estradiol level below which the male skeleton becomes estrogen deficient, and that elderly men with circulating bioavailable estradiol levels below this value were at highest risk of bone loss. Our work has since been confirmed by other groups, who have found a similar threshold level for serum estradiol below which fracture risk increases in men.

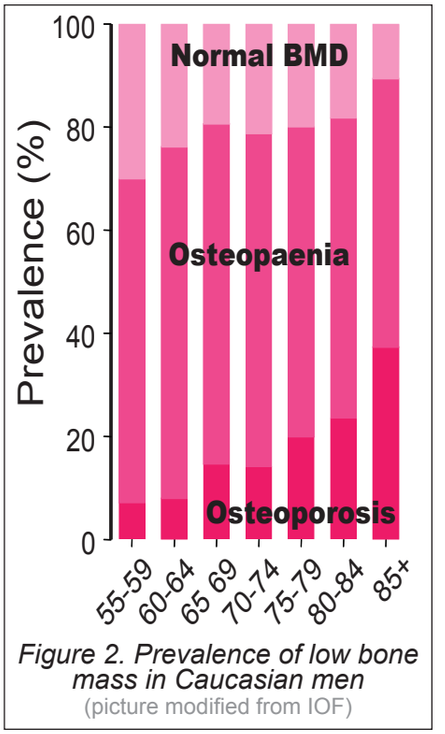


Figure 2. Prevalence of low bone mass in Caucasian men
(picture modified from IOF)

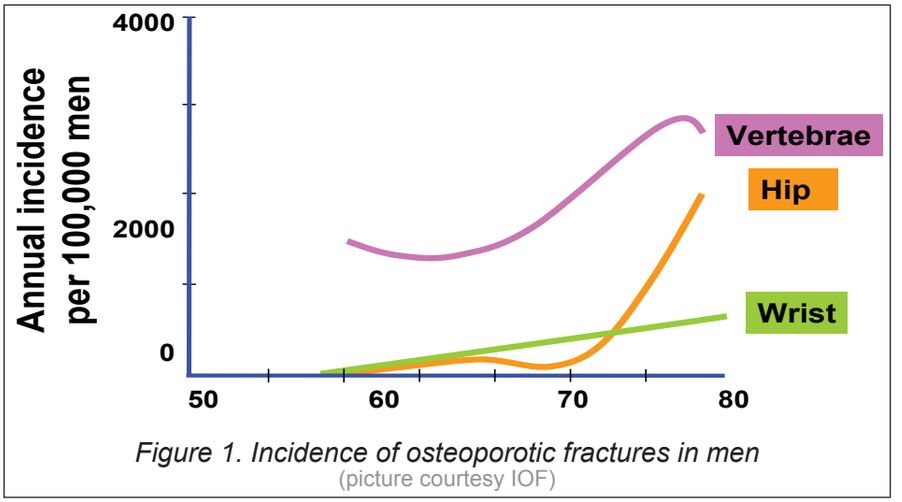


Figure 1. Incidence of osteoporotic fractures in men
(picture courtesy IOF)

Our findings also have significant practical implications. First, as assays for measuring serum estradiol levels are standardized using mass spectroscopy, it may be possible to identify men at risk for bone loss or fracture by measuring serum estradiol levels. Second, those men with low estradiol levels may be candidates for treatment with selective estrogen

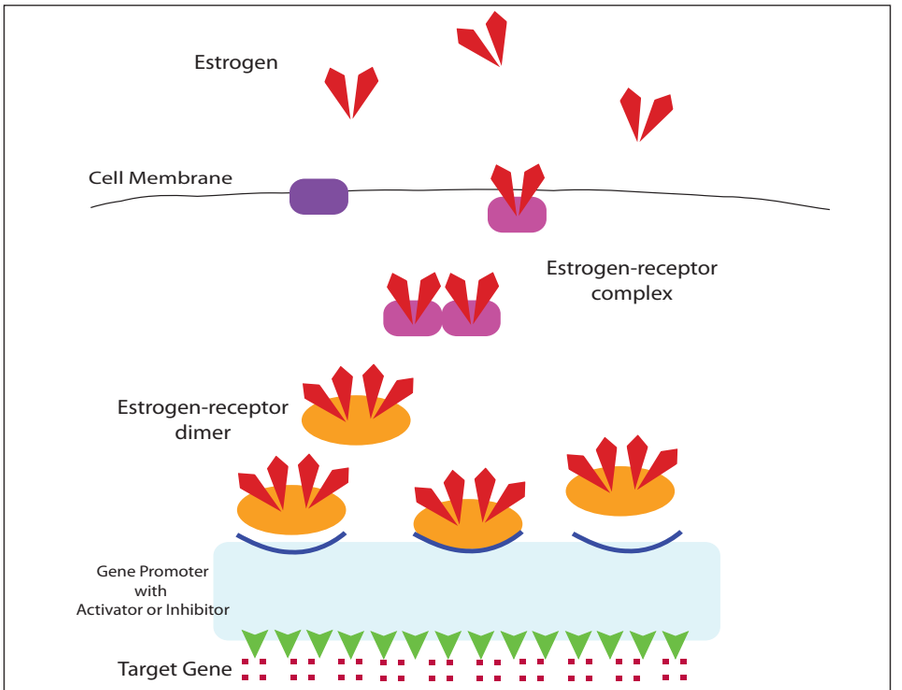


Figure 3. Pathway for estrogen activation or inhibition
(picture modified from Mayo Clinic)

receptor modulators (SERMs), such as raloxifene (or other, newer SERMs), that have an estrogen-like effect on bone without feminizing side effects. Finally, these studies have highlighted a heretofore unforeseen role for the female sex steroid, estradiol, in regulating bone loss in men.

In further studies, we are using novel imaging approaches to assess changes in bone structure and strength with aging in men and women. These include the use of high resolution peripheral quantitative computed tomography (HR-pQCT), which essentially provides a non-invasive "bone biopsy" at the wrist and tibia. Using these techniques, we are beginning to understand the structural basis for bone fragility associated with aging in men and in women. At a more basic level, we have identified circulating osteoprogenitor cells in peripheral blood in humans and are developing approaches to examine the expression of specific genes in these cells in the hope that the expression patterns of these genes may help identify patients at increased risk of developing osteoporosis. This work is still at a relatively early stage of development, but we are optimistic that it represents a fruitful direction to pursue. ■

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Sundeep Kohsla, M.D.

Dr. Khosla is Professor of Medicine and Physiology and Associate Director for Research at the College of Medicine, Mayo Clinic. Dr. Khosla received his A.B. degree from Harvard College and his M.D. from Harvard Medical School. He was subsequently a resident in Internal Medicine and a fellow in Endocrinology at the Massachusetts General Hospital. In 1988 he moved to Mayo Clinic, where his research interests include mechanisms of postmenopausal and age-related bone loss, sex steroid regulation of bone metabolism, and osteoblast/stem cell biology. He has received numerous awards and honors for his work, including the Frederic C. Bartter Award for Clinical Investigation from the American Society for Bone and Mineral Research, the Innovation Award from the National Osteoporosis Foundation, and election to the ASCI and AAP. He is also Associate Editor of the Journal of Bone and Mineral Research and a member of the editorial boards for the Journal of Clinical Investigation, Journal of Clinical Endocrinology and Metabolism, and Endocrine Reviews.

Research Notes

Bone Morphogenetic Proteins

By Marcus M. Martin, Ph.D.

Bone morphogenetic proteins (BMPs) were discovered in 1965. Almost 40 years later, at the beginning of this century, their clinical applications were finally realized. BMPs have greatly advanced the field of spinal surgery, allowing for faster healing of spinal fusion procedures and providing an alternative to iliac crest bone grafts for bone fusion. This review outlines two types of BMPs and the current and future uses of these proteins in the treatment of spinal pathology.

Introduction

Spinal interbody fusion surgery involves the uniting of two vertebrae across an intervertebral space. This procedure requires the use of orthopaedic rods and screws which act as an 'internal cast' to stabilize the vertebrae until the fusion, or bony re-growth, has occurred. The success of spinal fusion depends on the formation of a bridge between the adjacent vertebrae. Bone grafts have long been used to provide the bony bridge between vertebrae. Autograft bone derived from the iliac crest is the gold standard of bone grafts since it does not present an immunogenicity challenge and it contains the cells and matrix materials which facilitate bone growth. It possesses both osteoconductive and osteoinductive properties. Osteoconduction refers to the ability of the implanted material to support neovascularization, as well as the ingrowth of perivascular tissue into its structure. Osteoinduction denotes the ability of the implanted material to induce proliferation of undifferentiated mesenchymal cells and the formation of bone by osteoprogenitor cells.

However, the use of autograft bone, such as harvesting from the iliac crest may lead to increased morbidity, blood loss, injury to local nerves, damage to blood and lymphatic vessels, infection, disturbances in gait, prolonged hospitalization and protracted recuperative time. Alternative materials, therefore, needed to be found. These were required to satisfy four main criteria. These graft substitutes would need to be capable of inducing fusion, be consistent in quality, be biocompatible and safe for human use. Hence, recombinant human bone morphogenetic proteins (rhBMPs) were developed to fill this void[1].

History

In 1965, BMPs were discovered by Marshall R. Urist. His experiments involved the removal of the mineral component of bone and the implantation of the remaining demineralized bone into research animals. This material stimulated bone growth when implanted into the muscle tissue of rats, mice and guinea pigs. This brought the realization that bone contained substances which can stimulate the formation of new bone. The osteoinductive potential of bone was found to be derived from naturally occurring noncollagenous glycoproteins, coined 'bone morphogenetic proteins'. Urist's discovery went unutilized for nearly four decades, until finally the clinical application of these molecules was realized. At least 20 different BMP molecules have been identified. Of these BMPs, BMP-2 and BMP-7 have been FDA approved for use in humans[2]. As many as 250,000 vertebral arthrodesis procedures are performed annually in the US[3]. Of these, 5% - 45% progress to non-union states. BMPs promise to make a major contribution to the treatment of these conditions by facilitating faster bone healing following these procedures.

Mechanism

BMPs are members of the TGF β superfamily of biological molecules. BMP molecules share a similar structure and amino acid sequence at the carboxyl terminal region. Different BMPs are not interchangeable, though some such as BMP-2 and BMP-4 show significant homology. Through signal transduction, BMP receptors effect the mobilization of proteins associated with bone development. This initiates a cascade of events that can facilitate bone formation. BMPs may be active at multiple points throughout this cascade. First

BMPs induce cell migration to the site of administration. Osteoprogenitor cells, osteoblasts and mesenchymal stem cells respond to the chemotaxic signal. Mesenchymal stem cells are undifferentiated and can produce several connective tissue cells, including cartilage-producing chondrocytes and bone-producing osteoblasts. The proliferative response may be enhanced by molecular signals released by cells at the injury site. BMPs affect undifferentiated cells, but do not appear to have a cell-specific effect on mature differentiated cells[1].

Production of BMPs

BMPs are present in small quantities within bone. It would require hundreds of kilograms of bone to extract milligram quantities of BMP. To overcome these limitations, scientists focused their research efforts on the determination of the amino acid sequence of these proteins and sequencing of their associated genes. Through the use of recombinant DNA technology, researchers were able to produce these proteins in large quantities in established cell expression systems, using bioreactors, thereby producing purified BMPs for research and clinical applications.

Rh-BMP-2 was FDA approved in 2002 for implantation in the lumbar spine and for use in tibial fractures while BMP-7 is only approved for humanitarian use in the spine, mostly because it failed to demonstrate equivalence to iliac crest bone graft. The complete mechanism of action of these two BMPs is not yet known. However, the efficacy of both has been demonstrated in several animal and human studies.

Carrier

In order to utilize BMPs at a fusion site, a suitable carrier had to be found to localize the material at the site.

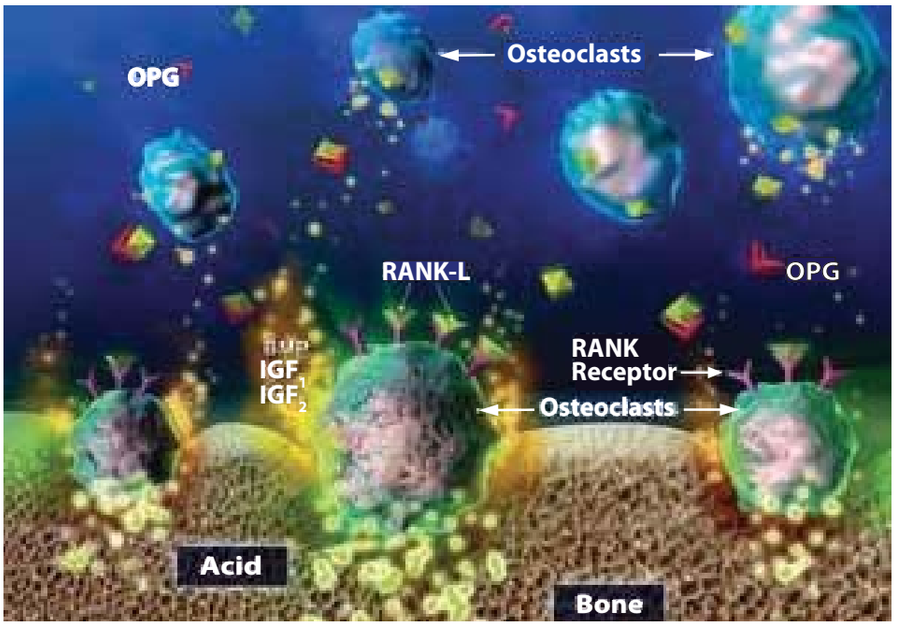

Figure 1. How BMPs work

At the cellular level, bone metabolism is largely mediated by the RANK ligand system. Osteoblasts secrete RANK-L which binds to the RANK receptor on the osteoclast causing bone resorption. As the osteoclast dissolves bone, IGF_1 and IGF_2, along with BMP, are released from the bone and cause osteoblastic growth, producing new bone. OPG competes with the RANK receptor to bind RANK-L, thereby inhibiting osteoblastic bone resorption.

(picture courtesy http://www.dentaleconomics.com)

When determining a carrier for BMP, the following characteristics were sought:

- Biocompatibility
- BMP-binding capacity
- Handling ease during surgery
- BMP release over an adequate period of time
- Space maintenance for new bone deposition
- Osteoconductive surface for osteoid deposition
- Ability to resorb at a rate compatible with new bone formation

After testing several candidate materials as BMP-2 carriers, an absorbable collagen sponge (ACS) derived from the Achilles tendon of USDA-cleared food-grade steers was chosen. This tissue is harvested before butchering. It is processed extensively in alkali solutions producing a surgically safe

sponge-like material. The material acts as a space occupier where new bone is desired, acting as a scaffold upon which vascularization and bone deposition can occur, as well as releasing the BMP chemotaxic signal to facilitate the migration of bone-forming cells to the desired location. The carrier used for BMP-7 is Type 1 bovine bone collagen[4].

Recombinant human bone morphogenetic protein-2

Recombinant human bone morphogenetic protein-2 (rhBMP-2) is marketed under the label 'Infuse Bone Graft'. It has been clinically evaluated for use in spinal fusion procedures. rhBMP-2 is carried on a bovine collagen sponge used in conjunction with a tapered, threaded intervertebral cage. Human trials of rhBPM-2 began in 1996.

Figure 2.
(picture courtesy Medtronic)

Several studies have demonstrated the safety and effectiveness of rhBMP-2 in lumbar spinal fusion. This molecule has been subjected to toxicology studies, biocompatibility tests, as well as assessments of reproductive impact, tumor growth potentiation tests, and pharmacokinetic studies.

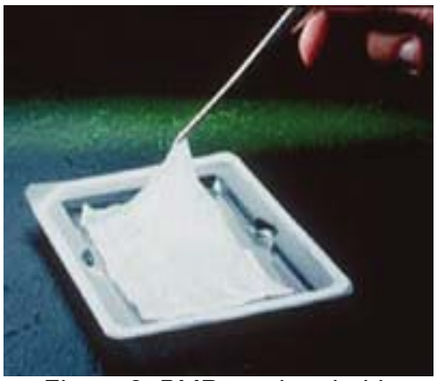

Figure 3. BMP on absorbable collagen sponge
(picture courtesy Infuse Bone Graft product inserts)

All data, thus far, indicate that rhBMP-2 is safe for use in clinical spinal procedures. These studies demonstrate that rhBMP-2 is safe even at doses thousands of times greater than physiological level. At the implant site, rhBMP-2 only persists for 3-4 weeks. rhBMP-2 also shows no carcinogenic effect. In clinical trials, patient populations treated with rhBMP-2 showed the same incidence of cancer as the population in which autografts were used.

Recommended Technique for use of INFUSE® Bone Graft and the LT-CAGE® Device

• Bone Graft is packaged with a collagen sponge and sterile water for reconstitution.

• The lyophilized rhBMP-2 is reconstituted with the sterile water to form a liquid solution, prior to surgery.

• The collagen sponge, which is the carrier for the rhBMP-2 solution, is cut and otherwise sized to fit inside two LT-CAGE® Devices (titanium screws which occupy the disc space and maintain the disc height).

• The sponges are then saturated with the rhBMP-2 protein for at least 15 minutes, rolled and placed inside the cages.

• Surgeons remove the damaged disc from the patient's spinal column and prepare the adjacent vertebrae for the insertion of the LT cages.

• Cages containing the soaked sponge are implanted in the space between the vertebrae, and the rhBMP-2 promotes the growth of new bone to fuse the spine at that location.

BMP-7

BMP-7 is marketed under the label 'OP-1'. It plays a role in the transformation of mesenchymal cells into cartilage-producing chondrocytes and bone producing osteoblasts. BMP-7 genes were isolated, placed into plasmids and incorporated into cells capable of expressing these proteins. This facilitated the production of the BMP-7 homodimer which can then be purified to greater than 97%

purity. Animal studies and human clinical studies have demonstrated the efficiency and safety of OP-1 as an enhancer of spinal fusion. BMP-7 has been shown to stimulate cell proliferation, osteoblast differentiation and collagen synthesis[4]. It may induce endochrondral ossification in segmental osteoperiosteal defects. OP-1 Putty is FDA approved under a Humanitarian Device Exemption (HDE) as alternative to autograft in compromised patients requiring revision posterolateral (intertransverse) lumbar spinal fusion.

Recommended Technique for use OP-1:

• The bone is debrided and decorticated so that the OP-1 Putty will come into direct contact with viable tissue.

Figure 4.
(picture courtesy Stryker®)

Figure 5. Op-1 putty
(picture courtesy Stryker®)

• Adequate homeostasis is provided to ensure that the material stays at the surgical site.

• The OP-1 Putty is carefully applied to the prepared site, being packed into the desired area to its maximum capacity.

• Using a suture material of choice, the soft tissues are closed around the defect containing the OP-1 Putty.

• After closure of the soft tissue around the defect, the surgical field is irrigated, if necessary, to remove any stray particles of the product.

Current and future uses

Currently BMP is used for bone fusion during orthopedic surgery. However, these proteins may soon assume a broader role in this process. The use of gene delivery systems, such as adenovirus, are being explored as a potential means of producing BMP at a desired anatomical site. Combinations of the different BMPs could also enhance the effectiveness of these molecules. Additionally, percutaneous treatment of non-unions or delayed fusions may be possible by using minimally invasive methods of BMP delivery to the injury site. The potential utility of this approach has been demonstrated in rats, where percutaneous injection of rhBMP-2 was shown to accelerate fracture healing. BMPs have made a significant positive contribution to spinal fusion procedures. Advances in drug delivery systems may see these molecules becoming even more of a staple in orthopedic surgery[5]. ■

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How is osteoporosis treated?

There is no cure for osteoporosis at this time. Treatment is a team approach from your spine surgeon, family physician and physical therapist. You need adequate amounts of Vitamin D and calcium in your diet. In some cases, medication is necessary to promote mineralization of bones. Currently, several therapies are available for prevention or treatment of osteoporosis. Bisphosphonates increase bone mineral density therefore, decreasing risk of fracture in women. Some of these therapies work by slowing bone loss, while others promote new bone formation.

Research Notes

Use of a Paravertebral Anesthetic Infusion System for Post-Operative Pain Relief

By Michael W. Hasz, M.D.

Patients who undergo lumbar spine surgery are often concerned about postoperative pain control. With adequate pain control, patients are able to more rapidly increase their level of activity after surgery and more likely to benefit from physical therapy. In addition, poor pain control has been cited as one of the most common reasons for an extended hospital stay after surgery.

Current pain control options include the use of narcotic (similar to morphine) medications in pill form, injection form, or intravenous patient controlled analgesia (PCA). Patients control the additional treatment modality in the form of a continuous paravertebral anesthetic infusion (On-Q® PainBuster®, I-Flow Corp., Lake Forest, CA). This has recently been added to the arsenal of pain control. The plastic pump delivers local anesthetic into the surgical site at a controlled preset rate, effectively decreasing pain in the area surrounding the incision.

Currently, we use each of the available modalities in our patients to varying degrees based upon the type of surgery performed and the patient's specific pain tolerance. Post-operatively, we commonly inject

Figure 1. On-Q® PainBuster®
(picture courtesy www.iflo.com)

the incision site with a local anesthetic such as lidocaine or bupivicaine, then use a long-acting oral pain medication and the intravenous PCA as a very effective combination. Unfortunately, the local anesthetic injection is only effective for a brief period of time, generally between four and eight hours. With a continuous anesthetic infusion pump (On-Q® PainBuster®), a lower dose of the anesthetic may be delivered to the area around the incision on a continuous basis and can be used for up to 72 hours in the postoperative period. Using long-term local anesthetics significantly reduces the need for narcotic pain medications and also limits the morphine associated side-effects such as sedation, constipation and respiratory depression.

In our experience, the infusion of this continuous local anesthetic around the surgical incision site has significantly decreased the amount of postoperative narcotics required, taken either orally or with PCA delivery. It has increased the mobility of patients: patients have been able to sit up, walk and work with physical therapy sooner than the patients who did not receive the continuous infusion pump. With this increased activity and improved pain control, patient satisfaction has also greatly improved.

In addition to early mobilization, the benefits for the patients include increased pulmonary function, decreased fever and reduced risk of

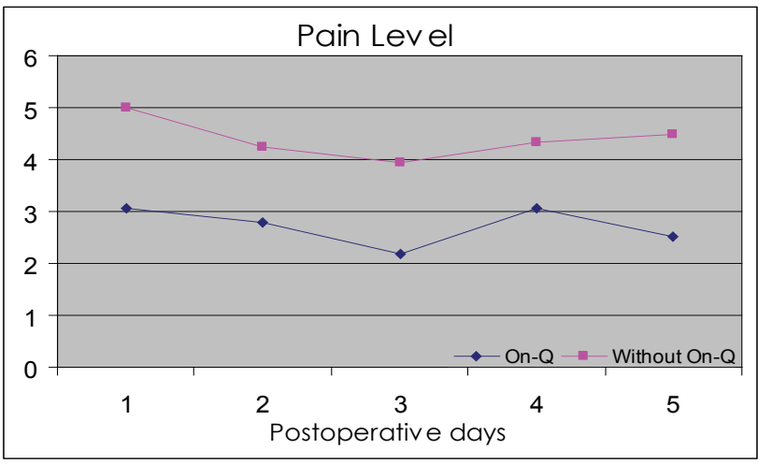

Figure 2.

deep venous thrombosis (blood clot in the leg) and pulmonary embolism (blood clot to the lung). There are additional benefits associated with the continuous infusion of local anesthetics for postoperative pain. It has been shown that the use of bupivicaine interacts with various prostaglandins (inflammatory mediators) in the postoperative period. One such prostaglandin is called prostaglandin E_2 (PGE_2). Prostaglandin E_2 receptors, subtype EP_1 (PGE_2EP_1) have been linked to several physiologic responses, such as fever, inflammation, and mechanical hyperalgesia (increased sensitivity to pain). Local anesthetics seem to decrease the sensitivity of these receptors to the presence of prostaglandins, thereby speeding recovery of injured tissues.

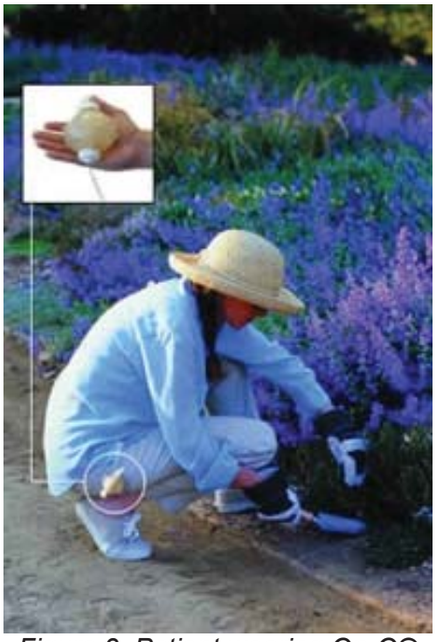

Figure 3. Patient wearing On-Q® PainBuster® infusion pump after spinal surgery.
(picture courtesy www.iflo.com)

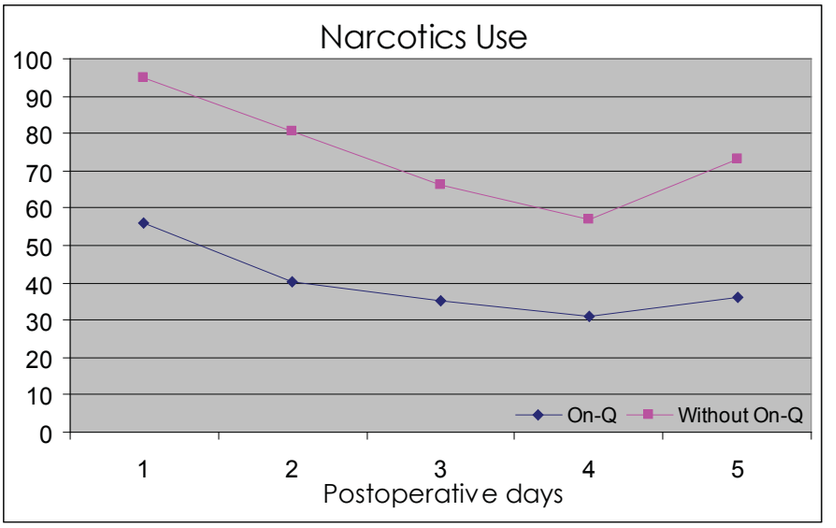

Figure 4.

The use of continuous wound catheters after surgery has been shown to improve pain control, reduce opioid use, increase patient satisfaction and shorten hospital stay across a wide range of surgical procedures such as cardiac surgery, abdominal hysterectomy, cesarean section, knee and shoulder surgery, and spinal fusion. The most recent study involving spinal fusion demonstrated that the On-Q® PainBuster® after spinal fusion surgery decreased postoperative pain and the need for narcotic medications. A group of 52 patients in Southern California underwent lumbar spinal fusion. An infusion pump was inserted into half of the patients. The recorded average daily pain level and use of narcotics was lower for patients with the local anesthetic pump than for patients without one. ■

Michael W. Hasz, M.D.,F.A.C.S.
Spine Surgeon

Dr. Hasz is Board Certified by the American Board of Spine Surgery and the American Board of Orthopaedic Surgery. He is a Fellow in the American Academy of Orthopaedic Surgeons and a member of both the American Association of Orthopaedic Surgeons and the North American Spine Society.

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Research Notes

Is Posterior Disc Arthroplasty an Answer (A Biomechanical Perspective)?

By Vijay K. Goel, Ph.D.

Anterior lumbar disc replacements are used to restore spinal alignment and motion of a degenerated segment. Compared to fusion of the segment, disc replacements may prevent adjacent segment degeneration. Presently, available anterior discs may be considered as first generation discs and have highlighted several issues like the approach itself, difficulty of revision, and postoperative facet pain. To address these issues, 360° motion preservation systems consisting of an artificial disc and posterior dynamic system (PDS) are being pursued. These systems address all the pain generators in a motion segment, including the nerves, facets, and disc. We have undertaken biomechanical studies on 360° motion preservation systems to address the issue "Is posterior disc arthroplasty an answer from a biomechanical perspective?"

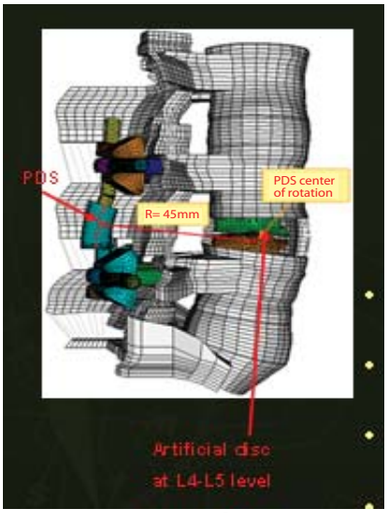

Figure 1. Artificial disc
(picture courtesy www.eng.utoledo.edu/~vgoel)

An experimentally validated 3-dimensional computer simulation model of the ligamentous L3-S1 segment was used to investigate the differences in biomechanical behavior of the lumbar spine for the following scenarios: intact segment, segment implanted with a 360° motion preservation system involving anterior disc, and a 360° motion preservation system involving a posterior disc. The computer simulation models were subjected to 400 N of follower load plus 10Nm moment in extension and flexion.

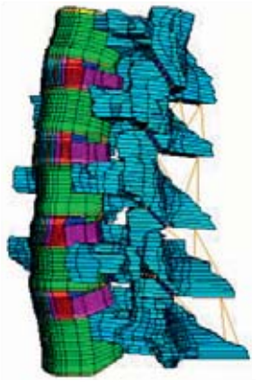

Figure 2. Cervical spine
(picture courtesy www.eng.utoledo.edu/~vgoel)

The ranges of motion for the 360° systems at the implanted and adjacent levels were similar to those of the respective intact levels. The stresses in various components were quite low as compared to the yield strengths of the material used for the fabrication of the devices.

In conclusion our findings show that a disc replacement with PDS restored the movement of the spine at all levels to near normal. Since the posterior disc with a posterior dynamic system will allow the surgeon to address all of the shortcomings of the first generation anterior discs using one approach that is widely accepted among the surgeons, we strongly feel that the posterior disc with a posterior dynamic system is the answer for a successful outcome following a 360° disc arthroplasty. ■

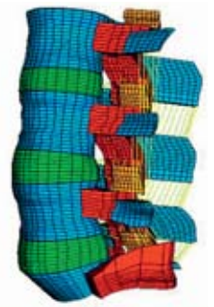

Figure 3. Lumbar spine
(picture courtesy www.eng.utoledo.edu/~vgoel)

Vijay K. Goel, Ph.D.
Department of Orthopedic Surgery
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Toledo, Ohio

As a researcher, Professor Goel has made several noteworthy contributions in the area of spinal biomechanics.

Acknowledgements: Work supported in part by grants from Disc Motion Technologies, Inc; Facet Solutions, Inc., and Spinal Kinetics, Inc.

Research Notes

Outcomes and Complications with X-STOP Interspinous Decompression in Patients with or without Spondylolisthesis for the Treatment of Spinal Stenosis

By Nishant Reddy, Kogulan Nadesakumaran, Prithvi Narayan, M.D., Mark McLaughlin, M.D., Niraw K. Shah, M.D.

Traditional surgical treatments of spinal stenosis include laminectomy, laminotomy, foraminotomy, facetectomy and laminoplasty. While such procedures may be effective, they carry the risks and complications of any invasive surgery, as well as irreversibly altering the spinal canal anatomy. The X-STOP Interspinous Process Decompression device has been reported to be an effective, minimally invasive alternative to treat spinal stenosis in certain patient populations. Previous studies have shown varied success rates and outcomes. The efficacy of the X-STOP device in patients with a grade 1 spondylolisthesis is unknown.

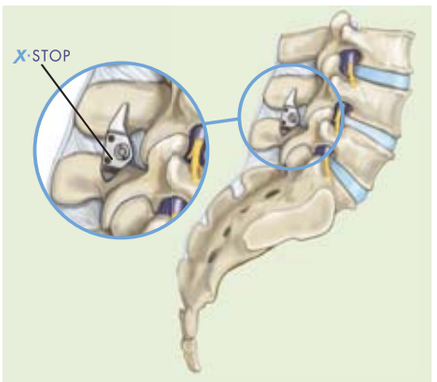


Figure 1. Spine with X-STOP implant
(picture courtesy Medtronic)

Methods

We conducted a retrospective study of all patients treated with the X-STOP device over the past two years in a single spine practice to look specifically at outcomes determined by patient satisfaction, improvement, changes in the ability to ambulate, and alterations in patient pain medication regimen. Estimated blood loss, length of stay, length of surgery, and complications resulting from the procedure were also recorded. Information was gathered utilizing patient charts and questionnaires.

Figure 2. X-Stop device
(picture courtesy Medtronic)

Results

On a scale of 1 to 5, (1- unsatisfied, 5- extremely satisfied) the average overall satisfaction regarding the X-STOP procedure for 15 patients was a 3.73. 11 out of 15 patients reported major or minor improvement as determined by: degrees of symptom relief, changes in medication regimens, and abilities to ambulate. The average increase in the ability to ambulate was 4.3 blocks. Ten patients reported no change in their pain medication regimen. Ten patients reported that they would have the surgery again.

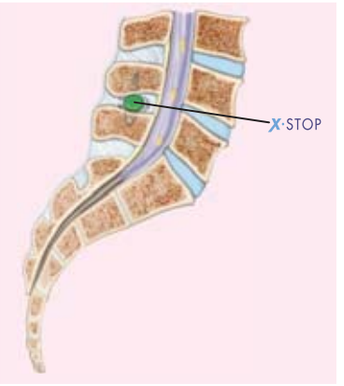


Figure 3. Cross-sectional view of X-STOP implant
(picture courtesy Medtronic)

Complications from the procedure included a superficial wound infection, a new contralateral radiculopathy, erosion of the spinous process in a patient with recurrent symptoms of leg pain, and a deep wound infection requiring incision and drainage. One patient developed a spinous process fracture prompting removal of the X-STOP device. All complications in this series occurred in patients with grade 1 spondylolisthesis.

Conclusion

While the X-STOP procedure did improve overall outcomes in our series, success rates were less than what is reported in the literature. Our series demonstrates significant complications in 4 of 15 patients. Patients with spondylolisthesis showed a decreased satisfaction, higher complication rates, and an increased need for further surgery. ■

According to the National Institutes of Health:

At some point, neck or back pain affects an estimated 9 out of 10 people. It is one of our society's most common medical problems.

The first attack of neck or low back pain typically occurs between the ages of 30 and 40. Spinal pain becomes more common with age.

With symptoms ranging from a dull ache to absolute agony, back pain can put your life on hold.

In fact, it is second only to the common cold in causing missed workdays for adults under age 45.

Office visits for low back pain: 25 million per year

Medical admissions for low back pain: 325,000 per year

Chronic Lower Back Pain?

An investigational device is being tested to see if it provides relief for chronic lower back pain.

You may qualify for this clinical research study if you:

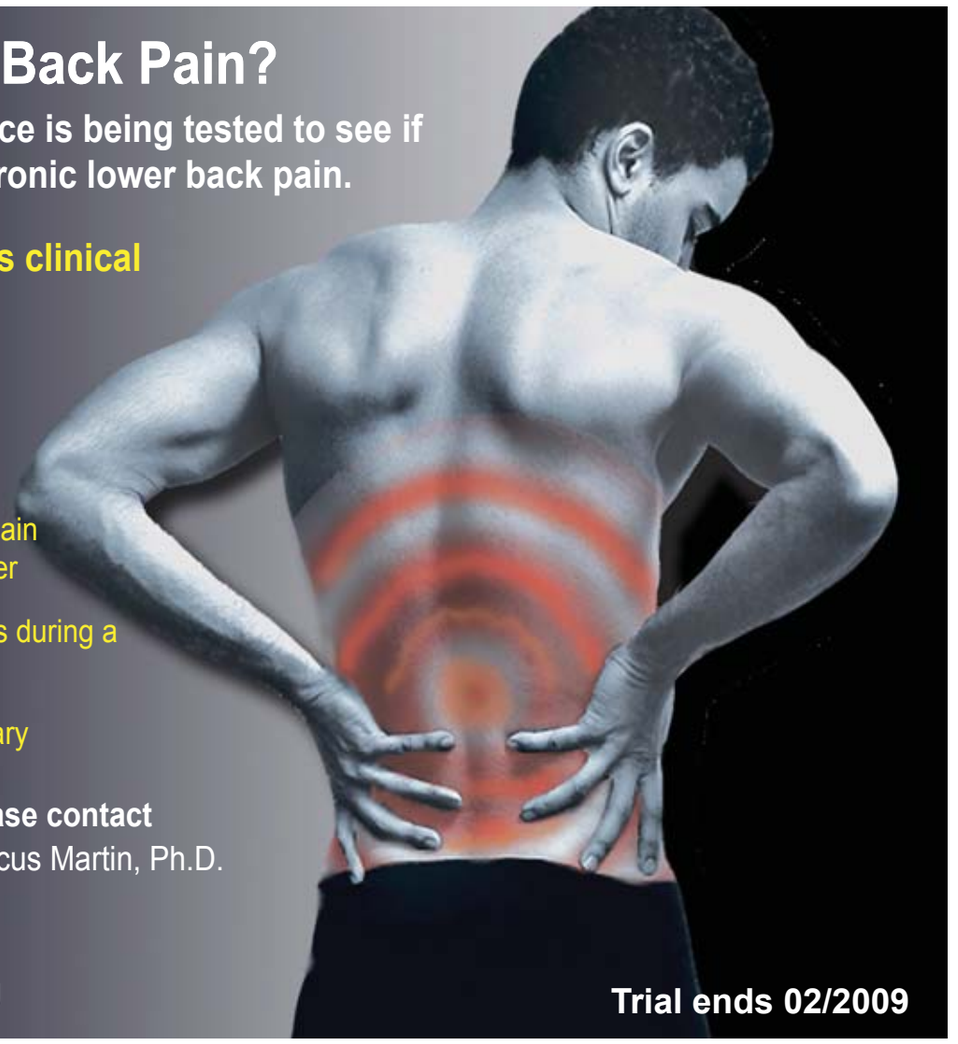
-Are 18-65 years of age

-Have had lower back pain for more than 3 months

-Have been taking the same pain medications 3 months or longer

-Able to complete 5 clinic visits during a 12-week period

-Willing to complete a daily diary



For more information please contact

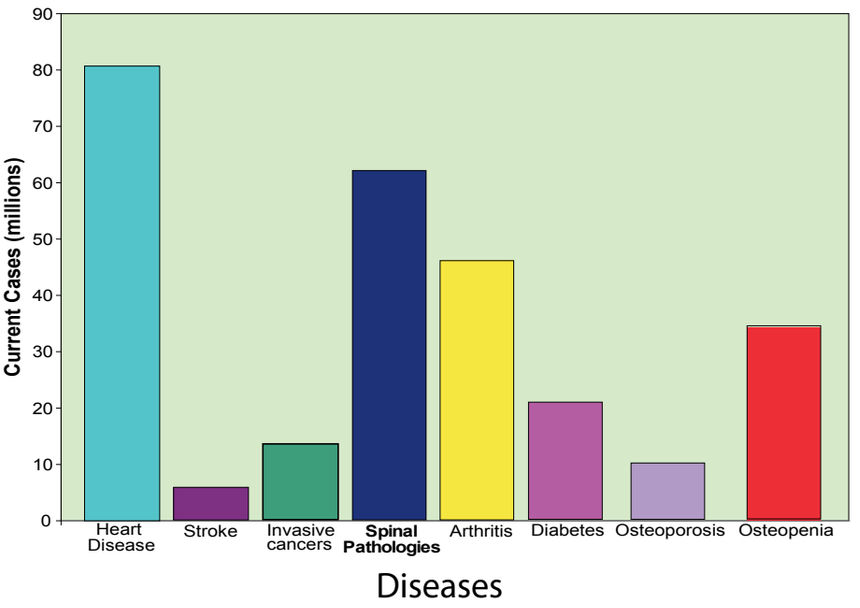
Anne Copay, Ph.D. or Marcus Martin, Ph.D.
Phone: (703) 766-5405
Fax: (703) 709-1397
email: mmartin@spinerf.org

Trial ends 02/2009

Neck and Back Pain Affects Millions

The Spinal Research Foundation is an international non-profit organization dedicated to improving spinal health care through research and education. The Foundation collaborates with spinal research centers of excellence around the world to prove the success of traditional approaches, as well as develop new techniques and technologies. These results are shared with both the medical profession and the general public to improve the overall quality and understanding of optimal spinal health care.

More than 85% of the population will suffer from severe neck and/or low back pain during their lifetime. Eight percent of these people develop chronic pain, which means that at any given time, 25 million people in the United States are directly affected by this condition and many more indirectly. Techniques to cure, manage, and prevent this limiting and disabling condition need to be developed. Educating the public, health care providers, and insurance providers is the first step in advancing spinal health care.



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Diabetes- http://www.diabetes.org/about-diabetes.jsp
Osteoporosis- http://www.nof.org/osteoporosis/diseasefacts.htm
Cancer- National Cancer Institute 1975-2005 statistics.

You can help!

The Spinal Research Foundation is America's leading non-profit health organization dedicated to spinal health. Friends like you have made it possible for us to make huge strides and groundbreaking research discoveries. Join us in our mission to promote spinal health. Support cutting edge research by making a donation to the Spinal Research Foundation.

Support cutting edge research

- Visit www.SpineRF.org to make a secure online donation.
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Spinal Research Foundation Regional Research Centers

The Spinal Research Foundation has named fourteen Regional Research Centers across the country that share one core mission: Improving spinal health care for the future. These centers offer the best quality spinal health care while focusing on research programs designed to advance spinal treatments and techniques.

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Thomas C. Schuler, M.D., F.A.C.S., President
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The Orthopaedic and Sports Medicine Center
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Colorado Comprehensive Spine Institute
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