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Perspective Article

Osteoporosis as it Affects Men, Andropausal and Senior Males

Louis ZG TOUYZ[1]* and Sarah JJ TOUYZ[2]

McGill Faculty of Dentistry, Canada
Glasgow Health Science School of Medicine, Scotland

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***Corresponding author**

Louis ZG TOUYZ, McGill Faculty of Dentistry, Canada,
Tel: 514-398-7203;
Email(s): louis.touyz@mcgill.ca (or) touyzlouis@gmail.com

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Abstract

This perspective appraises the pathology, etiology, clinical presentation and therapy of osteoporosis, in particular for men, and focuses on implications for oral healthcare.

Introduction

Osteoporosis (OP) is a condition that involves bone, and can potentially affect the whole skeleton. OP renders thinning of bone tissue and structures including the cortices and medullary trabeculae. Consequently, OP bones are weak and more susceptible to fracture. Fractures in spine, hip and wrist bones are common with OP. Frequent minor spinal fractures are symptomless, but collectively over time OP microfractures can eventually result in spinal deformity and consequent disability. The North America prevalence of OP is high, with nearly 1/3rd of the population over 60 years suffering from OP. About 50 million North Americans have a low bone mass, and about 44 million Americans and 4.4 million Canadians have OP. OP affects females earlier and more frequently than males, and is a condition that is typically associated with post-menopausal women. However, OP also affects many men. OP tends to occur about one to two decades later in men than in women, and can be just as debilitating and devastating.

Aim

This article appraises the etiology, pathophysiology, management and socioeconomic aspects of OP, while focusing on risk factors in men, and highlights OP management for males.

Etiology and pathophysiology

Pathophysiology: Bony Anatomy and Histology of OP: All bones have a thicker dense outer layer, the cortex, and an inner layer or medullary cancellous part, which is less dense. The cortex is compact bundle bone, while the medulla is traversed with thinner reticulated trabeculae, housing marrow spaces. Bones are biological calcified structures, sculpted by genetic programming to suit the functional purpose located in the body. Structural beams grow the cortex, trabeculae in the medulla, and house the bone marrow according to the needs and demands of the body. A periosteum covers the outer cortex, and has bone-forming cells known as osteocytes. Histologically, osteocytes are incorporated into the bone in Haversian systems, and line the thin trabeculae in endosteal sinuses (Figure 1).

Bone metabolism and blood formation (from the bone marrow) is moderated by many plasma biochemical co-factors (such as osteocalcin, erythropoietin), endocrine and autocrine molecules (such as parathyroid hormone, cortisol, growth hormone, estrogen), and mediated through osseous stem cells, hemopoetic cells, unicellular osteocytes/osteoblasts (bone-forming) and multinuclear osteoclasts (bone-removal). Alternate cycles of bone deposition and bone resorption are ongoing all the time, and occur throughout life. When bone resorption exceeds bone formation, often due to disrupted or imbalanced regulating feedback systems, OP develops. Therapy is directed at these cells and their functions to mediate the rate of bone deposition and resorption.

Vit-D: Vitamin-D (Vit-D) is thought to play an important role in bone mineral density homeostasis and OP. Vit-D is directly involved in calcium absorption from the gut, and is controlled by the parathyroid (PTH) feedback system. The first step of vit-D synthesis depends primarily on UV exposure on the skin from sunshine, with successive storage in the liver as an inactive metabolite, and subsequent renal activation stimulated by PTH. Vit-D can also be acquired through the diet, with similar steps of metabolism. Several factors can influence vitamin D levels. Usually, a lack in vit-D is mostly due to lack of UV exposure. For instance, certain countries with predominantly cold or rainy weather (such as Scotland or the winter months of Canada), people tend to cover-up in warm clothing and consequently have minimal exposure to the sun. Further, certain cultures and religions

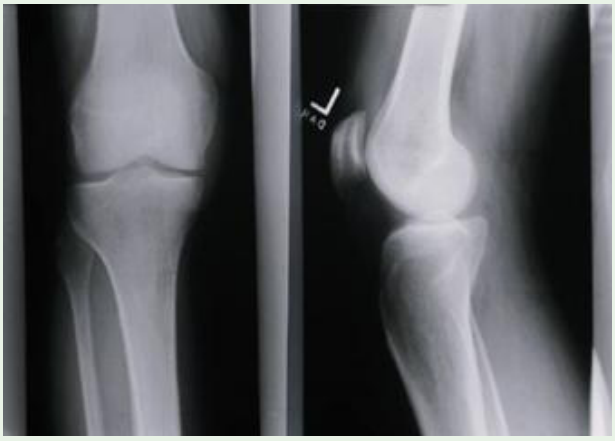

Figure 1: Front and lateral Radiograph of a right knee to show anatomical areas of bone. The femur, patella, tibia and fibula show bone differentiation into areas. Bones have a dense outer layer, the cortex, and an inner cancellous part. The cortex is compact bundle bone; the medulla is with thinner reticulated trabeculae, houses marrow spaces.

wear long sleeves or cover up with more layers, minimizing the amount of skin exposure to sunlight. More Vit-D is produced when young; this may be influenced by the number of hours spent outdoors in youth or reduced mobility and metabolism with age (SOURCE). This puts certain populations, particularly older generations, at risk for developing OP. Ensuring adequate Vit-D levels through adequate sun exposure or dietary supplements are essential for minimizing the risks of developing OP (Figure 2).

3-D Micrographs of medullary bone structure shows thinning of the cortical plates, and also diminishing of trabeculae, often with medullary micro-fractures. Overall this leads to weakening of the cortex and medullary parts of the bone, and generally increases chances of fractures [6,7] (Figure 3).

Diets as contributing factor in OP: Deficiency of Vit-D (subtypes Vit D-2 and Vit D-3) will result in Ricketts in children and Osteomalacia

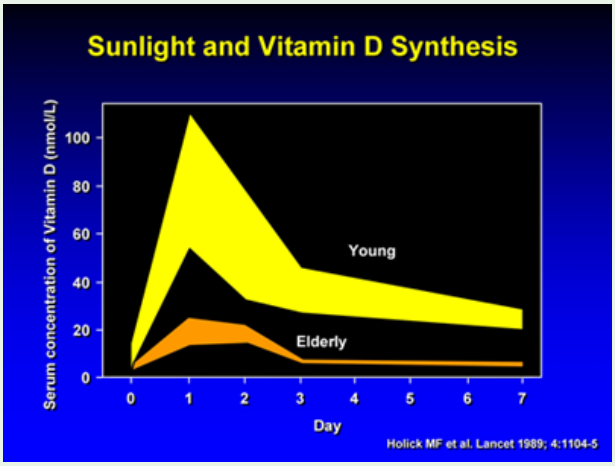

Figure 2: ***Vit-D and Sunshine:*** Among the causes of OP is a lack of Vit D. [Holick MF et al Lancet 1989, 4; 1104-5.]
NOTE: The hormones Estrogen, Androgen and PTH positively moderate Bone Metabolism; when these diminish with age, so too does bone deposition.

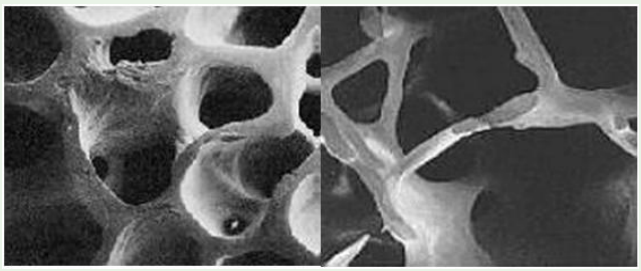

Figure 3: Micrographs of bone structure: Shown here on the right is OP affected medullary bone, with a micro-fracture, compared to the left side with healthy equivalent medullary bone. Note increases in size of bone marrow spaces, reduction of reticulating bone spicules, and micro-fractures of the trabeculae.
Ref: US Department of Health and Human Services. Bone health and osteoporosis: a report of the Surgeon General. Rockville, Md: 2000. [Photos reproduced from Dempster DW, et al. J Bone Miner Res.1986; 1:15-21… with permission of the American Society for Bone and Mineral Research] [6].

in Adults. Daily doses of sunshine help in dermal synthesizing of Vit-D. An adequate dietary intake of calcium, phosphorous (and when under 25 years also fluoride) is needed to delay OP. People with lactose intolerance tend to eat less dairy products and consequently have a low calcium dietary intake.

Secondary conditions, diseases and medications implicated in causing OP

Primary or Secondary hypogonadism, primary hyperparathyroidism, thyrotoxicosis, Growth Hormone deficiency (GH), osteomalacia, hypophosphatasia, connective tissue disorders, osteogenesis imperfecta, GIT malabsorption syndromes including coeliac disease, anorexia nervosa and excessive weight loss.

Co-factors as medications

Glucocorticoid-steroids, excess thyroxin, anticonvulsants (like phenytoin and phenobarbital); lithium, gonadotropin-releasing hormone and medroxyprogesterone are all implicated in OP [8].

Clinical presentation: Osteoporosis in men

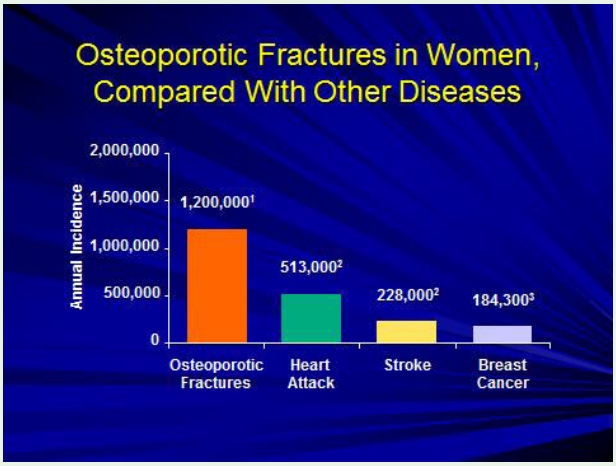

Figure 4: Osteoporotic fractures compared to other diseases [1,2,4,5]. OP prevalence exceeds heart attack, stroke, and breast cancer (in women).

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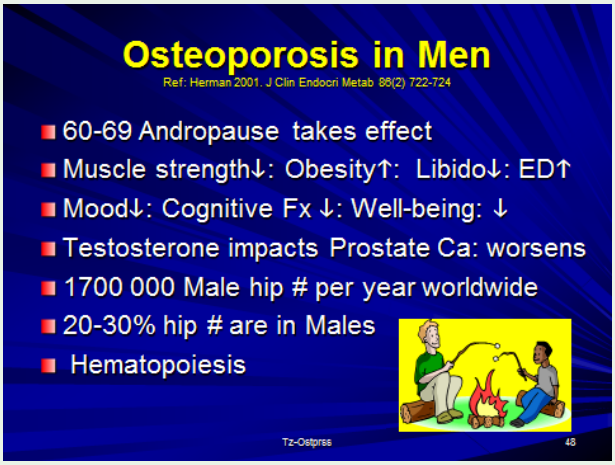

Figure 5: Common signs and symptoms of OP in Men. [Herman (2001) J Clin endocrine Metab.86;2;722-724.] Arrows up↑ indicate increase; and arrows down↓ indicate decrease.

OP is among the most common metabolic pathologies affecting the North American population (particularly those aged 65 and over), with OP frequencies exceeding that of stroke, breast cancer and coronary thrombosis, combined. [1-4] For instance, in North America nearly 4.5 million osteoporotic fractures are recorded compared to 1.24 million cancers per year (Figure 4).

North Americans of both sexes (Note: do you mean sexes (male and female)? Gender is more of how a person considers themselves i.e. transgender) suffer from Osteoporosis (OP). In the USA, ~34 million have low bone mass, 10 million people have OP, and although 40 percent of women over 50 years suffer with OP during their lifetimes, there are at least 14 million males with Low Bone Mass (LBM) or OP. These men are typically >60 years of age (when andropause takes effect), and often experience other andropause related signs and symptoms (Figures 5 and 6).

The risk of developing OP increases as people age; however, there is a discrepancy between the age of onset between genders due to the ages of onset of menopause and andropause. Most women start being

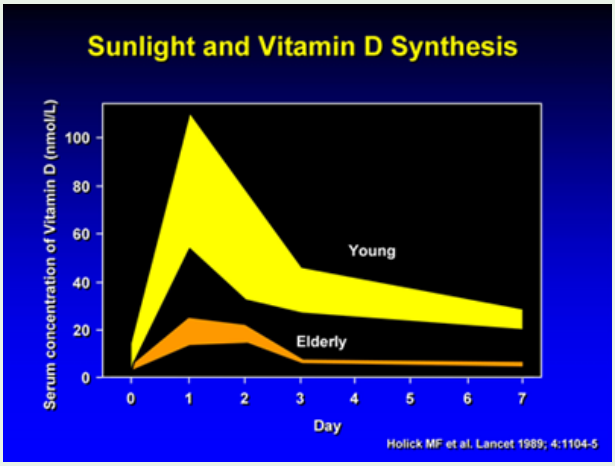

Figure 6: The symptoms of Andropause; arrows ↑indicate increase or decrease↓. Andropause is the male equivalent of female menopause.

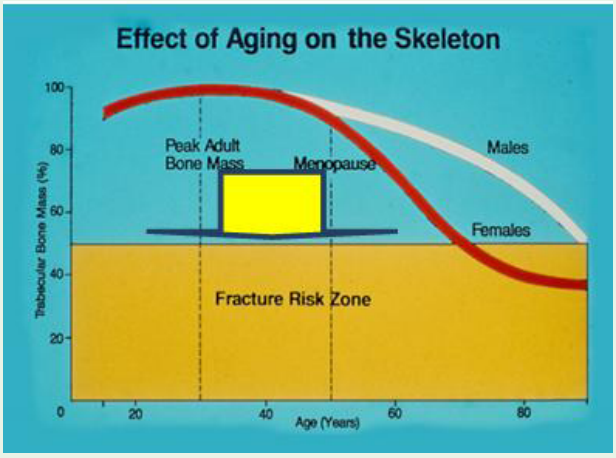

Figure 7: Effect of aging on the skeleton. For men, note the divergence (light blue line off the red line) of males after age 50 years.

affected from age 50, while males become prone to OP one to two decades (on average to fifteen years) later after females (Figure 7).

Men's decline in Bone Mass is slower; males start to lose their bone mass and develop OP nearly 10-15 years after women. Most women become prone to lowering bone mass and OP earlier, from about 50 years (around the age of menopause). Male hormones tend to decline more gradually with age and this impacts bone density [12].

Bone Mineral Density (BMD) mainly as Calcium hydroxyapatite and traces of other ions like Magnesium) is decreased as OP progresses. Optimal Peak Adult Bone Mass (PABM) is considered as 100%, but when the PABM reduces to <45%, the risk from OP increases exponentially. For many decades, reduction of bone mass and density was considered to be a slow and steady progression which occurred over decades, comprising of several vertebral micro-fractures. However, OP has now been deemed to be progress more rapidly than previously thought.

Symptomology of early OP vertebral fractures are not always clearly defined. These fractures produce slight pain, imprecise location and vague backache. Minor collapse from body of vertebral trabecular

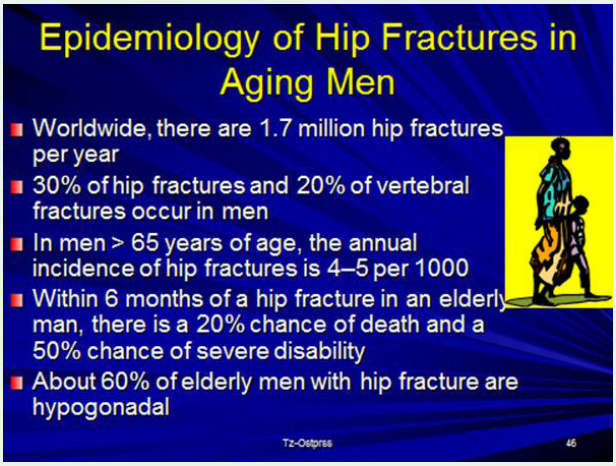

Figure 8: The global epidemiology of hip and vertebral fractures in men.

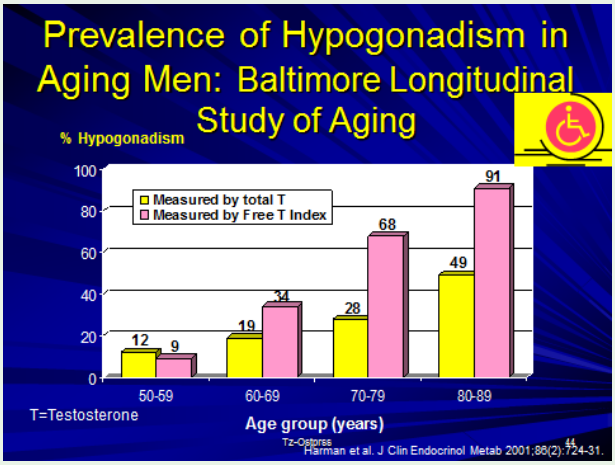

Figure 9: Prevalence of hypogonadism in Men. About 60% of men with hip fractures have low or significantly reduced male endocrine function. [Harman et al. (2001) J Clin Endocronol Metab 86(2) 724-731].

breakage starts slowly manifesting as kyphosis. From upright posture women gradually hunch forward as their vertebrae collapse. This spinal crumple inexorably progresses to kyphosis (hunch-back), until walking becomes impossible. Subsequently they need walking aids (sticks, walkers etc.), or a wheel chair to get around. Their height diminishes, and the folding forward impinges on thoracic space available for chest (heart and lungs), and the upper abdominal organs (stomach, liver, spleen, pancreas) and diaphragm. Loss of bone mass may be slow, but once fractures begin, other fractures tend to follow, especially after minor traumas, accidents or falls, and can result in devastating outcomes. Consequent to kyphosis, organ dysfunction precipitates indigestion, esophageal reflux, respiratory difficulties… all accompanied by discomfort and pain and even incontinence from changed intra-abdominal pressure. OP affects the size, mass, strength and volume of the entire skeletal system. The micro-fractures in OP are frequent in vertebrae, and over time contribute to the final collapse and overt shortening of the spine [7].

Once vertebral OP micro-fractures manifest, other OP fracture

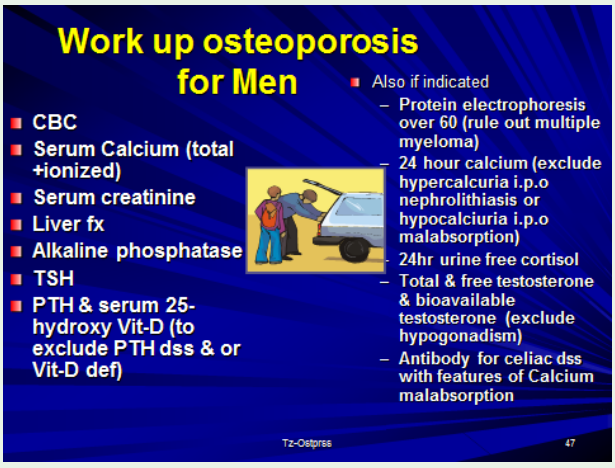

Figure 10: Clinical work-up for OP in Men. CBC= full blood count; fx =function; TSH=Thyroid Stimulating Hormone; PTH=Parathyroid Hormone; dss=disease; def=deficiency.

Table 1: The Major and Minor Risk factors for Men. A combination of both major and minor risks may influence the onset and /or Clinical diagnosis of OP. Xs = excess; < = less than.

Major Risk Factors	Minor Risk Factors (2 or more)
• Non-traumatic loss of vertebral height/kyphosis • Radiographic evidence of osteopenia • Older than 65 years • Hyper-parathyroidism • Hypogonadism • Systemic glucocorticoids • Prior fragility fracture before 40 years of age • Family history oseoporotic fractures • Propensity to fall • Malapsorption	• Low dietary calcium • Weight< 57kg • Cigarette smoking • Xs alcohol/coffee intake • Chronic use of anti-convulsants • Long term heparin • Rheumatoid arthritis

sites around the body often occur within one year. It is important to note that even minor traumas can result in significant fractures due to the vulnerable state of OP bone tissue. In particular, Hip and/or head of femur fractures occur frequently in both genders unwittingly suffering from OP. These tend to result in significant morbidity, including limiting perambulation, and often head of femur or total hip replacement is needed. Studies have shown that hypogonadism in men, as experienced in andropause, not only increases the likelihood of OP, but also the prevalence of hip fractures increases substantially with age. Because of this, early therapy to moderate bone loss and maintain bone mineral density, and to slow down decreasing bone mass, is indicated both women and men (Figures 8 and 9).

There are major and minor "Risk Factors and Clinical Indicators for Males prone to developing OP. Vertebral deformity (Table 1).

Red Flags and contributory co-factors include poor diets, smoking, alcohol consumption, lack of exercise all contribute to a genetically determined propensity to developing OP. Men when over 65 years old, will show signs of OP with these influences. An inactive sedentary lifestyle predisposes to develop in OP. Consequently vigorous exercise at least three times per week encourages minimizing OP development. Also people who uses steroids (like prednisone) to control allergic (chronic asthma), autoimmune diseases (Crohn's Disease) or transplants are prone to develop OP. Women taking medications for hormone suppression are candidates for OP [7-9].

Workup: Investigation of Male OP

After a full history and noting of physical signs and symptoms, other special investigations will confirm the diagnosis. A full blood count and other tests are mandatory; the results of other tests help re-affirm the diagnosis (Figure 10).

Bone mass peaks when people are in their mid-twenties to mid-thirties. Subsequently, bone mass starts decreasing over time. Peak Bone Mass is assessed with T scores, and compared with values compiled by the World Health Organization (WHO). Normal range is accepted at a positive T+ score above T =1, when T= 0, and still acceptable as healthy between 0 and -1. World Health Organization deems osteopenia to exist at T=< - 1, and OP If T= < - 2.5 (Table 1).

The healthy range is between zero loss (T= +2.5), and T= - 1 unit of Peak Bone Mass. More than one unit loss of PBM is labeled as Osteopenia. A T-score below T= -2.5 PBM is consistent with suffering from OP. So, clinical risk factors for developing OP include:

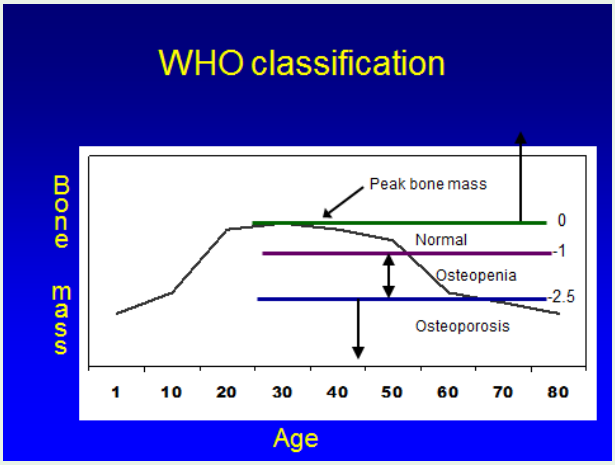

Figure 11: WHO Classification and Graph; showing WHO classification of measures for Bone Mass and Age in OP.

being over 65 years of age; a low BMD; a T-score of T=-2.5; prior fragility fracture, most commonly at the spine, hip or forearm. All these co-factors are aggravated by a genetic calcium metabolic predisposition to OP (Table 2 & Figure 11).

Osteoporosis manifests loss of bone mass due to an imbalance of plasma calcium-phosphorous levels with consequent release of calcium from bone. Primary OP (senile or post-andropausal) or Secondary OP (calcium deficiency, hyperparathyroidism, osteomalacia), both result in healthy men (~15%, with Standard deviation T-scores at T= -1 to -2) do have a lower than normal ratio, but in general if the Ca:P ratio reaches T= -2.5 SDs, OP will become apparent. A significant number of men over 70 have a BMD below T= -2.5 and nearly all of these men have various degrees of bone loss from OP. Decreased Bone Mineral Density. The normal Ca: P ratio has a range consistent with health.

Some clinical confirmation may be done quickly with tests for BMD; Ultrasound of the foot gives a rapid but unreliable provisional diagnosis. Measures of the vertebrae using Dual X-Ray Absorptiometry (DXRA) are preferable and more consistently reliable. This DXRA measures the Calcium/Phosphate crystal density per cm^2. Lower bone density may also be recognized on panoramic full mouth radiography, but it seems the skull in general is more resistant to bone resorption than other peripheral sites, like the hip, vertebrae, ribs and limbs.

Discussion

OP, andropause and men

Males are also at risk for developing OP. Risk factors are similar but different from females. Andropause in Men is the equivalent to female menopause but with female and male hormone changes respectively. Men reach andropause, which occurs at a variable age (50-70), but in general, about ten to fifteen years after women. These men are prone to decreases in bone mineral density, reduced muscle mass and strength, an increase in obesity, a declining libido, increase in erectile dysfunction, a decrease in hematopoiesis, are prone to bouts of depression with a decrease in cognitive function and general well-being.

Epidemiology of hip fractures in aging men

Both vertebral and hip fractures affect men. 20% of all vertebral fractures affect men; women show a higher percentage (>40%). Consequently women tend to be more kyphotic, earlier and more frequently, than men. Globally, there are nearly 1.7 million hip-fractures per year, and of these 30% occur in men. Hematopoiesis is reduced in elderly men, and this impacts calcium blood chemistry. For men over 65 the annual incidence is 4-5 per 1000. After six months of a hip fracture there is a 20% chance of death and a 50% chance of permanent severe disability. About 60% of elderly men with hip fractures are hypogonadal [12].

Major OP risk factors for men include hypogonadism, vertebral deformity, kyphosis or non-traumatic loss of vertebral height, radiographic evidence of osteopenia, age older than 65 years, hyperparathyroidism, use of systemic glucocorticosteroids, a prior fragility fracture before 40 years, a family history of osteoporotic fractures, malabsorption syndrome, and propensity to falls.

Minor OP risk factors for men influence developing OP. Any two concomitant findings of the following will predispose to developing OP in men: these include low dietary calcium intake, weight below 57 Kg (or10%of that at age 25), Cigarette smoking, excess alcohol and coffee intake, chronic use of anti-convulsants, long term use of heparin, rheumatoid arthritis, hyperparathyroidism.

Special clinical investigations needed to assess OP in males

These are similar but slightly different from that of females. The work–up includes: Complete blood count, serum calcium (total & ionized), serum creatinine, liver function and enzymes, alkaline phosphatase, TSH, PTH and serum 25-hydroxy Vit-D (to exclude PTH disease & or Vit-D deficiency). Other investigations (assist in eliminating differential causes): Protein electrophoresis over 60 year (rules out multiple myeloma), 24-hour calcium (excludes hypercalcuria in place of nephrolithiasis, hypocalcuria in place of malabsorption), 24 hour urine free cortisol, total and free testosterone, bioavailable testosterone (to exclude hypogonadism), antibodies to celiac diseases with features of calcium malabsorption.

Special clinical investigations needed to assess OP in females

These have been reviewed in other publications [2,3].

Osteoporosis and the jaws in males [14-20]

Men generally lose their teeth earlier than females. The major cause being neglected oral hygiene and consequent development

Table 2: T-Scores based on WHO criteria.

Clinical diagnostic Categories of Osteoporosis in Andropausal males. [4]	
Category	Definition by Bone Density T-Score
Osteopenia Normal Range	T-score between T= +2.5 and T= -1.
Osteopenia	T-score between T= -1 and T= -2.5
Osteoporosis	T-score less than T= -2.5
Severe Osteoporosis	T-score less than T= -2.5 AND a fragility fracture

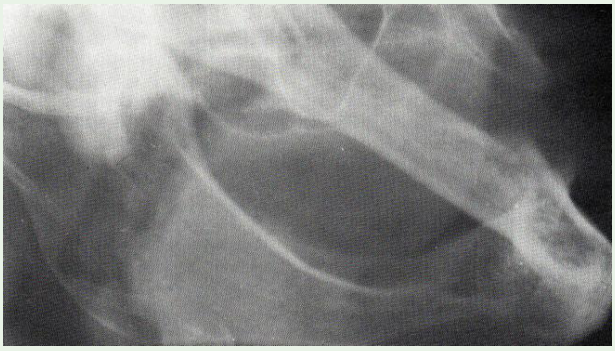

Figure 12: OP Edentulous mandible from a 55year white female with OP. Note thinning of bony cortical plates**.** OP in the jaws is observed in males who are heavy smokers and over the age of 65.

of gum disease. Socio-economic factors (cost of advanced dental therapies) impacts edentulism.

Dentate patients stimulate the jaw bone metabolism on an ongoing daily regimen. Accordingly OP is not always blatantly obvious on jaw radiographs. But since bite-wing radiographs often are taken with check-ups on a regular annual basis, changes may be observed by comparison indicating marrow changes. Also by comparison, panoramic radiographs may show changes indicating OP. Diagnosis by CT is feasible [17] More typical of OP is the development of localized OP defects, which may be confused with other bone pathology, such as simple bone cyst, giant-cell-granuloma, ossifying fibroma, osteosarcoma, aneurysmal bone cyst and others [14]. A biopsy for histopathology investigation is always necessary and will differentiate and/or confirm the diagnosis [16]. With focal OP marrow defect, nothing more than hematopoietic marrow cells are revealed. OP affects most bones, especially the spine pelvis and ribs, but less so the bones of the skull. While focal OP marrow defects are not commonly found in both the maxilla and mandible, they do occur in these bones [15-19] With OP, edentulous jaws will show thinner cortical plates, loss of alveolar bone, a thin mandibular ridge and less dense medullary bone [19] (Figure 12).

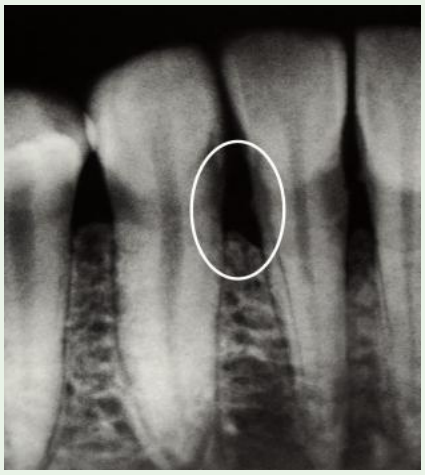

Figure 13: An intra-oral radiograph of a 60 year old with mild periodontitis (probing depths between 3.5mm and 5.5mm: PSR 2) secondary to poor oral hygiene. OP was confirmed with medical diagnosis.

Figure 14: Edentulous male suffering from OP. Note thin lips, deep naso-labial fold, vertical collapse, decreased columella, with over-closure. Proper prosthesis, often stabilized with a few implants can constitute excellent therapy, with huge improvements in appearance, speech, food mastication and quality of life.

Periodontitis: Gingivitis affects over 90percent of the population. At most 30 percent, but more realistically only 8-12 percent of people develops periodontitis. Nearly all periodontitis is mediated through stagnated biofilms which change their invasive destructive capacity over time. While some forms of aggressive periodontitis affect young people and diabetics due to systemic predisposing dysfunctional metabolic factors, most chronic forms of periodontitis affect middle-aged and older people. OP becomes prevalent indentate seniors, less frequently in males than females, but when seniors of both genders suffer from OP and periodontitis, there is a tendency for periodontitis to be more aggressive, rapid and destructive of supporting alveolar bone [17-20] (Figure 7 & 9). Stagnated biofilm produces bacterial toxins enzymes, antigens and mitogens, all of which have a Zone of Influence (ZOI) and biological effect. When teeth are also distressed by occlusal trauma, there is a Zone of Traumatic Effect (ZOTE). When OP is present, the combined effect of ZOI and ZOTE is accelerated alveolar bone loss. Periodontal disease and alveolar supporting bone loss can be successfully controlled through excellent oral hygiene, and professional maintenance, monitoring and therapy. The prognosis for males with appropriate therapy for OP sufferers is excellent (Figure 13).

Radiographs show loss of supporting alveolar bone (circle) [22, 24-26].

General Therapy and Management [26,27]

Therapy and management involves (1) dietary modification, (2) behavior changes (3) moderation of OP through medication (4) oral and dental implications.

Diet and Nutrition as therapy and control of OP [28]

Because low calcium intake and diets are implicated in OP development, dairy products are promoted as high sources of calcium containing foods. Dairy products include, milk (high or low fat), cream, cheeses (especially Boccancini, Cream Cheeses, Mozzarella), yoghurt, skim milk, milk shakes, ice-creams. Whole cow's milk (3.7G total fats), is about 88 percent water, but the solids contain essential nutrients of skeletal growth. Besides calcium, phosphates and magnesium, (all nutrients essential for healthy bone growth), bovine milk also contains: proteins, potassium, sodium carbohydrates

(lactose), Vit-A, Vit-D, Thiamine, Riboflavin, Niacin, Vit B-6 , Folic acid, Vit-B12, Pantothenate and Zinc.

To ensure stable calcium for bone formation the range of calcium intake is 200mg-to over 1000mg/day. The FAO/WHO minimum requirement is close to the minimum requirement, which is low for ideal health. However, the recommended calcium per day for adults is at least 800 mg, and 1200mg+ for teenagers and all seniors over 55 years. People consuming less protein will remain in calcium balance with lower levels of Calcium intake. Only one quarter of calcium intake from cow's milk is retained. Milk is a ubiquitous source of calcium, though a varied diet is easier to sustain (Table 3).

Other nutrient requirements and food sources:

Calcium: Other foods with significant calcium content include: dairy products, butter, yoghurt, almonds, prunes, and seaweed.

Vitamin D is needed for adequate calcium absorption and metabolism at 400 I.U. per day for 19-50 year olds. Over 50 years old, the required Vit-D is 800 I.U per day, double the usual need. With a daily exposure to sunshine of about half an hour, Vit-D is synthesized in the skin. For ages 19to 50, 4 cups of milk will provide 400 I.U. Vit-D; 8 cups of milk is needed for those over 50+ years to get the required 800 I.U Vit-D per day. Besides milk, other sources of Vit-D are in fish oils, nuts, dates, leafy greens and other fats.

Protein: First class protein contains essential amino acids which cannot be synthesized by human metabolism. Collagen is a body protein and its synthesis is a precursor to bone formation. 0.8G/kG body weight first class protein is recommended to sustain good bone density. Sources of protein are lean meat, fish, poultry, eggs, nuts and pulses (beans. lentils, peas etc.)

Sodium: A Total of 2G sodium is needed per day. Consuming excess >2Gper day will reduce bone density. High sodium intakes may disrupt stable metabolism and induce hypertension. Sources from salted foods and table salt added to food to enhance flavor.

Vitamin-C: a daily intake of 60mg a day is adequate. This is double the RDA of Vit C needed for bone synthesis. Excess intake of Vit-C may have pharmacological effects unrelated to the function of the vitamin. Sources are broccoli, parsley, guava, citrus, rose hips and fresh fruits and vegetables.

Phosphorous: The Phosphorous requirement is at least 1:1 for Ca: P, and probably needs more Phosphorous. The average Calcium intake per day is 400-1300mg/d and Phosphorous 800-1500mg/d. Sources vegetables, meats and fruits.

Vitamin K: The average mixed diet provides 300-500 μg/day Vit-K. Extra Vit-K is not recommended for improving bone density. Too much Vit-K, in combination with phytates, may decrease calcium absorption. Food sources include beans, soy products, fruit and leafy greens.

Table 3: Daily Calcium needs and cups of whole cow's milk needed to provide this.

Age in years	Elemental calcium	Cups (350ml) of milk
9-18	1300mg	4 cups
19-50	1000mg	3 cups
Over 50	1500mg	5 cups

Caffeine: A large coffee (355ml) has about 180mg caffeine. More than 4 cups per day is not recommended.

Isoflavine: In post menopause women Bone mass density will be sustained with 200mg 3 X day intake of Ipriflavones, and will slow down development of OP, and maintain Bone Mass Density [12,25].

Behavior modifications

Exercise, and particularly weight bearing activities, slows development of OP. Exercise forces the body to support full weight. This stimulates bone formation and modeling. Brisk daily exercise is needed for 30 minutes. Exercise at least three times weekly is the desirable minimum. Making exercise part of a daily routine assures benefits accrue over time. Playing sports is one pleasurable form of securing benefits of exercise, such as climbing stairs, playing ball games, (like racket ball, tennis, squash) dancing, and jogging. Simply walking daily for a vigorous 30-45 minutes, contributes enormously.

Medications [27,37]

A wide variety of drug therapy is available for post-andropausal OP in men. These include: mainly drugs derived from Bisphosphonates, and possibly hormone (testosterone derivatives) therapy.

Hormonal therapies: It include calcitonin, testosterone and (for females mainly) estrogen replacements [23,37,38].

Calcitonin and Parathyroid Hormone (PTH): A balance exists between calcitonin and PTH; calcitonin promotes calcium deposition, while PTH in physiological doses both encourages calcium deposition, but also, in excess doses PTH may promote calcium resorption. Stable calcium blood serum levels (9-11mgm/100ml) ensure healthy maintenance, but an imbalance causes calcium loss, mainly through the kidneys, and weakening of bones leading to osteoporosis. PTH will contribute to stable calcium/phosphorous blood levels, but excess PTH may cause thinning of cortical bones, giant cell granulomas in and around bones and soft tissue swelling. Excess PTH has other side effects: nausea, vomiting, fatigue, headaches are common, there is excess renal calcium secretion and bone weakening. Should a person suffer from neoplasia or be receiving radiotherapy, PTH therapy is contra-indicated. All anti-resorptive therapy should be stopped when on PTH, and anti-resorptive therapy should only start after PTH [36]. PTH works on the GIT promoting absorption of calcium, on the kidney increasing phosphorous retention, and on bone stimulating deposition or release of calcium. One commercial product for PTH available in North America is Teraparitide (Forteo®), administered sub-cutaneously (sc) and its cost is about 15 X times more expensive than most alternate therapies. Forteo® compares favorably to other successful medications.

Calcitonin (MiacalcinNS®) is available as a nasal spray delivering 200 I.U. sprayed into alternate nostrils daily. The annual cost of MiacalcinNS® is less than Forteo® and is well priced compared to other therapies.

Chemo-Drug Therapy for females should never be assumed to be the same for men. Professional guidance, supervision and advice for medications for OP in men, must be followed. For women Estrogen replacement therapy slows down OP, but also has side effects. Femigel® is an example, Thrombus formation is the major concern when women take hormones for OP [23,37,38]. Various forms of estrogen replacement are used, but are beyond the scope of this perspective.

Bisphosphonates [39-41]: These drugs inhibit bone resorption by constraining osteoclasts. Chemically they are similar to pyrophosphate which is an endogenous regulator of bone resorption. Two phosphonate groups are linked by phospho-ether to form a bisphosphonate (P-C-P). This molecule is easily manipulated and many variants allow many varieties of drugs with the same activity but a slightly modified formula to be registered. Bisphosphonates decrease the metabolic activity and numbers of osteoclasts, and accelerates their apoptosis. It also inhibits osteoclast recruitment and concentrates in lacunae around the osteoclasts. There are 2 major groups, one which contains Nitrogen, the other a Non-Nitrogen containing Group. The Nitrogen group disrupts mevalonate pathway, the Non-Nitrogen group, enters phosphate ATP which inhibits cell functions and hastens apoptosis. In physiological doses bisphosphonates have an affinity for bone, deposit in new bone in close proximity to and in osteoclasts, and will remain in bone for many years (up to a decade) [25].

Bisphosphonate medications may be administered orally, or by Intra-Venous (I.V.) route.

Oral medications include Fosamax® (alendronate sodium tablets; also available as a generic), Didrocal® (etidronate and includes $CaCo_3$); Actonel® (risedronate sodium tablets). Others include Evista® (raloxifene HCl); and Strontium renelate.

Intra Venous drugs include Aclasta® (zolendronic acid as an I.V.); Aredia® (Pamidronate disodium), and Zometa® (Zolendronic Acid).

Dental therapy and management of OP dental patients

Changing, modifying or stopping OP medication should not be done without communicating with the patients controlling physician.

For Male Dentate Patients with OP, most standard procedures can be successfully performed on OP patients. Smokers, are more prone to complications, like dry sockets post-extraction, and delayed healing after minor dento-alveolar or periodontal surgery. Smokers have a higher prevalence of severe periodontitis and are more resistant to periodontal treatment. Severity of alveolar bone loss increases when periodontitis presents in elderly female individuals suffering from estrogen deficiency. General alveolar ridge resorption is accelerated in women without hormone replacement therapy. Type IV bone (thin cortex and scanty medulla) is not ideal for implants; increased possibility of failure should be warned before placement, or alternate conservative therapy selected. However most OP patients sustain additive bone implants and react well to inductive (Decalcified Freeze Dried- DFDB) bone implants. Implants should be placed as early as possible for males. Frequently there is a direct correlation between mandibular and lumbar spine bone mass. A finding of thin delicate mandibular bone, without a definitive diagnosis of OP, warrants immediate referral and follows-up, by a physician [14]. OP is not always obvious on skull and jaw radiographs. Diagnosis of OP is often noted in the medical anamnesis. Careful note of medications (HRT, Vit-D & Calcium supplements, PTH, Calcitonin and /or bisphosphonates) used and whether there is a history of neoplasia, and patients suffering from OP should be informed of increased probabilities of complications arising during therapy.

Edentulous Patients with OP frequently have a prognathic appearance. Other clinically noted signs are: - Thinning of the lips, a deepening of the naso-labial fold, increased deepening labial vertical lines, an increased columella/philtral angle, ptosis of peri-oral muscles, jaw-collapse with over-closure; on Radiograph there may be thinning of cortical plates and marked reduction of alveolar ridges [15]. See Figures 12-14.

Constructing and fitting satisfactory full prosthesis for these patients is extremely challenging. Often, placement of at least two or more stabilizing osseo-integrated implants, are needed. Bone grafts are often indicated to improve denture retention and/or allow for implant placement. Should the bone be so thin, fragile or atrophied, a permanent fixed splint, from the inferior mandibular border holding trans-osseous stabilizers, may be indicated for prostheses.

One major serious oro-dental side effect of Bisphosphonate Therapy (BPT) is the development of Bisphosphonate Osteo-Necrosis of the Jaws (BONJ) [39-43]. BONJ is rare but serious complication, affecting less than 0.1% of cases treated with Bisphosphonate Therapy (BPT.) Patients prone to developing BONJ may suffer from Paget disease, multiple bone myeloma, primary neoplasia of breast (very rare in males, but does occur), prostate, liver, lung or kidney. BPT is also used for controlling hypercalcemia and metastatic bone lesions related to carcinoma. All these patients are candidates for developing BONJ, and require conservative non-invasive treatment.

Clinical presentation of BONJ: BONJ presents as exfoliating whitish, pale avascular bone. Pain is low level or absent. There's peripheral gum inflammation and PSR III (probing depths >5.5 mms). Extraction sockets do not heal. Bony ridge protuberances and mylohyoid ridges are affected, particularly in edentulous jaws [39-41]. Non-vital bone (no feeling or bleeding) protrudes into the mouth and frequently loses its mucosal covering.

In cases with the aforementioned conditions, and on high doses of BPT, these patients are not ideal patients for major invasive periodontal or dento -alveolar surgery. Maxillo-facial, dento-alveolar or periodontal surgery may precipitate BONJ in these cases [39,41]. Yet people treated with BPT for osteogenesis imperfecta, with regular level BPT and can successfully receive most dental and gum treatments without BONJ complications. BPT persists in the system for years, and should extractions or major periodontal infections require treatment, these should be done and stabilized whenever possible before implementing anti-resorptive therapy by BPT. Sufferers of BONJ-prone cases require regular monitoring, anti-septic lavages and rinses (typically 0.02% Chlorhexidine is used) and antibiotic cover. Hospitalization is desirable to articulate a team of a physician, an oral-medicine specialist and a maxillo-facial surgeon. New invasive oro-dental therapies should be eschewed, but non-vital involucra must be removed to avoid developing osteomyelitis. Care of general nutrition is similar to management of patients suffering from cancer [42-45].

Discussion

OP is not a condition confined to Females. OP in Males is a frequent occurrence. All men over 65 years old should include bone assessments as part of their annual check-ups. Early initiation of behavioral and drug therapy optimizes delay of onset of OP.

For diagnosis of OP, femoral neck measures and lumbar spine for low Bone Mass Density, specificity and positive predictive value are higher (over 82%) and more reliable than compared to only 73%

with only Oral Panoramic radiography alone [15]. Tobacco smoking seriously aggravates OP. Smoking accelerates onset and progress of OP by its toxic effects but particularly by reducing blood flow to all organs, including bones. Smokers should quit as soon as possible. Nearly all the bisphosphonate drugs (not MiacalcinNS*, which is a calcitonin nostril spray) are taken orally (per os… p.o.) over a long period of time. Didrocal* (Etidronate) is prescribed as 400mg po X 14 days every 3 months and $CaCo_3$ as 500mg p.o., daily for 3 months. Costs vary for each drug, and recommended scripting, posology and delivery regimens should be followed. These drugs are effective with clinical improvements recorded over decades. Annual costs are much more affordable than hormones (PTH) and consequently are widely successfully and frequently prescribed for osteoporosis [38]. Healthcare workers managing OP patients should have OP cases mouth fully checked out and stabilized, preferably by a dental specialist, before prescribing BPT. Dental health care workers need to be on the lookout for red-flags when treating OP patients.

Conclusion

OP is a chronic insidious, debilitating disease of aging, slowly affecting the quality of life of both genders. Very few people show no signs of OP as they age. The onset of symptoms may be slow, especially in Males, but the inexorable results of OP are progressive frailty and increased proneness to bone fractures with age. A healthy balanced diet, rich in calcium combined with daily rigorous exercise seems to be the sole natural formula for retarding OP. Traditional consumption of health liquids like water, soups or milk, is being replaced by increased drinking of soda-pop (USA teenagers up to 6 cans per day); and this pop-substitution for liquids, is contributing to increased prevalence's of OP [46]. The aging process may be related to the limited number of times human cells, particularly the whole range of bone forming cells, both cartilaginous and intra-membranous, can divide before reflecting signs of break up or dysfunction. This from the Hayflick phenomenon or limit, which is determined by the number of times a cell will multiply through mitosis, until it undergoes a programmed cell death. Telomeres loose small portions as cells multiply, till the dividing cell DNA becomes dysfunctional [47,48]. Age inevitably affects the entire body's metabolism, and the skeleton is not omitted from this process. The skull seems less affected by OP than the vertebrae, hips or long bones. Possibly more bone metabolic factors will be discovered to restore healthy bone function. Falls by elderly males remains the most prevalent cause of bone morbidity. Oral health may be affected by OP; regular home and professional maintenance will ensure functional dentate status well into the last light of twilight years. Edentulous oral cripples have a wide range of successful progressive options to replace mastication with restorative dentistry. Medications help to avoid and reduce bone fractures but do not totally stop, nor totally cure, existing OP. Constant vigil, monitoring, adjusting diets, physical habits and medication, are all needed to live with the reality of OP. Osteonecrosis of the jaws (ONJ) is a rare complication and precise management is unresolved; management is by prevention of ONJ, is feasible mainly by completing all invasive dentistry before prescribing bisphosphonates. Developed ONJ is treated by resecting dead bone and concomitant stringent oral hygiene.

Data on Drugs Cited:

Note: Cost is estimated in Cdn$ for one year's supply.*

Evista* (raloxifene HCl) is a registered trademark of Eli Lilly Company. 60mg, po.od…. Cost ~$706.

Miacalcin* (calcitonin salmon) Nasal Spray is a registered trademark of Novartis Pharmaceuticals Corporation. 1 Spray 200 I.U., alternate nostrils daily…….. Cost $740.

Fosamax* (alendronate sodium tablets) is a registered trademark of Merck & Company, Inc., 10mg, po, od,…… cost $460; or 70mg po qwk……$640.

Actonel* (risedronate) 5mg po od……Cost $622; or 35mg po qwk……Cost$473.

Forteo* (Teraparitide) 20mg sc od…… …… …….. Cost $9600.

Didrocal* (Etidronate)400mg x 14 days q 3months, & $CaCo_3$ 500mg X 76 q 3 mths……Cost$170.

od=every Day; po= by mouth; qwk=every week; i.u.=International Unit; q= every; sc= sub cutaneously;

*Dispensing fees are not included in all costs cited here: this may be between $40 and $60 extra.

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