Osteoporosis: Evolving Treatment Options
Janelle Sheen, PharmD

Prevalence
Osteoporosis is a major public health concern for approximately 44 million Americans. Of the ten million Americans that are estimated to have osteoporosis, eight million are women and two million are men. An additional 34 million Americans are estimated to have low bone density, placing them at increased risk for osteoporosis and fractures.¹

Prevention
Osteoporosis is a disease that is characterized by low bone mass and structural weakening of bone tissue that can lead to an increased risk of fractures. In 2005, osteoporosis was responsible for an estimated two million fractures and $19 billion in costs. By 2025, experts predict that osteoporosis will be responsible for approximately three million fractures and $25.3 billion in costs each year. Osteoporosis is often left undiagnosed due to the absence of symptoms, and it is typically not a disease that is addressed until vertebral collapse or a fracture has occurred.¹ It is important that health professionals are aware of the recommendations for the prevention, diagnosis, and treatment of osteoporosis.

Health care providers should educate their patients on the most efficacious prevention techniques, and these include recognizing risk factors as seen in Table 1, identifying those at high risk for falls, and reiterating healthy lifestyle changes.² These lifestyle modifications include aerobic exercise such as walking or bike riding for 30-60 minutes everyday. Smoking cessation has also been shown to decrease fracture risk by increasing bone mineral density (BMD). Alcoholic moderation is another important component of fracture prevention. It is recommended that both men and women consume alcohol in moderation, as >/= 3 drinks has been found to be detrimental to bone health.³ The longer a patient complies with osteoporosis recommendations, the lower the risk of a fracture.⁴

Calcium and Vitamin D
While all groups agree calcium and vitamin D supplementation are important, the recommended daily amounts of each vary from one professional group to another. In general, all adults should consume at least 800mg-1000mg of elemental calcium a day in at least two divided doses. Postmenopausal women over the age of 50 years should receive 1000mg-1200mg of elemental calcium per day in divided doses.³,⁵,⁶ Men over the age of 50 years should receive 800mg-1000mg of calcium per day.³,⁵,⁶ It is important to note that all calcium supplements differ in their elemental calcium content; for example, a 500mg Tums Regular Strength chewable tablet of calcium carbonate contains only 200mg of elemental calcium. More calcium supplement information refer to the “Quick Reference” below.

<table>
<thead>
<tr>
<th>Calcium “Quick Reference”</th>
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<tbody>
<tr>
<td><strong>Calcium Supplement Type</strong></td>
</tr>
<tr>
<td>Carbonate</td>
</tr>
<tr>
<td>Tricalcium phosphate</td>
</tr>
<tr>
<td>Citrate</td>
</tr>
<tr>
<td>Lactate</td>
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<tr>
<td>Glucosate</td>
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</table>
In the last several years there has been much debate about the appropriate recommended daily intake (RDI) of vitamin D. Current guidelines recommend 400-1000 IU per day of vitamin D₃ (cholecalciferol) for individuals age 50 and older. Adults < 50 need 400-800 IU of vitamin D₃ daily. Vitamin D₃ is the form of vitamin D that best supports bone health. These recommendations were revised due to a growing body of evidence that calcium and vitamin D deficiency is widespread.

Table 1: Risk Factors for Osteoporosis ¹,²,⁸

| Caucasian or Asian race | Skeletal disorders: osteogenesis imperfecta, rickets, hypophosphatasia, and spinal cord injury. |
| Female gender | Endocrine and metabolic: hypogonadism, hyperparathyroidism, thyrotoxicosis, Cushing syndrome, metabolic acidosis, and Gaucher’s disease. |
| Postmenopausal women* with family history | Other disease states: cystic fibrosis, systemic lupus, rheumatoid arthritis, end stage renal disease, malabsorption, bone marrow diseases, and hypercalcioia. |
| Advanced age (especially with recurrent falls) | Medications: glucocorticoids, phenytoin, gonadotropin releasing hormone agonists, methotrexate, excess thyroid hormone, heparin, cyclosporine, and depot-medroxyprogesterone acetate. |
| Poor health, frailty, below healthy weight | |
| Personal history of fracture as an adult | |
| Inadequate physical activity | |
| Excessive alcohol intake | |
| Anorexia | |
| Current cigarette smoking | |
| Low calcium intake (lifelong) | |

*Which can also include: menopause before age 45, having both ovaries removed, or the absence of menstrual periods for a year or more prior to menopause.

Screening for Osteoporosis

The diagnosis of osteoporosis is established by measurement of BMD. Dual-energy x-ray absorptiometry (DXA) measurement of the hip and spine is used to establish or confirm a diagnosis of osteoporosis, predict future fracture risk and monitor patients by performing serial assessments.³,⁹ The BMD diagnosis of normal, low bone mass, osteoporosis and severe or established osteoporosis is based on the World Health Organization (WHO) diagnostic classification. A BMD that is within 1 SD of a “young normal” adult (T-score at -1.0 and above) is considered normal. Low bone mass (osteopenia) is a T-score between -1.0 and -2.5 and osteoporosis is a T-score at or below -2.5.

The decision to perform bone density assessment should be based on an individual’s fracture risk profile and skeletal health assessment. The following are indications for BMD testing:

- Women age 65 and older and men age 70 and older, regardless of clinical risk factors
- Younger postmenopausal women and men age 50 to 69 about whom there is concern based on clinical risk factor profile
- Women in the menopausal transition if there is a specific risk factor associated with increased fracture risk such as low body weight, prior low-trauma fracture or high risk medication
- Adults who have a fracture after age 50
- Adults with a condition (e.g., rheumatoid arthritis) or taking a medication (e.g., glucocorticoids in a daily dose ≥ 5 mg prednisone or equivalent for ≥ three months) associated with low bone mass or bone loss
- Anyone being considered for pharmacologic therapy for osteoporosis
- Anyone being treated for osteoporosis, to monitor treatment effect
- Anyone not receiving therapy in whom evidence of bone loss would lead to treatment
- Postmenopausal women discontinuing estrogen should be considered for bone density testing

Treatment

Osteoporosis treatment has been greatly advanced within the last century. Candidates for treatment include those with a hip or vertebral fracture, those with a BMD T-score less than or equal to -2.5, postmenopausal women and in men 50 years and older who have low bone mass or osteopenia with a T-score of -1.0 to -2.5, and lastly those at significant risk for osteoporosis.³,ⁱ⁰ Traditionally, hormone therapy (HT) had been used for the prevention and treatment of osteoporosis. However, since the Women’s Health Initiative (WHI) trial, the U.S. Food and Drug Administration (FDA) has discouraged using HT primarily for osteoporosis. Currently the
manufacturer’s labeling for all HT products states that HT should only be used in low doses and for physicians to prescribe other non-hormone containing products for the treatment of osteoporosis.\textsuperscript{10,11} Table 1 compares the currently available osteoporosis treatments.

**Bisphosphonates:** The most commonly prescribed medications for the treatment of osteoporosis are the bisphosphonates. Agents in this class indicated for osteoporosis include the oral medications risedronate (Actonel\textsuperscript{®}, Actonel\textsuperscript{®} with Calcium, Atelvia\textsuperscript{®}), alendronate (Fosamax\textsuperscript{®}, Fosamax\textsuperscript{®} Plus D), and ibandronate (Boniva\textsuperscript{®}). Bisphosphonates work by inhibiting osteoclast adherence to the bone surface; therefore decreasing bone resorption. With proper use of these agents, the risk of fracture is reduced by 45-55\% at all skeletal sites including vertebral, nonvertebral, and hip.\textsuperscript{11} The most common adverse effects are nausea, abdominal pain, and dyspepsia. Esophageal, gastric, or duodenal ulceration and bleeding can occur if administration directions are not followed. These medications should be taken in the morning with at least four ounces of water, and at least 30 minutes before consuming any food or other medications. The patient should not recline or lie down for at least 30 minutes after taking a bisphosphonate to reduce the risk of gastrointestinal irritation.\textsuperscript{7}

Contraindications for bisphosphonates are hypersensitivity, hypocalcemia, inability to sit or stand upright for 30 minutes, and any abnormalities of the esophagus. Bisphosphonates are also cautioned to have increased gastrointestinal side effects with the use of non-steroidal anti-inflammatory medications, and decreased efficacy when coadministered with metallic cations such as antacids and iron supplements.\textsuperscript{7} Use of bisphosphonates in patients with renal impairment is cautioned when serum calcium is high in order to decrease osteoclastic bone resorption.\textsuperscript{7}

Raloxifene is contraindicated in active thromboembolic disease and the product should be discontinued at least 72 hours prior to prolonged immobilization.\textsuperscript{7} The use of this product is cautioned in patients with high risk for thromboembolism, cardiovascular disease, a history of cervical/uterine cancer, and women with a history of hypertriglyceridemia.

**Calcitonin:** Calcitonin nasal spray (Fortical\textsuperscript{®} or Miacalcin\textsuperscript{®}) is a thyroid hormone that is naturally released when serum calcium is high in order to decrease osteoclastic bone resorption.\textsuperscript{7} Treatment with this medication can reduce the incidence of new fractures by 36\%, but efficacy with nonvertebral fractures has not been consistent. The reduction in new fracture risk for calcitonin nasal spray (Fortical) is not significant enough compared to other osteoporosis medications to warrant it being used as a first line treatment. Therefore, calcitonin is reserved primarily for use in patients who have failed primary therapy, contraindications, or have had intolerable adverse events to other more efficacious treatments.\textsuperscript{10,11}

Adverse reactions to calcitonin include rhinitis and back pain most frequently, but other side effects may occur. Nasal adverse events may be more common in patients over 65 years of age, and if nasal ulceration occurs, temporary withdrawal may be necessary. Hypersensitivity is the main contraindication for this medication because the nasal spray is currently derived from salmon.\textsuperscript{7}

**Teriparatide:** Teriparatide (Forteo\textsuperscript{®}) is a version of human parathyroid hormone that causes decreased osteoblast apoptosis and results in increased bone formation. Teriparatide has been found to reduce the risk of new vertebral fractures by 65\% and nonvertebral fracture by 53\% with a 20 mcg/day dosage.\textsuperscript{11} It is important to note that teriparatide is only indicated for a duration of under two years and because it is an injection, these factors limit its use to a second-line therapy.\textsuperscript{4,10} It should not to be used concomitantly with bisphosphonates because they may decrease the efficacy of teriparatide. Adverse reactions include hypertension, syncope, angina, and dizziness. Nausea, dyspepsia, rash, transient hypercalcemia, rhinitis, pharyngitis, arthralgia, and weakness occur frequently but it has not been shown to prevent nonvertebral fractures.\textsuperscript{7}

There are several contraindications with teriparatide: patients with Paget’s disease, unexplained elevated alkaline phosphatase, open epiphyses, and prior skeletal radiation exposure. There is currently a black box warning in the manufacturer’s labeling concerning osteosarcoma. This warning states that there is an
increased risk of osteosarcoma associated with the duration and dose of teriparatide. Therefore, any patients at risk for osteosarcoma should avoid use of this medication.

**Injectable Treatments:** A growing number of injectable treatments are available for the treatment of osteoporosis. Ibandronate (Boniva®) is a bisphosphonate given four times a year while zoledronic acid (Reclast®) is given only once yearly. Both of these are given by intravenous infusion. A new agent is now available for subcutaneous injection, called denosumab (Prolia®). Denosumab is administered every six months and works by inhibiting osteoclast formation, function, and survival, thereby decreasing bone resorption and increasing bone mass and strength in cortical and trabecular bone. These treatments offer more options for patients looking for alternative agents for osteoporosis.

**Table 1: Osteoporosis Treatments**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosage</th>
<th>Route</th>
<th>Cost Legend</th>
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<tbody>
<tr>
<td>Alendronate (Fosamax®, Fosamax® Plus D)</td>
<td>5mg/day, 10mg/day, 35mg/week, 70mg/week</td>
<td>Oral</td>
<td>*</td>
</tr>
<tr>
<td>Calcitonin (Fortical®, Miacalcin®)</td>
<td>200IU/day (nasal), 100IU every other day (inj.)</td>
<td>Nasal spray / SQ or IM Injection</td>
<td>**</td>
</tr>
<tr>
<td>Denosumab (Prolia®)</td>
<td>60mg every 6 months</td>
<td>SQ Injection</td>
<td>***</td>
</tr>
<tr>
<td>Ibandronate (Boniva®)</td>
<td>150mg/month (oral), 3mg every 3 months (inj.)</td>
<td>Oral and IV Injection</td>
<td>**</td>
</tr>
<tr>
<td>Raloxifene (Evista®)</td>
<td>60mg/day</td>
<td>Oral</td>
<td>**</td>
</tr>
<tr>
<td>Risedronate (Actonel®, Actonel® with Calcium, Atelvia®)</td>
<td>5mg/day, 35mg/week, 75mg for 2 days monthly, 150mg monthly</td>
<td>Oral</td>
<td>**</td>
</tr>
<tr>
<td>Teriparatide (Forteo®)</td>
<td>20mcg/day</td>
<td>SQ Injection</td>
<td>***</td>
</tr>
<tr>
<td>Zoledronic acid (Reclast®)</td>
<td>5mg once yearly (treatment), 5mg every two years (prevention)</td>
<td>IV Infusion</td>
<td>***</td>
</tr>
</tbody>
</table>

**Recent Concerns With Osteoporosis Drugs:** Recent data suggest a rare but possible risk of atypical femur fractures with long-term bisphosphonate use. The proposed mechanism is that long-term use might inhibit bone turnover and delay healing of micro-cracks which occur with normal daily activity. However, causality has not been established as these fractures also occur in osteoporotic patients who have not been treated with bisphosphonates. Experts recommend stopping bisphosphonates after five years in patients at low risk for osteoporotic fractures, and recommend checking bone density at least every two years. Therapy can be restarted if bone density falls more than 4% in the spine or 5% in the hip. At high risk due to very low bone density, previous fracture, or corticosteroid use, should consider continuation of the bisphosphonate. Physicians should consider the risks and benefits for each individual patient.

There has also been data suggesting a correlation between bisphosphonates and osteonecrosis of the jaw (ONJ). While rare, it has been linked to dental procedures including tooth extractions. Symptoms of osteonecrosis are severe pain and swelling in the jaw and loose teeth. Proper oral hygiene, including teeth brushing and flossing, can prevent jaw osteonecrosis. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of bisphosphonate treatment reduces the risk for ONJ. Clinical judgment of the treating health care provider should guide the management plan of each patient based on individual benefit/risk assessment.

**Conclusion**

Osteoporosis can be a devastating disease. Fortunately, new medications have been developed that offer safer and more efficacious options for the prevention and treatment of osteoporosis. Prescribers should be aware of the novel treatments and their place in therapy. Fractures are associated with significant morbidity and mortality. Six months after a hip fracture, only 15% of patients can walk across a room without aid. One in
five of those patients who were ambulatory prior to their fracture will now need long-term care. Lastly, an average of 24% of hip fracture patients age 50 years and over will die in the year following their fracture. It is crucial to implement effective osteoporosis treatment and prevention strategies in eligible patients.

References:

Update to Herpes Zoster Vaccine
Zostavax® is indicated for prevention of herpes zoster (shingles) in individuals 50 years of age and older and is not indicated for the treatment of zoster or postherpetic neuralgia or as a substitute for live varicella virus vaccine. It is not indicated for use in children or persons less than 50 years of age as there is insufficient data to recommend vaccination in these groups at this time.1,2,3 Even though the safety and efficacy of Zostavax® have not been studied in patients with a history of herpes zoster infection, these persons can still be vaccinated without any additional safety concerns.2,4

References:

To report medical fraud, contact the Medicaid Quality Assurance Bureau. NM Medicaid Fraud@state.nm.us or (505) 827-3100 or (505) 827-3185.

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