



## SECONDARY OSTEOPOROSIS

### Drugs and Diseases that can Cause Bone Loss, Falls and/or Fractures

**T**here are several well known risk factors for osteoporosis and osteoporotic fractures such as age, sex, low body weight, a low bone mineral density, a past fragility fracture, having a parent who had a hip fracture and a past history of fall(s). Less well known are which medications and medical conditions can increase the risk of osteoporosis and osteoporotic fractures either by causing more thinning of bones, by increasing the risk of falls or both. Osteoporosis that results from having another disease or condition or from the treatment of another condition is called secondary osteoporosis. This fact sheet will present a brief summary of the commoner causes of secondary osteoporosis.

#### MEDICATIONS

##### SYNTHETIC GLUCOCORTICOIDS (E.G. PREDNISONE)

Glucocorticoids are produced naturally by the body as cortisol or cortisone, and are necessary for normal metabolism, growth and responding to physical stresses such as infection, injury and inflammation. However, high levels of glucocorticoids (both natural and synthetic) are associated with reduced activity of the bone-forming cells and increased activity of the cells that break down bone, which may result in bone loss. Synthetic glucocorticoids (e.g. prednisone, dexamethasone) are widely used in a variety of conditions because they are very effective anti-inflammatory

drugs. Hydrocortisone and cortisone acetate are used to treat individuals who are deficient in cortisone.

Glucocorticoids are taken in a number of different ways. Bone damage more commonly results from the long-term use of glucocorticoid pills, such as prednisone, when taken at a dose of 7.5 mg (or more) daily for 3 (or more) months (these do not have to be consecutive) in the previous year. Glucocorticoid joint injections, inhalers, skin creams or eye drops have not been shown to increase the risk of osteoporosis. If treatment with glucocorticoid pills such as prednisone is required, bone health should be carefully monitored.

##### BREAST CANCER DRUGS

Aromatase inhibitors anastrozole (Arimidex®), letrozole (Femara®) and exemestane (Aromasin®) are used in the treatment of breast cancer. They prevent estrogen production, which results in extremely low blood levels of estrogen. These drugs have been shown to cause bone loss, and some studies have also shown increased risk of fractures, particularly at the spine and wrist.

##### PROSTATE CANCER DRUGS

Androgen deprivation therapy is a type of treatment for prostate cancer in which the source of male sex hormone is removed. Androgen deprivation therapy has been associated with reduced bone mineral density, which is greatest during the first year of therapy in men aged 50

years and older. This results in an increased risk of fractures.

##### “HEARTBURN” DRUGS

Proton pump inhibitors, such as Prevacid®, Losec®, Pantoloc®, Tecta®, Pariet® and Nexium®, are drugs that are used to treat acid-related diseases such as reflux, heartburn and ulcers. These drugs reduce the amount of acid produced in the stomach. Long-term use (several years) of proton pump inhibitors, particularly at high doses, has been associated with an increased hip fracture risk in older adults. This may be due to less calcium absorption from foods in the presence of lower stomach acid.

##### DEPO-PROVERA

When used for contraception, the long-term use of injectable Depo-Provera has been shown to result in a significant reduction in bone mineral density. Most of this bone loss is reversible after the drug is discontinued.

##### EXCESSIVE THYROID HORMONE REPLACEMENT

Normal thyroid hormone blood levels maintain good bone health. In individuals who are on thyroid replacement therapy (Synthroid®, Eltroxin®), the dose needs to be monitored to ensure that the blood levels of thyroid hormone stay in the normal range. Monitoring is especially important in older adults because the dose required may decrease with age. Excessive thyroid replacement in

older adults has been associated with abnormal heart rhythms and muscle weakness, both of which increase the risk of falls and fractures. Excessive thyroid hormone replacement can also reduce bone mineral density and bone quality, which may also lead to fractures.

### ANTI-SEIZURE AND MOOD-ALTERING DRUGS

The anti-seizure drugs carbamazepine (Tegretol®) and phenytoin (Dilantin®) have been associated with a reduction in bone density and this is believed to be due to low vitamin D and decreased intestinal absorption of calcium. Drugs that act on the central nervous system can cause falls by causing drowsiness, confusion, a drop in blood pressure, abnormal heart rhythms or a change in the normal functioning of the nerves and/or muscles of the body. Examples are some antidepressants, some types of sleep aids such as benzodiazepines and some antipsychotic medications. The risk of falling increases as more of these medications are taken, particularly during the start or the sudden discontinuation of these drugs. Antidepressants and sleep aids have also been associated with an increased risk of hip fractures during the first few weeks of starting these drugs.

### BLOOD PRESSURE MEDICATION

Recent studies have shown that some of the common drugs used to treat high blood pressure can increase the risk of falls and fractures in older adults. This occurs during the first few weeks of treatment because of a drop in blood pressure. Some of these drugs have also been associated with an increased risk of hip fracture when the drug is started. These drugs are important for reducing the risk of heart attack and stroke, but in order to prevent falls, caution should be taken when first starting them.

### DIURETICS

Diuretics, such as furosemide

(Lasix®), are commonly used to treat the fluid retention and swelling caused by heart failure. They work by increasing urination and they also promote calcium excretion from the kidneys. As a result, they have been associated with reduced bone mineral density at the hip. They have also been associated with an increased risk of hip fracture within the first 7 days of starting treatment in older adults, which is likely due to an increase in falls.

### PROSTATE DRUGS

Alpha adrenergic blockers such as tamsulosin (Flomax®) are commonly used for the treatment of benign prostatic hyperplasia (enlarged prostate or BPH) in men. Older adults are more susceptible to the side effects of these drugs, which may include dizziness, weakness, changes in blood pressure and falling. As a result, older men are at increased risk of hip fracture in the first month after starting an alpha adrenergic blocker.

### OTHER DRUGS

There are other drugs that have limited scientific evidence for affecting fracture risk. These include:

1. The use of *acetaminophen* (e.g. Tylenol®) for a period of at least 3 years (dose uncertain) compared to non-users has been associated with an increased risk of fracture.
2. *Narcotic* and *opioid* medications used for pain, such as morphine, have been associated with an increased risk of fracture secondary to falling due to the effects on the central nervous system, which may lead to dizziness or changes in balance.
3. *Aluminum-containing antacids* such as Maalox®, Mylanta®, Amphogel®, Gelusil® and Roloids® are often taken for the treatment of heartburn. These over-the-counter medications may inhibit phosphate absorption from the intestine, which may reduce

bone mineral density. In patients with impaired renal function, the aluminum may impair bone mineralization and this may be associated with fractures.

4. *Thiazolidinediones* such as rosiglitazone (Avandia®) and pioglitazone (Actos®) are drugs used to treat type 2 diabetes. In men and women aged 40 years and older who were started on these drugs, there was an increased risk of fracture and this risk increased with longer duration of thiazolidinedione use (4 years or more).
5. *Antirejection/immunosuppressive therapy* such as cyclosporine (Neoral®) and tacrolimus (Prograf®) used after organ transplant may increase bone loss.
6. *Heparin* is a blood thinner. When used for a short period of time the effect on the skeleton is minimal, but with long-term use it may reduce bone density.
7. Some *cancer chemotherapy drugs* may cause ovarian failure in women, resulting in premature menopause, or testicular failure in men, resulting in low testosterone levels, both of which lead to bone loss. In addition, some cancer treatments include glucocorticoid therapy that may further increase bone loss.

### MEDICAL CONDITIONS

A variety of diseases or conditions can increase bone loss and/or fall risk. Some of the more common examples are discussed below.

### RHEUMATOID ARTHRITIS AND OTHER RHEUMATOLOGICAL CONDITIONS

An inflammatory disease of the joints, rheumatoid arthritis is often treated with glucocorticoids, usually prednisone. Pain and loss of joint function can lead to inactivity, which can further contribute to bone loss. Research suggests that osteoclast

(a bone removing cell) activity and bone resorption is increased at the affected sites. In addition to rheumatoid arthritis, ankylosing spondylitis has been associated with bone loss. Several other rheumatological conditions may affect the joints, resulting in poor balance and increased risk of falls, including lupus, psoriatic arthritis and severe osteoarthritis of the hip or knee.

### MALABSORPTION SYNDROMES

Malabsorption can result from bowel diseases such as Crohn's disease, ulcerative colitis and celiac disease, and other conditions that affect the bowel such as weight loss surgery. These conditions reduce the absorption of nutrients from the intestine including dietary calcium and vitamin D. The result is lower levels of calcium and vitamin D, which can increase bone loss and falls risk, leading to fractures.

### SEX HORMONE DEFICIENCY (HYPOGONADISM)

In women this generally results in the early stoppage of menstrual periods (amenorrhea). Common causes include premature menopause (before the age of 45), eating disorders such as anorexia nervosa, exercise-induced amenorrhea (typically seen in high performance athletes and dancers), pituitary disease, chemotherapy and chronic illness. Some of these conditions can be treated with hormone therapy.

In men low levels of testosterone can be caused by a number of conditions including liver disease, pituitary disease, chemotherapy, chronic illness and ageing. Some of these conditions can be treated with testosterone.

### PRIMARY HYPERPARATHYROIDISM

The parathyroid glands produce parathyroid hormone, which controls blood calcium levels. In primary hyperparathyroidism a tumour (generally benign) in one or more of these glands causes the production of more parathyroid hormone than

is needed. This causes an increase in bone turnover, which results in excess calcium release from bone and a rise in the level of calcium in the blood. As a result, the risk of osteoporosis and fractures also increases.

### CHRONIC KIDNEY DISEASE

Many patients with chronic kidney disease are treated with glucocorticoids such as prednisone, which puts them at risk for developing osteoporosis. In addition, chronic kidney disease may cause several different metabolic bone diseases (called renal osteodystrophy) that are associated with reduced bone formation, hyperparathyroidism, and vitamin D deficiency. In renal osteodystrophy bone quality is poor, and this increases the risk of fracture.

### CHRONIC LIVER DISEASE

Chronic liver disease is associated with reduced bone formation, vitamin D deficiency and low sex hormones, all of which may result in bone loss. In addition, some forms of liver disease may be treated with glucocorticoids such as prednisone, which may cause even greater bone loss. Up to 50% of patients with chronic liver disease develop osteoporosis.

### DIABETES

There is evidence to suggest that both men and women with type 1 diabetes are at higher risk for low bone density and for osteoporotic fractures. Poorly controlled type I and type II diabetes are often associated with hypoglycemic episodes (low blood sugar) and/or neuropathy (poor sensation) in the feet. Both of these complications of diabetes can increase the risk of falls and fractures.

### CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

COPD is a type of chronic lung disease that usually results after

prolonged smoking but can also occur due to other causes. COPD can consist of chronic bronchitis or emphysema or both, and is often associated with a chronic cough, phlegm production, shortness of breath on exertion or at rest (depending on the severity) and frequent chest infections. There is a strong association between COPD and low bone mass or osteoporosis, usually from a combination of factors such as smoking history, low body weight, poor nutrition and treatment with oral glucocorticoids.

### UNTREATED HYPERTHYROIDISM

Normal thyroid hormone levels maintain good bone health. Too much thyroid hormone interferes with the body's ability to absorb calcium into the bones and increases bone turnover, which can cause bone loss over time.

### NEUROLOGICAL DISORDERS

Many neurological disorders are associated with an increased risk of fractures (broken bones) because they increase fall risk, bone loss or both. For example:

1. Conditions or injuries resulting in *immobility* are associated with bone loss. This includes stroke, multiple sclerosis and spinal cord injury.
2. Conditions or injuries that result in *poor balance*, or problems with *gait* or *movement*, are associated with an increased risk of falls and fractures. These include cerebral palsy, multiple sclerosis, Parkinson's disease, spinal cord injury, stroke, confusion (due to dementia or delirium), dizziness and vertigo, and lower limb muscle weakness.
3. *Neuropathy* (numbness or reduced sensation) of the feet or legs can also lead to poor balance. This includes diabetic neuropathy, sciatica and other types of neuropathy.

OTHER MEDICAL CONDITIONS THAT MAY INCREASE RISK OF OSTEOPOROTIC FRACTURE	DRUG TREATMENT MAY CAUSE BONE LOSS	CONDITION MAY INCREASE BONE LOSS	CONDITION MAY INCREASE FALL RISK
Cushing's syndrome		•	
Pituitary disease		•	
Multiple myeloma	•	•	
Leukemia and Lymphoma	•		
Thalassemia major		•	
AIDS/HIV	•	•	
Low blood sugar			•
Dehydration			•

The Table above summarizes other conditions or diseases that may increase the risk of fracture by increasing either bone loss or fall risk or both.

## HOW TO MINIMIZE THE HARMFUL EFFECTS OF MEDICATIONS AND OTHER MEDICAL CONDITIONS ON BONE

### TALK TO YOUR DOCTOR

This fact sheet may not include all medications or all medical conditions that can contribute to fractures. If you are taking any medications or suffer from any medical conditions that may increase bone loss or the risk of falls, talk to your doctor and request a *fracture risk assessment*,

which is a more in-depth assessment of your bone health. To do this your doctor may suggest you have a bone mineral density (BMD) test. This is a painless test that can help to predict your likelihood of fracture. Your doctor will also need to consider other risk factors including your age, sex, fracture history, parental history of hip fracture and glucocorticoid use.

### CALCIUM, PROTEIN AND VITAMIN D

The Osteoporosis Canada (OC) fact sheet *Nutrition: Healthy Eating for Healthy Bones* can help you determine if you are getting enough calcium and vitamin D. OC recommends that as much as possible, calcium intake should be from food, and supplements should

only be taken if one cannot consume sufficient calcium from the diet. On the other hand, there are few food sources of vitamin D and sun is an unreliable source, so OC recommends daily vitamin D supplementation all year round for all Canadian adults. A balanced diet, following Canada's Food Guide, will ensure that you get sufficient protein and other nutrients essential for bone health.

### REGULAR EXERCISE

Exercise helps build and maintain strong muscles and bones. The OC fact sheet *Exercise for Healthy Bones* provides good general guidelines for choosing the exercise that is right for you.

### SMOKING AND ALCOHOL

Any type and amount of smoking contributes to bone loss and increases the risk of osteoporosis in both men and women. Drinking an average of three or more alcoholic beverages per day may also increase bone loss and fracture risk. OC recommends no smoking and no more than an average of two alcoholic drinks daily.



Make your  
**FIRST** break  
your **LAST**

**INSIST ON ASSESSMENT**

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## OSTEOPOROSIS

THE INFORMATION CONTAINED IN THIS FACT SHEET IS NOT INTENDED TO REPLACE MEDICAL ADVICE. READERS ARE ADVISED TO DISCUSS THEIR INDIVIDUAL CIRCUMSTANCES WITH THEIR PHYSICIAN.

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