

The Canadian Pemphigus and Pemphigoid Foundation

Managing the Side-Effects: Bone Care

Common drug therapies for pemphigus and pemphigoid patients have a number of unwanted side effects. Glucocorticoids, such as prednisone, can put you at risk of bone loss, which may lead to osteoporosis and fragility fractures. A fragility fracture is one that occurs spontaneously or following minor trauma such as falling from a standing height or less.

In this information bulletin, we discuss the things you can do to help reduce your risk for a fragility fracture. We recommend that all pemphigus and pemphigoid patients read this bulletin – especially patients who expect to be on glucocorticoids, such as prednisone, for more than three months.

The Challenge for Pemphigus and Pemphigoid Patients - A Higher Risk of Bone Loss and Fracture

One of the most significant risk factors for the development of osteoporosis and for fracture is long-term (i.e., more than three months) use of glucocorticoids such as prednisone. Although used to control the inflammation in your skin, glucocorticoids have a negative effect on your bones because:

- They speed up the activity of cells that break down old bone
- They stop bone-forming cells from building new bone
- They decrease the amount of calcium absorbed from food and supplements
- They increase the loss of calcium in the urine, and
- They reduce the level of sex hormones in men and women (these hormones help protect bone).

This doesn't mean that you should stop taking prednisone or other glucocorticoids. It does mean that you need to carefully monitor your bone health while taking these drugs. This is done by doing bone mineral density (BMD) tests (which look for bone loss), by paying close attention to falls prevention, and by proper supplementation with vitamin D and the inclusion of calcium and protein rich foods in your daily diet.

What is Osteoporosis?

Osteoporosis is a process that makes bones weak. If you have osteoporosis, it means you have less bone (lower bone density) and the bone you do have is of poorer quality. As a result, your bones can break (fracture) more easily. These types of fractures are called fragility fractures because they occur with little or no trauma. A fracture that occurs from a simple fall is considered a fragility fracture. Osteoporosis has been called "the silent thief" because there are no symptoms until you experience a broken bone. A fracture is often the first sign of osteoporosis. Fractures of the wrist, spine, hip and shoulder are most common. Fractures can have severe consequences, including pain, deformity, disability and even death.

Each year in Canada, there are about 30,000 hip fractures, which is just the tip of the iceberg as many more Canadians suffer fractures of the spine, wrist, shoulder, and other bones because of osteoporosis. Over 90% of hip fractures in Canada occur in people over 60 years of age, and over one quarter of these occur in men. Fragility fractures are the most serious consequence of osteoporosis and represent 80% of all broken bones in those over age 50.

The number of pemphigus and pemphigoid patients who develop osteoporosis is unknown. Since osteoporosis is very common in the older population, pemphigus and pemphigoid patients are encouraged to take steps to reduce their risk for osteoporotic fractures.

One of these steps is doing a bone mineral density (BMD) test. A BMD test is a painless and accurate way to measure the density of your bones and it

uses very low doses of radiation. It is recommended for all women and men after the age of 65, or in younger individuals with additional risk factors (such as prior fragility fractures or prolonged glucocorticoid/prednisone use). When used in combination with other risk factors, a BMD test can help determine your fracture risk and it can assist your physician in making decisions about your treatment.

Pemphigus and pemphigoid patients should take note that continuous use of a glucocorticoid such as prednisone for three months or more is a significant risk factor for losing BMD and for suffering a fragility fracture. Hence, if you are taking glucocorticoids, your dermatologist or doctor should be monitoring your bone density. However, BMD testing alone is not the best way to determine a person's risk of fracture. A comprehensive fracture risk assessment, which incorporates the BMD results and also looks at other risk factors, will lead to a much more accurate determination of a person's need for treatment.

The Importance of a Comprehensive Fracture Risk Assessment

In order to assess your risk of fracture, your doctor will need to ask you some detailed questions about your lifestyle, your family history and your health in order to identify other risk factors for fragility fractures and falls. Falls can lead to fracture, which is why your doctor will ask if you have fallen in the past 12 months and will assess your gait, balance and general fitness. Besides a low BMD, other risk factors for fragility fracture include older age, number of years of being postmenopausal for women, whether you have already had a fragility fracture, low body weight, current smoking, high alcohol intake (an average of 3 or more drinks per day), if either of your parents has had a hip fracture, and glucocorticoid use (3 months or more in the previous year at a prednisone equivalent dose of 7.5 mg or more daily).

Your doctor should also do a physical examination, including measuring your weight and height, and screen for signs of an asymptomatic and undiagnosed spine fracture. Spinal fractures can occur without pain, and sometimes if there is pain it is misdiagnosed as a "pulled muscle." If you have lost height or have localized back pain, you may need an x-ray of your spine to check for spine fracture(s).

Tools for Assessing Risk of Fracture

There are two new closely related tools that are available for Canadian physicians to assess a person's 10-year risk of fracture. These are the CAROC and FRAX tools and they help determine whether a person is at low risk (less than 10%), moderate risk (10 – 20%) or high risk (more than 20%) of fracture over the next 10 years. Persons who have had a previous fragility fracture of the hip or spine and those who have had more than one fragility fracture of other bones are considered to be at high risk, regardless of their BMD test results. For more information on fracture risk assessment, contact Osteoporosis Canada and ask for the Diagnosis fact sheet.

So You Have Been Diagnosed with Osteoporosis (In other Words, You Have a High Risk of Fracture) - Now What?

Physical Activity and Bone Health

Physical activity, particularly weight-bearing activity, is one way to strengthen bone and to reduce the risk of fragility fractures. Weight-bearing exercise is any activity where our feet and legs carry our body weight, such as walking, low-impact aerobics or dancing. This type of exercise stimulates the bone cells to help maintain a good balance between the bone-building cells and those that take bone away. As well as being good for bone health, physical activity is also important for muscle strength and balance, both of which help to decrease the risk of falls and osteoporosis-related fractures.

Weight-resistance exercises are also beneficial. These activities involve moving objects or our own weight to create resistance. Free weights, weight-training machines or exercise bands are all examples of weight-resistance exercise. Resistance exercises done in a weight-bearing position are the most useful. While swimming is not weight-bearing, aqua fit exercises that have a resistance component may be beneficial. Resistance exercises can be very helpful in promoting muscle strength which decreases the risk of falls.

It is important to realize that even short periods of activity are beneficial – you can break your weight-bearing sessions into as little as 5 – 10 minute segments and still benefit from the activity. For ex-

ample, individuals who suffer from knee pain when they walk for half an hour or more can try walking for ten minute intervals at a time, 3 times per day and derive the same benefit as having walked once per day for 30 minutes.

For some patients with pemphigus and pemphigoid, lack of mobility becomes an issue. Their skin lesions make it very difficult to move because clothing can rub and create more lesions, or the lesions themselves may be in places that make it painful to walk or move. If you are having trouble being physically active for these reasons, you should consult your dermatologist and occupational therapist to develop an exercise program that works best for you.

Essential Nutrients for Bone Health

The three main dietary needs for bone health are vitamin D, calcium and protein, and all of these are equally important.

Protein is a nutrient that is necessary for building and repairing all body tissue. In addition to calcium and other minerals, bone is made up of the protein collagen, which gives the bone both strength and flexibility. Not having enough protein in one's diet can contribute to osteoporosis and fractures by lowering bone mass and decreasing muscle strength (which can also increase the risk of falls). Canada's Food Guide recommends two to three servings per day of 2-3 oz. (57-85 grams) of meat or alternatives. Some examples of foods in the meat and alternatives group include beef, pork, poultry, fish, eggs, beans, peanut butter and tofu. One serving of protein is roughly the size and thickness of your palm, excluding the thumb and fingers.

There are very few good food sources of vitamin D, which means that we cannot rely on foods to get sufficient vitamin D. Most vitamin D is manufactured by the skin when exposed to sunlight and so it is known as the sunshine vitamin. In Canada, the sun is not a reliable source of vitamin D. In addition, as we get older, our skin loses its ability to produce vitamin D from the sun. Sunscreens also may reduce the skin's ability to make vitamin D from sun exposure. Because of this, Osteoporosis Canada and the Canadian Pemphigus and Pemphigoid Foundation's Medical Advisory Council recommend routine vitamin D supplementation for all Canadian adults all year round. They recommend a vitamin D supplement of 800 to 2000 IU daily for those over

50. Those under age 50 are recommended to take a vitamin supplement of 400 – 1000 IU a day. Persons under age 50 who also have osteoporosis, or are at risk for rapid BMD loss (such as those on glucocorticoids) are recommended to take 800 – 2000 IU of vitamin D daily.

Regarding calcium, Osteoporosis Canada and the Canadian Pemphigus and Pemphigoid Foundation recommend 1200 mg calcium daily from all sources for those over 50. For those under 50, the recommendation is 1000 mg calcium daily. Dairy products are the best source of calcium. Other good dietary sources of calcium include fortified orange juice and fortified soy and rice beverages. Eating canned salmon and sardines with the bones also provides a good source of calcium. Canada's Food Guide recommends that persons under age 50 have at least 2 servings of dairy products or alternatives each day. For those over age 50, the recommendation is 3 servings each day. The recommendations for those who have osteoporosis or who are taking prednisone (a glucocorticoid drug).

The best way to get your calcium is from food sources. If it is not possible to get adequate calcium from your diet, supplementation may be required. Only take as much calcium through supplements as is needed to make up any shortfall in your diet and only do so after consultation with your healthcare provider. Excess calcium from supplements can cause some unwanted side effects. Therefore, DO NOT take any calcium supplements if you are getting enough calcium in your diet for your age. If you are not sure what to do, ask your doctor.

Two types of calcium supplementation are widely available. These are calcium carbonate and calcium citrate.

Calcium carbonate has the most elemental calcium per tablet (elemental means the amount of calcium available for your body to actually absorb). However, calcium carbonate is not as easy to absorb as calcium citrate. Calcium carbonate supplements should be taken with food to help their absorption.

Calcium citrate has less elemental calcium per tablet but is more easily absorbed, and therefore does not need to be taken with food. It also causes less stomach upset than calcium carbonate. If you need a calcium supplement, your doctor can help you decide which type is best for you.

If you have difficulty chewing because of open sores on your gums, cheeks, tongue and/or palate, or if sores in your throat interfere with swallowing, there are both gelatin capsule and liquid forms of calcium and vitamin D that may be easier to swallow than tablets. Talk to your doctor or pharmacist if eating and swallowing are issues for you.

An important note for pemphigus and pemphigoid patients: Those on tetracycline and taking calcium supplements should note that calcium can interfere with the body's ability to absorb the tetracycline antibiotic (this includes doxycycline, minocycline, and tetracycline). To avoid this problem, take calcium supplements 2 - 4 hours before or after taking tetracycline antibiotics.

Avoid Foods and Lifestyle Factors that Cause an Increased Risk of Fracture

It is important to avoid the following:

- **Excess salt** can increase calcium loss through the urine. Keep the intake of salt to a minimum. Saltiness is an acquired taste that takes 2 weeks to re-develop, so if you don't like the unsalted taste of your food, you will no longer notice it after two weeks.
- **Smoking** increases a person's risk of fracture. Only 5% of people can successfully quit smoking on their own. Ask your doctor to help you quit if you smoke.
- **Drinking** 3 or more servings of alcohol a day has also been found to increase a person's risk of fracture.

If You Have Osteoporosis (High Fracture Risk) and Require Medication

Based on your fracture risk assessment results, you may be counselled by your physicians to consider taking medication to reduce your risk of fracture.

- **High Risk** – These individuals are usually advised to take medication to reduce their fracture risk.
- **Moderate Risk** – Some who are at moderate risk, particularly if they have additional risk factors for fracture or rapid BMD loss (such as prolonged glucocorticoid use), may also benefit

from treatment to prevent fractures.

- **Low Risk** – These individuals usually do not require treatment with medication, but should still follow the "Bone Care Checklist" and their fracture risk should be re-evaluated after 5 years or if they develop new risk factors.

If you have been found to be at moderate or high risk for fracture, there are several approved medications that are effective in reducing a person's risk of fracture. Talk with your doctor about which medication, and what regimen, is best for you.

Once you are on a medication, it is important to ensure that you continue to get adequate calcium and vitamin D and engage in physical activity. Ask your doctor if you are eligible for a blood test that checks your vitamin D level. Some people need more than the recommended amount of vitamin D but this should be checked and monitored on an individual basis by your physician. Drug treatments, a healthy diet, adequate vitamin D and exercise all work together to keep your bones as strong as they can be.

Osteoporosis Canada recommends the following medications as "first line" therapies to reduce the risk of hip, spine and other fragility fractures: alendronate (Fosamax®, Fosavance® and generics), denosumab (Prolia®), risedronate (Actonel®, Actonel® Plus Calcium, Actonel DR™ and generics) and zoledronic acid (Aclasta®).

Teriparatide (Forteo®) is a first-line medication to reduce the risk of spine and other fractures in patients at high risk for fractures.

Other medications available for the treatment of osteoporosis include estrogen hormone therapy, etidronate, the SERMs (Selective Estrogen Receptor Modulators) raloxifene (Evista® and generic) and nasal calcitonin (Miacalcin® and generic). For long-term glucocorticoid users who are intolerant of first-line therapies, calcitonin or etidronate may be considered for reducing further loss of bone mineral density.

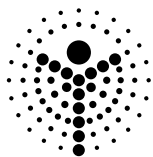
All of these medications have the potential to provide significant benefit when taken appropriately. However, medications can also have side effects. It is important to discuss your medication with your healthcare provider in order to make sure that the benefits outweigh the risks for you and that you are aware of what to watch for in case you do experience a possible side effect.

Osteonecrosis of the Jaw (ONJ)

One potential side effect of long-term use of a bisphosphonate such as alendronate or risedronate that may be of special concern to pemphigus or pemphigoid patients is osteonecrosis of the jaw. Osteonecrosis of the jaw (ONJ) is a rare condition in which the jaw bone's ability to heal is impaired and may cause a painful wound that does not heal. The affected bone can become infected and die.

A diagnosis of ONJ is made by examining the soft tissue covering the jaw bones in the mouth. If the jaw bone is not covered by a healthy soft tissue lining and remains uncovered or exposed for more than 8 weeks, this confirms the diagnosis of ONJ.

ONJ has been noted in some cancer patients receiving high doses of intravenous bisphosphonates every month to reduce the spread of their cancer to bone. In osteoporosis patients, bisphosphonate medications are used in much lower doses than in cancer patients and there is currently no definite proof that there is an increased risk of ONJ at these lower doses that are more regularly used. The risk of ONJ with regular dose bisphosphonate treatment in osteoporosis patients is estimated to be between 1 in 10,000 and 1 in 100,000 and may be no greater than the risk of ONJ in the general population who have not taken any bisphosphonates. The recommendations for osteoporosis patients on regular doses of bisphosphonates are the same as for all Canadians. Maintain good oral hygiene and visit your dentist every 6 months.



Osteoporosis Canada

Ostéoporose Canada

This information bulletin was developed in partnership with Osteoporosis Canada.

Managing Our Health Program provides information to patients on ways in which they can enhance their general health and better cope with the symptoms of their illness and/or the side effects of their treatment therapies. For more information, visit www.pemphigus.ca.

Disclaimer: The information in this Bulletin has been developed by the Canadian Pemphigus and Pemphigoid Foundation in consultation with its Medical Advisory Council and subject matter experts. It is important to note that the information is not intended to replace informed medical advice. You should consult your dermatologist or other healthcare professional (e.g., physician, dentist, pharmacist, etc.) for individual medical advice. While the information is presented with due care, the Canadian Pemphigus and Pemphigoid Foundation does not guarantee that it is free from all errors or omissions.

Need More Help?

As a first step, you should always consult your dermatologist and your doctor to get advice on how to best protect yourself from the side effects you may experience from the drug therapies you are on to treat or manage your condition(s). You may also wish to consult reliable resources such as those provided by Osteoporosis Canada. For example, if you have been diagnosed with osteoporosis, Osteoporosis Canada's Canadian Osteoporosis Patient Network (COPN) is a valuable resource. A free bi-weekly e-newsletter – with the latest in osteoporosis research and other articles of interest to people living with osteoporosis – is delivered directly to your inbox every two weeks or by hard copy every 3 months. To sign up, or for more information on osteoporosis, go to www.osteoporosis.ca or call 1-800-463-6842 to speak with an information counselor.

Your local Canadian Pemphigus and Pemphigoid Foundation Support Group Leader may also be able to put you in touch with other pemphigus or pemphigoid patients who are facing similar challenges in your region. In the meantime, make sure to keep physically active, maintain a healthy diet, take your vitamin D and keep in touch with your healthcare providers.

A Bone Care Checklist

- Do daily weight-bearing exercise. (Before you start, consult your doctor and, if necessary, an Occupational Therapist or Physiotherapist.)
- Eat calcium-rich foods.
- Avoid excess salt.
- If over 50, aim to get 1200 mg of elemental calcium from all sources (diet and supplements) and between 800 and 2000 IU of vitamin D from supplements.
- Work with your doctors to monitor your bone health on a regular basis.
- Consult your pharmacist for advice on when and how to take medications and vitamin supplements to maximize their effectiveness.