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Osteoporosis - Causes & Therapy

In osteoporosis, the bone loses mass and deteriorates leading to reduced bone strength and increased risk of fractures. At least 1 in 3 women and 1 in 5 men will suffer from an osteoporotic fracture during their lifetime.⁽¹⁾ Lifestyle factors such as lack of exercise, smoking, poor diet, and alcohol use can contribute to the disease. In addition, some health conditions such as Cushing's syndrome, rheumatoid arthritis, and diabetes have been associated with the disease. Often overlooked is that some drugs may contribute to the disease. The following chart highlights some causes and the recommended therapy.



Drugs that may contribute to Osteoporosis

Drug Therapy	How it Causes Osteoporosis	Recommended Therapy
Glucocorticoids (at a dose equivalent to 5 mg of prednisone or more for 3-4 months)	Stimulates breakdown of bone and inhibits bone reformation	Try to always use glucocorticoids short term at the lowest effective dose. If used long-term, treat with Vitamin D, Bisphosphonate or Prolia especially those at high risk, and calcium if insufficient from diet
Aromatase Inhibitors (used in Breast Cancer) (<i>exemestane, letrozole, anastrozole</i>)	Inhibits estrogens beneficial effect on bone	Vitamin D and calcium if not enough in diet; Once bone loss occurs bisphosphonates are preferred agents Note: tamoxifen protects and reduces fracture risk
Gonadotropin Releasing Hormones Antagonists (<i>Leuprolide Depot</i>)	Inhibits estrogen and testosterone beneficial effect on bones by reducing levels of estrogen and testosterone	Vitamin D, Bisphosphonate Recommended
Depo-Provera (<i>medroxyprogesterone depot</i>)	Inhibits estrogen and LH which reduces the beneficial effect of estrogen and testosterone on bones	Vitamin D for all; calcium if not sufficient from diet
Thyroid Replacement Therapy (<i>levothyroxine</i>)	Over-supplementation of TSH causes exogenous hyperthyroidism causing direct effects on bone remodeling causing bone loss	No treatment required as long as TSH is within recommended reference range
Anticonvulsants	Not fully understood; enzyme induction leads to increased catabolism of vitamin D to inactive metabolites. It is also suspected that fractures are often caused by the seizures themselves rather than the drug.	High risk drugs: Phenytoin (highest risk,) primidone, carbamazepine, and Phenobarbital should be treated with minimum vitamin 800 IU QD; Monitor BMD Medium Risk: Valproate & Lamotrigine; does not affect BMD in adults; No risk: Levetiracetam does not require treatment

Drugs that may contribute to Osteoporosis (Cont'd)

Drug Therapy	How it Causes Osteoporosis	Recommended Therapy
Antidepressants (examples: SSRIs such as <i>sertraline, escitalopram, fluoxetine etc</i> or tricyclic antidepressants such as <i>amitriptyline, trimipramine etc</i>)	Increased risk of falls and medications may have small role to cause fractures (TCAs have greater risk of falls than SSRIs) May be related to smoking, alcohol and physical inactivity often seen in depressed patients.	Preventative therapy is currently not warranted
Antipsychotics (ex. <i>risperidone, quetiapine, haloperidol etc</i>)	Increased risk of falls; Conventional antipsychotics affect prolactin which lowers estrogen/testosterone (inhibits beneficial effect on bones)	Preventative treatment is currently not warranted
Proton Pump Inhibitors (such as <i>pantoprazole, lansoprazole etc</i>) and H ₂ Antagonists (such as <i>famotidine and ranitidine</i>)	Cause not fully understood but may impair calcium absorption; fracture risk increases with duration of use	PPIs should be used for the shortest duration of time at the lowest possible dose; If treated with calcium should use calcium citrate which does not depend on stomach acid for absorption. H ₂ Antagonists may have lower risk of osteoporosis compared to PPI. Ranitidine could increase risk of falls leading to fractures so famotidine is the preferred option.
Thiazolidinediones	Periphery fractures increased	Should not be used due to increased risk of heart failure; consider if therapy is warranted
Anticoagulants	Heparin causes bone loss by decreasing bone formation. Warfarin may affect bone through its effect on vitamin K	No specific treatment recommended. Benefits of warfarin and heparin outweigh risks of osteoporosis
Vitamin A and synthetic retinoids	Vitamin A >3000 mcg/day of retinol equivalents had increased risk of hip fracture.	Reassess need for Vitamin A; Suggest getting from common food sources such as liver, milk, egg yolk, butter and some fruit/vegetables
Loop diuretics (bumetanide, furosemide)	Impair calcium absorption in the loop of Henle of kidney	Risk is small; treatment not warranted. Thiazide diuretics actually improve bone mass density

Drugs may contribute to osteoporosis but the total effect is usually small. It still should always be taken into consideration. It may be a reason to stop a medication, add on a medication that could offer protection or choose a better option that does not have the same effect on the bones.

Drugs used to treat Osteoporosis

Drug Therapy	How it Protects against Osteoporosis	Doses and Duration
Calcium	Osteoblasts use calcium to build up bones	Age 19-50: 1000 mg daily calcium requirement (including from diet and supplements) Age: 50 + 1200 mg daily calcium requirement (including diet and supplements) Ideally, all sources of calcium should come from dietary sources
Vitamin D (cholecalciferol)	Helps the body absorb calcium and improves the function of muscles, which improves your balance and decreases likelihood of falling	Healthy adults 19-50: 400-1000 iu of daily 50 +: 800-2000 iu daily Note: it is almost impossible for adults to get sufficient vitamin D from diet alone. Osteoporosis Canada recommends routine vitamin D supplementation for all Canadians year round.
Bisphosphonates: (ex. Alendronate, risedronate, zoledronic acid, or etidronate)	Bind to the surfaces of bones and slow down the bone eroding action of the osteoclasts.	Dosage varies on drug product. They can be given daily, weekly, monthly or yearly. Usually given on an empty stomach ½ hour before eating with a big glass of water. Patient must stay upright (not lie down) for ½ hour after taking to prevent damage to the esophagus. One drug product is available that can be taken with food.
Forteo (recombinant parathyroid hormone)	Activates the osteoblasts which build bones	20 mcg injected subcutaneously once a day. This medication should not be taken longer than 24 months.
Prolia (denosumab)	Inhibits the development of osteoclasts (which normally breakdown bone)	Only for use in females at this time. (Studies in men are still ongoing) 60 mg injected subcutaneously twice per year.
Testosterone	Only for use in men with hypogonadism. Testosterone has beneficial effects on bone.	Dose varies depending on drug product. Available in IM, oral, patch and gels.

References

1. <http://www.osteoporosis.ca/osteoporosis-and-you/osteoporosis-facts-and-statistics/>
2. Drug Information Provided by osteoporosiscanada.ca
3. Bowles. *Drug-induced osteoporosis. Women's and Men's Health*

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