

Osteonecrosis of the Jaw (ONJ)

In the last 20 years or so, there have been new drug therapies introduced to treat osteoporosis (weak, brittle bones) and cancers that affect the health and strength of bones. Osteonecrosis results when bone tissue doesn't get its normal blood supply. A poor blood supply causes loss of bone tissue and bone breakdown.

Osteonecrosis of the jaw (ONJ), also called vascular or aseptic necrosis, is a rare condition but it can be very serious. The exact cause is unknown but it has occurred in some cancer patients receiving bisphosphonates, steroids (high doses), and certain targeted chemotherapy agents, particularly after having a tooth pulled or oral surgery. (See back for more about bone remodeling.) ONJ caused by medication seems to prefer bones of the head – particularly the jaw bones. ONJ is diagnosed when there is exposed, necrotic (dead) bone tissue in the upper or lower jawbone for at least 8 weeks. Note: In 2022, the American Association of Oral and Maxillofacial Surgeons (AAOMS) said that medications associated with ONJ are proven to be safe and effective for most patients and recommended continued use to prevent bone loss.

Prevention - Better than Treatment

With thorough dental and mouth monitoring and care before and during drug therapy, the risk of developing ONJ can be significantly reduced. Preventing ONJ is preferable to treating it after it occurs.

What you can do – before starting drug therapy

- See your dentist before you begin your treatment.
- Make sure your dentist is familiar with the treatment you will be receiving.
- Have your dentist assess and manage your oral health such as tooth or gum infections, cavities, gum disease, and dry mouth (xerostomia). Have your filling, dentures, partials, and implants checked. Oral disease should be eliminated or stabilized.
- At the pre-treatment visit(s), try to have all your dental treatments EXCEPT having teeth pulled or bony surgery (such as implants). If you must have a tooth pulled or you have other oral trauma, do it before you start drug therapy and then wait 14–21 days before starting your drug therapy. Sometimes, the dentist may monitor your healing for up to 12-16 weeks before recommending you start bisphosphonates.
- If you had dental work done, check on the healing of your hard and soft tissue.

What you can do – while on drug therapy

- ✓ Maintain good oral hygiene throughout your drug therapy. Brush teeth and clean your mouth properly.
- ✓ Make any changes in oral/dental care necessary to continue monitoring.
- ✓ Report any new oral/dental problems as soon as they occur. Report any changes in your drug therapy.
- ✓ Monitor dentures for adequate fit and cleanliness (to avoid injuring tissue in the mouth)

If you have symptoms of ONJ (Pain, swelling, infection, poor healing of the gums; loose teeth; and numbness or the feeling of heaviness in the jaw) : Contact your oncologist about seeing an oral and maxillofacial surgeon. Be sure to let your regular dentist know as well.

Risk Factors

A person's risk for ONJ is based on multiple factors and usually includes trauma/injury to the jawbone (having a tooth pulled or getting an implant). Most studies estimate the average risk of ONJ for patients with cancer who take bisphosphonates is between 3% and 5%. The risk of ONJ seems to increase after long-term use of bisphosphonates in older people who have multiple myeloma, often after having oral surgery. Other possible risk factors include having:

- infection or inflammation in the mouth; radiation therapy to the head or neck
- a compromised immune system or an autoimmune disease
- diabetes, an infection, poor circulation, anemia (low red blood count), having 2 or more medical conditions
- poor oral health, gum disease, or dental surgery
- an alcohol or tobacco habit; poor nutrition; genetic factors
- cancer and getting IV bisphosphonates and wearing dentures (having all 3 doubles the risk of ONJ)

Bone remodeling

Osteoclasts are specialized cells that absorb and remove bone tissue so that new bone tissue can develop. This normal process of bone breakdown is called *resorption*. Medications that block it are called *antiresorptives*. **Osteoblasts** are specialized cells that mineralize bone and form new bone tissue. In healthy bone, osteoclasts and osteoblasts work together to “remodel” bone and keep it strong and healthy.

Medications that affect bone remodeling

- **Bisphosphonates** slow or stop osteoclasts and allow osteoblasts to work more effectively in forming bone. This improves bone mass and strength, and helps avoid bone fractures. Common U.S. bisphosphonates include alendronate (Fosamax®, Binosto®), ibandronate (Boniva®), pamidronate (Aredia®), risedronate (Actonel®), zoledronic acid (Zometa®, Reclast®, Aclasta®), etidronate (Didronel®), and tiludronate (Skelid®).
- **RankL inhibitors**, like denosumab (Xgeva®, Prolia®), decrease the number of osteoclasts formed and decrease the activity of osteoclasts. Unlike bisphosphonates, RANK-L inhibitors do not bind to bone, and their effects on bone remodeling wear off within 6 months of ending drug therapy treatment.
- When given with bisphosphonates or rankL inhibitors, some targeted chemotherapy medications may affect bone remodeling, delay wound healing, and have a toxic effect on oral cells. Some targeted chemo agents are risk factors for ONJ even when given alone (imatinib/Gleevac®, sunitinib/Sutent®, sorafenib/Nexavar®, and bevacizumab/Avastin®). Other drugs that may increase the risk of OJN include selective estrogen receptor modulators (raloxifene, fusion proteins [aflibercept], mTOR inhibitors [everolimus], and immunosuppressants [methotrexate and corticosteroids].

In the 2014 AAOMS Position Paper on ONJ, four stages of ONJ were defined including a Stage 0 category. Studies show that half of the patients with Stage 0 disease will, over time, progress to higher stages of ONJ that include exposed bone. They also cautiously recommended a drug holiday 3 months before and 3 months after any invasive dental surgery **if the patient has been on extended bisphosphonate therapy and medical conditions permit** the drug holiday. A drug holiday is not recommended for those taking denosumab because it may increase the risk of bone fracture.