Medication Related Osteonecrosis of the Jaw

What is osteonecrosis of the jaw?

'Osteo' means bone. 'Necrosis' means death of cells or tissue in the body. Osteonecrosis of the jaw (ONJ) is a serious bone disease where there is a loss of blood supply to the bones of the jaw. This blood supply is needed to keep cells and tissues healthy and alive.

The loss of blood supply leads to exposed (uncovered) bone of the maxilla (upper jawbone) or mandible (lower jawbone). These bones should be covered by gum tissue. With ONJ, the bone is exposed through an opening in the gum tissue or because the gum tissue is completely missing.

Symptoms of ONJ may be:

- Pain.
- Swelling.
- Infection of the gums.
- Loosening of the teeth.
- Exposed bone (often at the site where a tooth has been removed).
- Numbness or tingling in the jaw or a "heavy" feeling of the jaw.

ONJ may have no symptoms for weeks or months and may only be found by feeling or seeing exposed bone.

ONJ is sometimes confused with osteoradionecrosis of the jaw, which is caused by radiation therapy and is treated differently than ONJ. This article will discuss osteonecrosis of the jaw.

What causes ONJ?

The exact cause of ONJ is not known, but possible causes may be:

- Dental work.
- Infection.
- Inflammation (swelling).
- The slowdown of angiogenesis (making of new blood vessels).

While the exact cause of ONJ is not known, there are medications that are used to treat cancer that have been found to be related to a diagnosis of ONJ.

Who is at risk for ONJ?

Some cancers affect your bones more than others, like multiple myeloma or cancers that have spread to the bone (called bone metastasis). Other health issues like diabetes can also put you at risk for ONJ. Ways that cancer can affect bones are:

- Tumors that have grown into the bones (called invasion) can cause the bone to wear away. This leaves small holes in the bone, called *osteolytic lesions*. When the bone starts to break down and wear away, it

is called resorption. Resorption leaves bones weak and fragile.

- Tumors can also cause changes to your bone formation (growth). Bone can build up, called *osteosclerotic lesions*. These lesions can be painful and can easily break.

Medications can be used to treat osteolytic lesions and osteosclerotic lesions caused by cancer. In some cases, these medications can cause ONJ.

Which medications are linked with ONJ?

There are some medications that are used to treat cancer that can increase your risk of ONJ such as bisphosphonates, denosumab, and anti-angiogenic medications.

Bisphosphonates

Bisphosphonates are a group of medications that slow the breakdown of bone that happens with bone metastases or multiple myeloma (cancer of plasma cells, which enter and destroy bone). Bisphosphonates improve bone strength, slow down how quickly the bone wears away (called resorption), and lessen the build-up of unstable bone. These problems can lead to:

- Fractures.
- A faster spread of bone metastases.
- Spinal cord compression (when the bone in the spine presses against the spinal cord).
- Hypercalcemia (high levels of calcium in the blood caused by bone breakdown).

Currently approved bisphosphonates include:

- Alendronate (Fosamax®).
- Etidronate (Didronel®).
- Ibandronate (Boniva®) – currently used only for osteoporosis.
- Pamidronate (Aredia®).
- Risedronate (Actonel®).
- Tiludronate (Skelid®).
- Zoledronic acid (Zometa®).

Denosumab

Another medication used to slow or prevent bone breakdown and bone issues is denosumab (Xgeva®). Denosumab is a monoclonal antibody, which is a medicine that targets a specific protein or cell. Denosumab targets a protein called RANKL, which is needed for bone breakdown, but too much is made in bone metastases. By targeting RANKL, denosumab blocks or slows down bone breakdown.

Anti-angiogenic medications

Anti-angiogenesis inhibitors work by affecting a tumor's blood supply. These medications are used in many cancer treatment plans.

Prevention is the Key

Most cases of ONJ are related to a dental issue, and if these are avoided, ONJ may be as well. Some things you can do to reduce your risk are:

- Before taking a medication that can cause ONJ, you should be seen by an oral maxillofacial surgeon or dental oncologist familiar with ONJ.

- If there are any dental concerns (needing dental surgeries, extractions, root canals, or removal of abscessed teeth), therapy with the medication should wait (if possible). You should not start the medication until the dental concerns are taken care of and healed.
- If you are taking a medication that can cause ONJ, you should have regular dental exams (up to every 3-4 months) that include cleaning, looking at denture fit if needed, and education on oral care while taking these medications.
- Maintain good oral hygiene. If invasive dental work is needed, you should talk with your provider about your options. You may want to stop taking your medication for a period of time leading up to the procedure. Ask your provider when you should stop your medication.

How do we treat ONJ?

- The primary goals of treatment for ONJ are to reduce pain, treat or prevent infection, and slow down progression. This may include:
- Having a panoramic and/or intra-oral x-rays done to rule out other dental problems (impacted teeth, cysts, bone changes).
- You should be seen by an oral maxillofacial surgeon or dental oncologist familiar with ONJ.
- Oral rinses with chlorhexidine (Peridex®) should be used 3-4 times a day.
- Dentures can be worn but may need resizing or cushioning to prevent more injury to the bone.
- An appliance can be used to cover and protect the exposed bone.
- Antibiotics may be given if needed.
- Avoid surgery on these bones, if possible. These bones may not heal well after surgery and it may actually worsen the problem.
- In more advanced cases, surgery to remove the involved bone can improve quality of life, reduce pain, prevent the necrosis from spreading, and help promote soft tissue healing. When used, surgery may include the removal of foreign material and/or dead, damaged, or infected tissue or bone, and in some cases, reconstruction of the bone.

ONJ is rare, but as people with multiple myeloma and bone metastases are living longer and being treated with medications associated with ONJ for many years, it is important to be aware of it. The medications associated with ONJ benefit patients who are at a high risk of bone issues, and there are currently no other medications that have this benefit. You must weigh the risks and benefits when deciding to use these medications. You can talk with your provider about making treatment decisions that are right for you. You should follow any directions for mouth care that you are given and report any signs or symptoms of ONJ to your provider right away.

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