



## ***Bisphosphonates & Dentistry, A Current Review...*** by Dr. Jay M. Goldberg

**Introduction:** Bisphosphonates are a class of drugs used to treat osteoporosis and certain cancers. Recently, adverse effects associated with these medications, **bisphosphonate associated osteonecrosis of the jaws or BON**, has been reported in the dental and medical literature. Position statements have been released recently by the American Academy of Oral Medicine and the American Association of Endodontists on the subject and this article attempts to present an overview on the subject and treatment recommendations.

**Background:** Bisphosphonates are synthetic analogues of inorganic pyrophosphate that have a high affinity for calcium. All bisphosphonates accumulate over time in mineralized bone matrix. If not incorporated into the bone mineral matrix, they are eliminated in urine. During bone resorption, bisphosphonates are released from bone and can be reincorporated into new bone or phagocytized by osteoclasts. Osteoclasts involved in the process lose the ability to resorb bone and undergo apoptosis (programmed cell death). Finally, bisphosphonates also possess antiangiogenic properties making them tumoricidal and an important agent in chemotherapy.

Bisphosphonates are commonly used to treat certain resorptive bone diseases such as osteoporosis, Paget's disease and hypercalcemia associated with certain malignancies such as multiple myeloma and bone metastasis from the breast and prostate. **As a group they are potent inhibitors of osteoclastic activity.** In patients with osteoporosis, the drug is intended to arrest bone loss and increase bone density, decreasing the risk of pathological bone fracture that results from progressive bone loss. In addition, bisphosphonates are given to patients with cancer to help control bone loss that results from metastatic skeletal lesions found in multiple myeloma, and metastatic solid tumors found in the bone (breast, lung and prostate cancers).

**Clinical Signs and Symptoms:** Investigators have reported cases of BON in patients receiving I.V. bisphosphonates to control and treat metastatic bone cancers. The patients were taking pamidronate (Aredia) and zoledronic acid (Zometa). In addition, there were reports of a few cases in which the patients were taking oral doses of alendronate (Fosamax) to treat osteoporosis. **The most common history involved in this process is absent or delayed soft and hard tissue healing after dental extractions.** Trauma to the area, as in appliance induced soft tissue trauma has also been shown to initiate

this pathologic process. Early stage BON may reveal pain without any radiographic evidence of bone necrosis. It is believed this process is initiated when necrotic bone becomes infected after it is exposed to the oral environment. The osteonecrosis may progress leaving areas of extensive bone exposure and dehiscence. Peripheral nerves may become involved and sensory nerves may be affected (parasthesia).

**Treatment:** Treatments for BON include debridement, surgical sequestrectomy, mandibular resection, partial and complete maxilloectomy and hyperbaric oxygen therapy. **All therapies to date as reported in the literature have reported little to no healing in patients who have undergone treatment for BON. Therefore, until further information is available, it would appear prudent to consider all patients taking bisphosphonates to be at risk.**

### **Recommendations:**

- **The best treatment is prevention.**
- **Recognize the risk factors of BON:**
  - **Systemic:**
    - I.V. use of bisphosphonates
    - Multiple myeloma
    - Cancer metastatic to bone such as breast, lung and prostate
  - **Local:**
    - Dental extractions
    - Trauma from dentures
    - Presence of oral infections
    - Poor oral health
- Preventive care may include: caries control, conservative periodontal and restorative procedures and if necessary appropriate endodontic therapy. Remember, extraction sites were identified as a common cause of BON.
- For patients at higher risk for BON, surgical procedures such as tooth extractions, endodontic surgery or placement of dental implants should be avoided if possible.
- Patients at low risk for BON include those taking oral bisphosphonates such as Fosamax.
- Include the entire health care team, including the patient's oncologist when developing treatment plans for these patients.
- Finally, cases of bisphosphonate osteonecrosis of the jaws should be reported to the U.S. FDA MedWatch Online at: <http://www.accessdata.fda.gov/scripts/medwatch/>.