

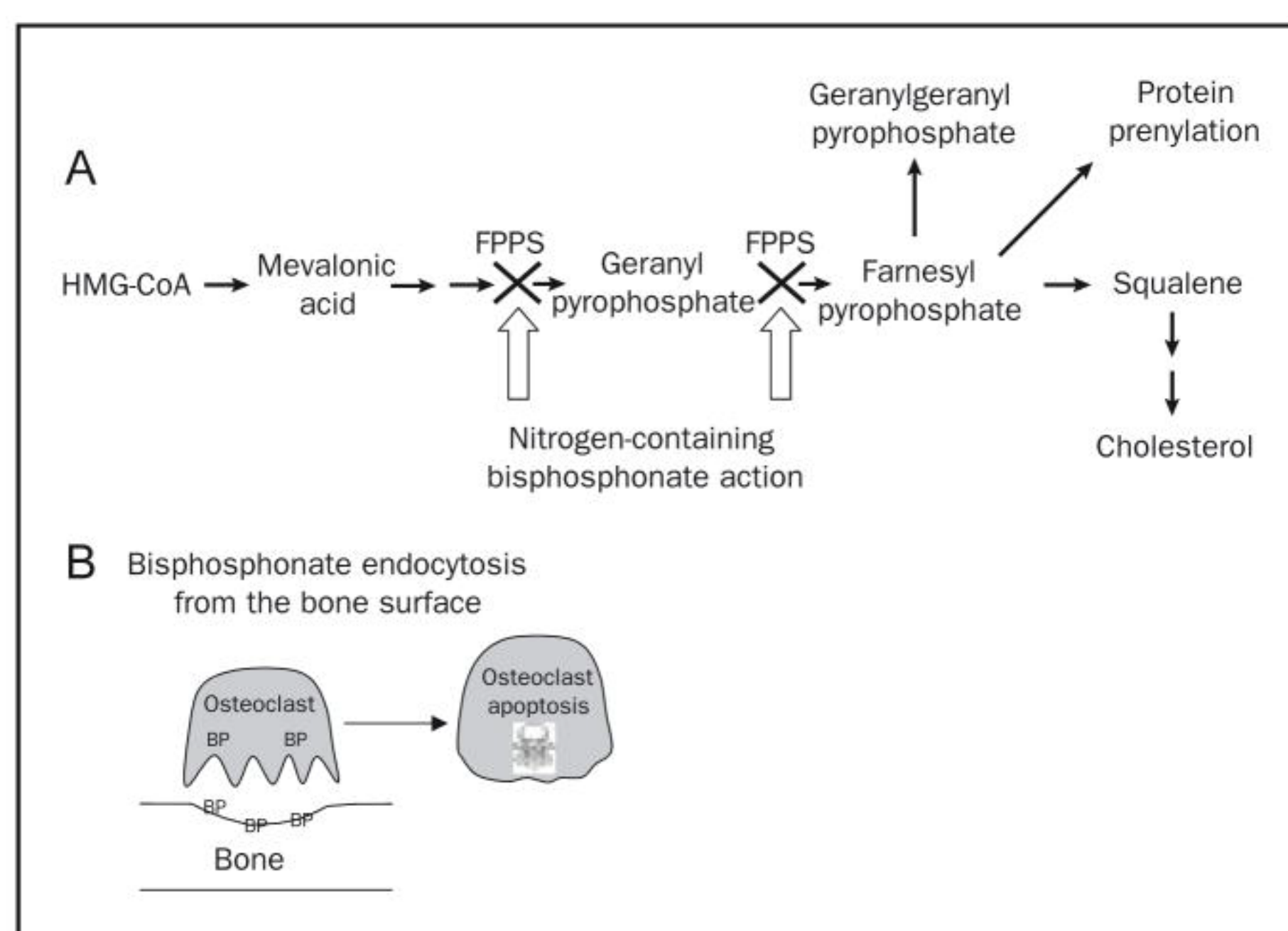
INTRODUCTION

- Oral surgery, including tooth extractions and surgical manipulation of the gingiva, jaws, and other oral structures, is one of the most major risk factors of developing osteonecrosis of the jaw in patients on bisphosphonate therapy
- The type of bisphosphonate and route of administration affects the incidence
- The length of time since the patient's bisphosphonate therapy can also affect the incidence
- Early and proper examination and intervention of the dental patient will determine the outcomes

“Cancer patients treated with IV bisphosphonates who undergo dentoalveolar procedures have a 5 to 21- fold increased risk for BRONJ than cancer patients treated with IV bisphosphonates who do not undergo dentoalveolar procedures”
-American Association of Oral and Maxillofacial Surgeons

PATHOPHYSIOLOGY

- Bisphosphonates inhibit osteoclastic bone resorption, used mostly for patients with various bone diseases
 - Osteoporosis, multiple myeloma, metastatic cancer, Paget's disease
 - These are disease processes that promote bone resorption via osteoclasts
- Bisphosphonates (containing Nitrogen) inhibit an enzyme (FPPS) contained in osteoclasts which causes the osteoclasts to apoptose
 - The osteoclast endocytoses the bisphosphonate
- Simple bisphosphonates
 - Mimics ATP which affects synthesis and induces osteoclastic apoptosis



DENTAL MANAGEMENT

- Detailed questioning of patient's current and past bisphosphonate use, as well as oral versus IV
- Examination should be performed before patient starts drug
 - Extract any hopeless teeth
 - Perform subgingival scaling
 - Replace poorly fitting dentures (avoid soft tissue trauma)
- Avoid elective procedures, root canal treatment > extraction
- Promote regular dental visits, good oral hygiene practices
- If extractions are absolutely necessary, perform as atraumatically as possible (no flaps), CHX mouthrinse 2x/day for 2 months following
- Root canal treatment with coronal amputation (such is our case)
- Always inform patient of potential risks!

ORAL VS. INTRAVENOUS

- Oral**
Risk of developing osteonecrosis is low
Increased risk associated with risk factors such as increased age, periodontitis, oral glucocorticoid use, prolonged history of BP use, cancer patients, even presence of bony exostoses/tori
Best way to lower risk is through regular dental visits and good oral hygiene
- IV**
More at risk than the patients on oral BP's (better absorption, longer half-life)
Unclear if temporarily discontinuing the drug (drug holiday) prevents necrosis, offers no short-term benefit
Preventative care is very important for these patients (caries, infection control)
Avoid elective jaw surgeries during treatment

CONCERNS FOR ORAL SURGERY

- Because BP's inhibit osteoclasts, it interferes with bone remodeling and bone repair
- This leads to an increased risk of **osteonecrosis of the jaw (ONJ)** in patients who are taking/who have taken bisphosphonates
- Risk of ONJ following dental surgery such as extractions or implant placement
 - Necrotic bone normally gets resorbed by osteoclasts following these procedures
 - But osteoclasts are being inhibited, and the necrotic bone stays, and blood supply is compromised leading to further necrosis
- There is no diagnostic test to assess which patients are at risk for developing ONJ
- 94% of ONJ cases are due to IV bisphosphonate use for cancer patients

“When compared to cancer patients receiving antiresorptive treatment, the risk of ONJ for patients with osteoporosis exposed to antiresorptive medications is about 100 times smaller.”

RECOMMENDATIONS

- Drug holidays have been controversial when it comes to bisphosphonates
Recommendations for patients on bisphosphonates for **osteoporosis/osteopenia**
Recommendation to stop **oral** bisphosphonates 3 months prior to dental surgery, and 3 months following dental surgery
Oral BP's are at much less risk than IV (elective dental surgery is not contraindicated)
Drug holiday recommended for patients with higher risk of developing ONJ
Higher dose of BP (over 4 cumulative years) and patients with other risk factors (RA, diabetes, smoking, current glucocorticoid use)
However, FDA in 2011 stated there is limited data regarding decision making for drug holidays

REFERENCES

- Drake MT, Clarke BL, Khosla S. Bisphosphonates: mechanism of action and role in clinical practice. *Mayo Clin Proc.* 2008;83(9):1032-1045. doi:10.4065/83.9.1032
- Kalra S, Jain V. Dental complications and management of patients on bisphosphonate therapy: A review article. *J Oral Biol Craniofac Res.* 2013;3(1):25-30. doi:10.1016/j.jobcr.2012.11.001
- Ruggiero SL, Dodson TB, Assael LA, Landesberg R, Marx RE, Mehrotra B; American Association of Oral and Maxillofacial Surgeons. American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate-related osteonecrosis of the jaws--2009 update. *J Oral Maxillofac Surg.* 2009 May;67(5 Suppl):2-12. doi: 10.1016/j.joms.2009.01.009. PMID: 19371809.
- Ruggiero SL, Dodson TB, Fantasia J, Goodday R, Aghaloo T, Mehrotra B, O'Ryan F; American Association of Oral and Maxillofacial Surgeons. American Association of Oral and Maxillofacial Surgeons position paper on medication-related osteonecrosis of the jaw--2014 update. *J Oral Maxillofac Surg.* 2014 Oct;72(10):1938-56. doi: 10.1016/j.joms.2014.04.031. Epub 2014 May 5. Erratum in: *J Oral Maxillofac Surg.* 2015 Jul;73(7):1440. Erratum in: *J*
- Oral Maxillofac Surg. 2015 Sep;73(9):1879. PMID: 25234529.
Stanton, David. "Management of XRT & Chemotherapy Patients." Lecture, University of Pennsylvania School of Dental Medicine.
- Soutome S, Hayashida S, Funahara M, Sakamoto Y, Kojima Y, et al. (2018) Factors affecting development of medication-related osteonecrosis of the jaw in cancer patients receiving high-dose bisphosphonate or denosumab therapy: Is tooth extraction a risk factor?. *PLOS ONE* 13(7): e0201343. <https://doi.org/10.1371/journal.pone.0201343>