Information sheet:

Bisphosphonates in Surgical and Implant Dentistry

Bisphosphonates are a class of drugs used to treat osteoporosis in a significant proportion of the population. They behave by reducing the rate of breakdown of the mineral part of the skeleton to increase bone density and strength. They are also used in higher doses to treat patients with metabolic disease or cancers that involve bone to reduce the rate of bone breakdown.

Bisphosphonates come in different strengths and are given at different doses depending on what is being treated. They are very successful at what they are prescribed to do - improving bone density in patients suffering from osteoporosis. Therefore they are prescribed widely.

However they also reduce the rate of bone healing and in extreme cases can render the bone of the jaws prone to dying, becoming exposed into the mouth and infected following even minor surgery such as extractions or gum surgery. Currently there is no known cure other than extremely good hygiene and application of topical antiseptics. At its worst, large volumes of jawbone can be lost to this debilitating condition. Unfortunately many of my patients who take bisphosphonates are unaware of the potential effects that this class of drugs has and the risks associated with oral surgery procedures.

The Association of Dental Implantology UK has recently asked Dr Jon Suzuki, an authority on the subject, to write a White Paper on the subject for guidance of colleagues and patients.

Dental Surgical Management of patients receiving oral or intravenous bisphosphonates
A White Paper by Professor Jon B. Suzuki DDS PhD MBA for the Association of Dental Implantology (UK) July 2009

The paper is available from the ADI website and can also be found as a separate file on the LCIAD website under Patient Information.

In summary, the current ADI guidelines published on their website http://www.adi.org.uk/members/only/bisphosphonates are as follows:

- Patients on IV bisphosphonates are at the highest risk of developing bisphosphonate-associated osteonecrosis (BON), particularly if they have been receiving IV treatment for more than six months. Elective dental implant treatment cannot be recommended for these patients. If treatment is required, this should be undertaken in a hospital environment with intravenous antibiotic therapy and full aseptic technique being considered as appropriate.

- Patients on IV bisphosphonates for less than six months should be at low risk of developing problems in relation to non-surgical periodontal and restorative care.
However, surgical treatment, e.g. extractions, should only be undertaken if absolutely necessary and should be approached cautiously and conservatively. If possible, a single intervention should be undertaken and an interval of two months left to verify acceptable healing before considering further surgical intervention.

- Patients on oral bisphosphonates treatment for three years or less probably have only a slightly increased risk of developing BON and as such, elective dental therapies including extractions and dental implants are not contraindicated. The patient should however be informed of the risk and appropriate consent obtained.

- Patients on oral bisphosphonates treatment for more than three years are at an increased risk of developing BON and this risk may increase with the duration of bisphosphonates therapy and other co-factors such as smoking. Therefore, surgical treatment, e.g. extractions, should be approached extremely cautiously and conservatively. If possible, a single intervention should be undertaken and an interval of two months left to verify acceptable healing before considering further surgical intervention.

- All patients on bisphosphonates treatment should rinse for one minute using a chlorhexidine aqueous solution 0.2% prior to dental treatment and to continue rinsing twice daily for 14 days after treatment.

- All patients on bisphosphonates treatment should be prescribed systemic antibiotics (see table 14 of White Paper) for one to two days prior to any dental procedures, which involve trauma to bone, e.g. extractions, implant placement and periodontal surgery.

- All patients on bisphosphonates treatment should be encouraged to attend for regular dental assessment and maintenance. The importance of ensuring a high standard of oral hygiene and good diet should be emphasised to reduce the need for possible future dental surgical intervention.

- Patients who smoke should also be encouraged to cease.

ADI Review Group:
- Anthony Bendkowski
- Robert Dyas
- Bill Schaeffer
- Eddie Scher
- Mark Atkinson

(This information sheet contains general information and must be read in conjunction with your personalised treatment plan, which gives specific advice).
Dr Koray Feran, 2011
Dental Surgical Management of patients receiving oral or intravenous bisphosphonates

A White Paper by Professor Jon B. Suzuki DDS PhD MBA for the Association of Dental Implantology (UK)

July 2009
Introduction

Bisphosphonates are a drug group that can be immensely beneficial to patients with osteoporosis and many other serious medical problems, however, it has become apparent that certain dental treatments, including implant surgery, can be more risky. Osteonecrosis of the jaw is a painful and debilitating condition that has been linked to bisphosphonate therapy, and dentists must understand how to minimise the risks.

The ADI invited Professor Jon Suzuki to write a White Paper on dental surgical management of patients receiving bisphosphonates. Professor Suzuki is a leading expert on this subject, and his experience has included being chairman of the Food and Drug Administration (FDA).

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Dental Surgical Management of Patients Receiving Oral or Intravenous Bisphosphonates

The medical use of oral and IV bisphosphonates is dramatically expanding throughout the world and is realising broader applications with respect to several systemic diseases, conditions and neoplasias (Table 1).

Bisphosphonate drugs are currently used in the medical management of osteoporosis, osteopenia, multiple myeloma, Paget’s disease, heterotopic ossification, hypercalcaemia of malignancies, breast cancer therapies and prostate cancer androgen deprivation therapy. The IV or “drip” bisphosphonates are primarily used for multiple myeloma, hypercalcaemia of malignancies, breast cancer therapies and Paget’s disease. Clinician judgment dictates which of the bisphosphonates are used for patients undergoing cancer chemotherapies (Woo et al., 2006).

The broadest patient group affected by oral bisphosphonates are patients with osteoporosis. Osteoporosis is currently a major worldwide health issue, which predisposes women and men to skeletal fractures. Osteoporotic fractures may result in significant morbidity and mortality for the patient, and generally has a major impact on day-to-day living. The risk of fracture is significantly reduced with the use of bisphosphonates which, as a class, improve bone density. Skeletal bone density is usually measured by Dual-Energy X-ray Absorptometry (DEXA) and patient data is reflected as a “T-score.” 1-1.5 S.D. from the mean T-score of young females (e.g. 24 years), indicates a diagnosis of osteopenia. 1.5-2.5 S.D. from the mean indicates a diagnosis of osteoporosis.

Within the past few years, several case reports of bisphosphonate–associated osteonecrosis of the jaw (BON) have been published. (Marx 2003; 2007; Ruggiero et al., 2004; Bagan et al., 2005; Bagan et al., 2006; Nase and Suzuki, 2006).

Position papers have been published by dental groups including The American Dental Association (2006; 2008), American Associations of Endodontists (2007), American Association of Oral and Maxillofacial Surgeons (2007) and American Society of Bone and Mineral Research (Khosla et al., 2007). (Their respective clinical profiles are summarised in Table 3).

Several IV bisphosphonates are currently prescribed in the United Kingdom (Table 2): Aredia, Bondronat, Bonefos and Zometa.

The most commonly recommended and prescribed oral bisphosphonates in the United Kingdom include (Table 4): Fosamax (alendronic acid) 5-10mg daily, Fosamax (alendronic acid) 70mg once weekly and Actonel (risedronate sodium) 5mg daily or 35mg weekly.

If these oral bisphosphonates are not efficacious, then the following oral bisphosphonates may be considered: Didronel (disodium etidronate) for osteoporosis 400mg daily for 14 days and then 1.25g calcium carbonate for 76 days (total cycle = 90 days).

Other bisphosphonate drugs used less frequently are: Bondronat (ibandronic acid) 50 mg daily - usually for bone metastases in breast cancer, Bonefos/Loron (sodium clodronate) 1.6 - 3.2 mg daily - usually for bone metastases in breast cancer and multiple myeloma, Proteolos (strontium ranelate) 2 g per day and Skelid (ti-ludronic acid) 400 mg daily for 12 weeks.

There are distinct advantages for oral bisphosphonates and, in most instances the benefits far outweigh the risks for osteonecrosis of the jaws. Oral bisphosphonates prevent 50% of vertebral fractures (250,000 fractures per year in the United States). In addition, oral bisphosphonates prevent 35-50% of non-vertebral fractures (350,000 – 500,000 fractures per year in the United States, Cummings et al., 2002).
Current Terminology of Osteonecrosis of the Jaw

The predominant term in common use in the United States is “bisphosphonate-associated osteonecrosis” (BON) (Table 5: Am Dent Assoc., 2008; Migliorati et al., 2005). This current terminology supersedes previous nomenclature for this condition. Other acronyms with corresponding name designations include: osteonecrosis of the jaw (ONJ), bisphosphonate-related osteonecrosis of the jaw (BRONJ) and bisphosphonate–induced osteonecrosis of the jaw (BIONJ, Nase & Suzuki, 2006).

Incidence of BON

There are significant differences in the incidence of BON with respect to intravenous (IV) and oral administration of bisphosphonates (Table 6). The IV method of bisphosphonate administration may result in an incidence of BON approaching 20% (Boonyatakorn et al., 2008; Cummings et al., 2002).

BON as a result of oral administration of bisphosphonates, ranges in incidence from 0-0.34% incidence or 1:10,000 to 1:100,000 patient treatment years (Mavrokokki et al., 2007; Grbic et al., 2008).

However, a recent publication (Sedghilzadeh et al., J Am Dent Assoc., 2009) reports a higher incidence (4%) of BON in a United States Dental School (University of Southern California, USA) setting.

Biological basis of BON

Recent research reports presented at the 2007 American Society for Bone and Mineral Research Meeting, Honolulu, HI, USA, has confirmed recognised pharmacological impact of bisphosphonates on impairment of osteoclasts (Weinstein et al., 2007). Delayed bone formation and impaired angiogenesis have also been reported (Aguirre et al., 2007).

Clinical reports support clinical observations with matrix necrosis of the mandible in patients with BON (Allen and Burr, 2008; Nase and Suzuki, 2006). (These mechanisms are summarized in Table 7).

Co-morbidities for BON

Recently, several potential co-morbidities for BON have been reported (Bamias et al., 2005). Periodontitis as an infection or dental extractions as a procedure (Boonyapakorn et al., 2008) may be factors with concomitant administration of bisphosphonate medications for BON.

Steroid therapy (Marx et al., 2005; Odvina et al., 2005) is a potential risk factor and a co-morbidity for BON.

Diabetes mellitus - Khamasisi et al., 2007 reported a possible association between uncontrolled diabetes mellitus and bisphosphonate associated osteonecrosis of the jaw.

Environmental factors including smoking (Yarom et. al., 2007) may be an initiating factor or co-morbidity for BON.

Case reports of dental surgical procedures resulting in BON in patients taking oral bisphosphonates have been recently published.

A crown lengthening surgery in a patient on oral bisphosphonates developed complications post-operatively (Nase and Suzuki, 2006). This case report describes the adverse clinical sequellae of a patient on oral bisphosphonates with successful dental and periodontal outcome, following periodontal surgery.

Additional case reports have been published on patients on IV bisphosphonates with lesions persisting for greater than 8 weeks and having no history of radiation therapy to the jaw (Wade and Suzuki, 2007). (Co-morbidity factors are summarized in Table 8).
Recommendations for Dental Therapies on Bisphosphonate Patients

Position papers have been published by organisations within the dental profession (Table 3). Most recently, the American Dental Association newsletter updated recommendations for managing dental procedures for patients on oral bisphosphonate therapy. These recommendations of the American Dental Association (ADA, 2008) (Tables 9, 10) are supportive and modify the original recommendations made in July 2006 by the American Dental Association. The recommendations are primarily a resource for dentists for bisphosphonate patients.

Diagnosis of BON is made from clinical presentations, medication history, and information from attending physicians. The clinical presentation of BON includes delayed onset and variable pain, periodontal swelling, soft-tissue infection, mobility of teeth, purulence, and exposed bone in the oral cavity.

The recommendations by the American Dental Association can be applied to other clinical situations for patients taking bisphosphonate medications. Routine dental treatment, such as restorations and scaling, is acceptable. Dental and periodontal examinations are highly recommended before or early during oral bisphosphonate treatment. Improved oral hygiene reduces risk of BON.

The CTX telopeptide test has originally been recommended to develop improved prognosis for BON (Marx, 2006). However, the CTX test exhibits biological and patient variability (Table 11) and lacks sufficient supporting scientific data for its use. Therefore, the CTX blood test is “inconclusive” for the determination of BON risk (ADA, 2008).

“Drug holidays” have also been recommended by previous reports to reduce risks of BON (Marx, 2006). There are no peer-reviewed clinical studies which support the application of a “drug holiday” to reduce risk of BON. Therefore, it is questionable to recommend cessation of bisphosphonate medications prior to dental therapies (ADA, 2008) (Tables 12, 13).
Dental Treatment for Bisphosphonate Patients

Specific recommendations have been updated based upon peer-reviewed case reports and clinical observations. It is recommended that the dentist complete therapy on one tooth or one sextant in a bisphosphonate patient and observe wound healing and any adverse effects for a two-month period of time. Antimicrobial rinses such as chlorhexidine should be recommended twice per day during this two-month observation period. Dental infections should be treated as quickly as possible after diagnosis; e.g. endodontic lesions, severe periodontal disease, abscesses of dental origin, purulence, and sinus tracts. These lesions must be managed quickly to reduce the risk of BON.

Non-surgical periodontal therapies or minimal flap surgical approaches should be treatment planned first. Systemic antibiotics may be recommended concomitant with or prior to dental therapies (Table 14).

There is no evidence regarding regenerative periodontal surgical procedures and bisphosphonate patients. These patients should be treatment planned with caution.

In addition, dental patients may be at increased risk for BON when “extensive implant placement or guided bone regeneration is necessary to augment deficient alveolar ridges prior to implant placement” (ADA Council on Scientific Affairs, 2008).


A recent report in the United States (Fugazzotto et al., 2007) has indicated that a history of oral bisphosphonate was not determined to be a contributing factor to the development of BON following surgical implant placement. This published report includes dental implants placed both into tooth extraction sockets (immediate implants), and into edentulous ridges.

This paper’s conclusion is primarily based on a total of 61 patients in private practice. BON was not recorded immediately post-operatively nor during a follow up period averaging 3.3 years. In this United States study, of the total of 61 patients, only 26 had used oral bisphosphonates for 4 years or greater prior to implant surgery. In fact, 22 patients were administered 35 mg alendronate (Fosamax) per week while 4 patients used 70 mg of alendronate (Fosamax) per week. A biological gradient of increasing time of oral bisphosphonates may play a major role in the incidence of BON. Therefore, the risk for BON in at least 22 patients of this study may be lower than the suggested minimal levels resulting from the standard regimen of alendronate (Fosamax).

Interpretations of implant safety in oral bisphosphonate patients should be reviewed in light of the patients’ medication and medical history.

Both human and animal studies on the impact of oral bisphosphonates on orthodontic therapy have been published. Preliminary findings indicate that orthodontic therapies and expected outcomes may have to be adjusted for bisphosphonate patients. Adachi et al., (1994) and Liu et al., (2004) reported bisphosphonate therapy in rats. Orthodontic tooth movement may be protracted, and root resorption may be a sequellae of bisphosphonate use in animal models.

Rinchuse et al. (2007) in two case reports on orthodontic patients taking bisphosphonates also observed protracted tooth movement.

In conclusion, it must be recognized that oral and IV bisphosphonates have a distinct benefit to health and improvement of mineral bone density.

**Dental professionals should not recommend discontinuation of these medications for any reason.**

Websites (Table 15) are available for contemporary updates on BON risk factors and management.
Conclusions and Recommendations

- All physicians prescribing bisphosphonates whether intravenously or orally, should actively encourage patients to attend for dental examination, preferably before starting these drugs.

- Patients on IV bisphosphonates are at the highest risk for BON and this risk increases for patients on IV bisphosphonate after 6 months of treatment.

- For patients on IV bisphosphonates for up to 6 months, non-surgical periodontal and restorative care is generally considered to be of an acceptably low risk of developing BON. Emergency dental care, e.g. extractions, should be cautiously and conservatively prescribed and follow the American Dental Association (ADA) guidelines of one initial treatment and then wait for 2 months to determine satisfactory healing before attempting any additional procedures.

- For patients on IV bisphosphonates for over 6 months it is recommended that dental treatment, and particularly surgical interventions be undertaken as a hospital in-patient with appropriate intravenous antibiotics and sterile operating procedures.

- Elective dental surgery such as dental implant placement is not recommended for patients receiving IV bisphosphonates.

- For patients who have been taking oral bisphosphonates for less than 3 years, most dental treatment including surgical procedures (extractions, implant placement, periodontal surgery) is generally considered to be of acceptably low risk of developing subsequent BON.

- For patients who have been on oral bisphosphonates for more than 3 years, BON risk increases and dentists should follow the American Dental Association (ADA) guidelines of one initial treatment and then wait for 2 months to determine satisfactory healing before attempting any additional procedures.

- The risk of developing BON following dental treatment may increase with the duration of continued bisphosphonate treatment. However, there is no current data to support this concept of a “biological gradient” effect.

- Multiple implants or site preparation surgeries may increase BON risk, but there is no current data to support this concept either.

- It would appear a reasonable precaution to recommend an antimicrobial mouthwash (e.g. chlorhexidine 0.1%) for all patients on bisphosphonates prior to every dental procedure, and continue for 14 days post treatment.

- The prescription of systemic antibiotics is recommended for 1-2 days prior to any dental procedures that will be near or through alveolar bone, i.e. extractions, implants, periodontal surgery (Table 14).

- It is important that patients be encouraged to maintain a high standard of oral hygiene. Dental treatment should not be undertaken if the oral hygiene is not acceptable. Treatment should be rescheduled and oral hygiene instruction provided.

-CTX calcium serum test has inconsistent results and may not be predictable for BON. It is not recommended at this time until further studies prove its validity.

- There is no supporting data that cessation of bisphosphonate medication for a period of time i.e. a “drug holiday” reduces the risk of developing BON.

- Regular dental maintenance for all patients on bisphosphonate therapy is necessary to ensure continued oral health and reduce the need for surgical intervention.

- As more research about BON emerges, the recommendations regarding treatment of patients on bisphosphonates will evolve and dentists should always be aware of the latest recommendations.
### Table 1
Bisphosphonates: Therapeutic Uses

<table>
<thead>
<tr>
<th>Intravenous</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypercalcaemia of malignancy</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>Bone metastases of solid tumors</td>
<td>Paget’s disease</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>Heterotopic ossification</td>
</tr>
<tr>
<td>Paget’s disease</td>
<td></td>
</tr>
<tr>
<td>Osteoporosis</td>
<td></td>
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</table>

### Table 2
Intravenous (“Drip”) bisphosphonates - UK

<table>
<thead>
<tr>
<th>Name</th>
<th>Indication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bonefos (sodium clodronate, tablet or drip IV)</td>
<td>Hypercalcaemia of malignancy</td>
<td>by slow IV infusion, 300mg daily for 7-10 days max., or by single-dose infusion of 1500mg</td>
</tr>
<tr>
<td>Aredia (disodium pamidronate)</td>
<td>Hypercalcaemia of malignancy, according to serum calcium concentration</td>
<td>15-60mg in single IV infusion or in divided doses over 2-4 days; max. 90mg per treatment course</td>
</tr>
<tr>
<td></td>
<td>Paget’s disease of bone</td>
<td>30mg once a week for 6 weeks (total dose 180 mg) or 30mg in first week, then 60mg every other week (total dose 210 mg); max. total 360mg (in divided doses of 60mg) per treatment course; may be repeated every 6 months</td>
</tr>
<tr>
<td>Zometa (zoledronic acid)</td>
<td>Reduction of bone damage in advanced malignancies involving bone</td>
<td>by IV infusion, 4mg every 3-4 weeks</td>
</tr>
<tr>
<td>Bondronat (ibandronic acid, tablet or drip IV)</td>
<td>Reduction of bone damage in bone metastases in breast cancer by intravenous infusion</td>
<td>6mg every 3-4 weeks</td>
</tr>
<tr>
<td></td>
<td>Hypercalcaemia of malignancy</td>
<td>by IV infusion, according to serum calcium concentration, 2-4mg in single infusion</td>
</tr>
<tr>
<td></td>
<td>Postmenopausal osteoporosis</td>
<td>by IV injection over 15-30 seconds, 3mg every 3 months</td>
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### Table 3
Summary of Position Papers on the Clinical Profile of Osteonecrosis of the Jaw

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Case definition</strong></td>
<td>Exposed bone in the jaws that persists for at least 8 weeks, in the absence of previous radiation and of metastases in the jaws.</td>
<td>Exposed bone in the oral cavity for more than eight weeks and no history of radiation therapy to the jaws.</td>
<td>ONJ is defined as exposed bone in the oral cavity that did not heal within 8 weeks and had not had radiation therapy to the head and neck region.</td>
<td>The classic clinical presentation includes pain, soft tissue swelling, mobility of teeth, purulence and exposed bone.</td>
</tr>
<tr>
<td><strong>Incidence</strong></td>
<td>Spontaneous reports of ONJ submitted indicates a reporting rate of less than 1 per 100,000 patient treatment years.</td>
<td>ONJ has been estimated to be 0.7/100,000 person-years of exposure to oral bisphosphonates.</td>
<td>The risk with oral bisphosphonate therapy is estimated between less than 1 per 100,000 patient treatment years.</td>
<td>Oral incidence reported at 0.7 cases per 100,000 person-years.</td>
</tr>
<tr>
<td><strong>Recommendations</strong></td>
<td>In osteoporosis patients, no specific interventions prior to bisphosphonate therapy are required except to encourage routine dental care.</td>
<td>A comprehensive dental exam should be completed on all patients beginning therapy with bisphosphonates (or as soon as possible after beginning therapy).</td>
<td>Good oral hygiene and regular dental visits are recommended.</td>
<td>Dental and periodontal exam; treat dental infections and periodontal diseases.</td>
</tr>
<tr>
<td><strong>Do you stop oral bisphosphonates before surgery?</strong></td>
<td>Some clinicians have suggested that a drug holiday from bisphosphonates may be beneficial but there is no evidence to support this.</td>
<td>There is no evidence supporting for drug holidays.</td>
<td>Drug “holidays” may not reduce risk.</td>
<td></td>
</tr>
<tr>
<td><strong>Recommendations</strong></td>
<td>Routine dental treatment need not be modified on the basis of oral bisphosphonate therapy.</td>
<td>Patients taking oral bisphosphonates should have similar dental care (such as good dental hygiene and cleaning, restorations and endodontics) recommended for the general population.</td>
<td>Pat</td>
<td></td>
</tr>
</tbody>
</table>

### Do you perform surgery on patients receiving oral bisphosphonates?

Patients requiring surgery to the oral cavity who have risk factors such as diabetes or corticosteroid use, close monitoring is recommended. Systemic antibiotics and antimicrobials should be considered.

Patients should be informed of the risk of developing BON if invasive surgery is planned or necessary. Conservative surgical technique with primary flap closure is advised. Alternative treatment plans consisting of endodontics instead of extraction and bridges and partial dentures versus implant reconstruction should be presented to the patient.

Elective dental surgery may be necessary if conservative dental treatment fails.
<table>
<thead>
<tr>
<th>Name</th>
<th>Indication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Actonel</strong> (risendronate sodium)</td>
<td>Pagets disease of bone, Post-menopausal osteoporosis, Prevention of osteoporosis (including corticosteroid-induced osteoporosis)</td>
<td>30mg daily for 2 months; may be repeated if necessary after at least 2 months; 5mg daily or 35mg once weekly; 5mg daily</td>
</tr>
<tr>
<td><strong>Bondronat</strong> (ibandronic acid, tablet or drip IV)</td>
<td>Reduction of bone damage in bone metastases in breast cancer by intravenous infusion, Post-menopausal osteoporosis</td>
<td>50mg daily; 150mg once per month</td>
</tr>
<tr>
<td><strong>Bonefoss</strong> (sodium clodronate, tablet or drip IV)</td>
<td>Osteolytic lesions, hypercalcaemia and bone pain associated with skeletal metastases in patients with breast cancer or multiple myeloma</td>
<td>1.6g daily in single or 2 divided doses increased if necessary to a max. of 3.2mg daily</td>
</tr>
<tr>
<td><strong>Didronel</strong> (disodium etidronate)</td>
<td>Osteoarthritis</td>
<td>400mg qd for 2/52 in conjunction with 1.25g CaCO₃ over a 76-90 day cycle</td>
</tr>
<tr>
<td><strong>Fosamax</strong> (alendronic acid)</td>
<td>Post-menopausal osteoporosis and osteoporosis in men, Prevention of post-menopausal osteoporosis, Prevention and treatment of corticosteroid induced osteoporosis</td>
<td>10mg daily (or 70mg once weekly for post-menopausal osteoporosis); 5mg daily (for post-menopausal women not receiving hormone replacement therapy, 10mg daily)</td>
</tr>
<tr>
<td><strong>Fosavance</strong> (alendronic acid and colecalciferol)</td>
<td>Post-menopausal osteoporosis in women at risk of vitamin D deficiency</td>
<td>1 tablet once weekly</td>
</tr>
<tr>
<td><strong>Protelos</strong> (strontium ranelate)</td>
<td>Osteoporosis</td>
<td>2g od</td>
</tr>
<tr>
<td><strong>Skelid</strong> (tiludronic acid)</td>
<td>Osteoporosis</td>
<td>400mg od for 12 weeks (may be repeated if necessary after 6 months)</td>
</tr>
</tbody>
</table>
### Table 5
**Current Terminology of “Osteonecrosis of the Jaw”**

<table>
<thead>
<tr>
<th>Term</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisphosphonate associated osteonecrosis (current term*)</td>
<td>BON</td>
</tr>
<tr>
<td>Osteonecrosis of the jaw</td>
<td>ONJ</td>
</tr>
<tr>
<td>Bisphophonate-related osteonecrosis of the jaw</td>
<td>BRONJ</td>
</tr>
<tr>
<td>Bisphophonate-induced osteonecrosis of the jaw</td>
<td>BIONJ</td>
</tr>
<tr>
<td>Bisphopshonate-associated osteonecrosis of the jaw</td>
<td>BONJ</td>
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</tbody>
</table>


*Council on Scientific Affairs J Am Dent Assoc. 2008;139(12):1674-77

### Table 6
**Incidence of BON**

<table>
<thead>
<tr>
<th>IV</th>
<th>Oral</th>
</tr>
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<tbody>
<tr>
<td>20%¹</td>
<td>0.34%² - 4.0%³</td>
</tr>
</tbody>
</table>

¹Boonyakaporn et al. Oral Oncol. 2008;44(9):857-69

### Table 7
**Biological basis of BON**

| Impairs osteoclasts | Weinstein, ASBMR 2007 |
| Delayed bone formation | Aguirre, ASBMR 2007 |
| Impaired angiogenesis | Aguirre, ASBMR 2007 |
| Matrix necrosis in the mandible | Allen, 2008; Nase and Suzuki, 2006 |
### Table 8
Potential co-morbidities for BON

<table>
<thead>
<tr>
<th>Condition</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodontitis</td>
<td>(Boonyakaporn, 2008)</td>
</tr>
<tr>
<td>Extractions</td>
<td>(Boonyakaporn, 2008)</td>
</tr>
<tr>
<td>Steroid treatment</td>
<td>(Odvina, 2005)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>(Khamasisi, 2007)</td>
</tr>
<tr>
<td>Smoking</td>
<td>(Yarom, 2007)</td>
</tr>
</tbody>
</table>

### Table 9
ADA Recommendations

- Routine dental treatment is OK
- Dental examination before or early during bisphosphonate treatment
- Oral hygiene instruction (OHI) reduces risk
- CTX blood test is inconclusive
- “Drug holiday” may NOT reduce risk of BON


### Table 10
Dental treatment for patients on bisphosphonate treatment

1. Observe wound healing for one tooth or sextant (2 months min.)
2. Antimicrobial rinses bid
3. Treat ASAP. Endo, sinus tracts, purulence, severe periodontitis, apical abscess
4. Non-surgical periodontal treatment with limited flaps
5. Bone regeneration? - no evidence
6. Implants? - caution advised


### Table 11
CTX test problems

- Measures primarily trabecular bone (teeth are anchored in cortical bone, whilst implants pass through both cortical and trabecular bone)
- Measures skeletal bone
- May not be accurate for jaw bones
Table 12
Fosamax has extended benefit for 5 years after discontinuation of Tx

- 1100 female patients, age range 55-81 years
- 10 years on Fosamax treatment
- Osteoporosis protection for 5 years after stopping the drug
- Conclusion - “Protective benefit for at least 5 years after drug cessation”
- “Drug holiday” may NOT reduce risk of BON


Table 13
Bone biopsy data

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bone Mineralization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate (Fosamax)</td>
<td>2-3 years normal mineralization</td>
</tr>
<tr>
<td>Risendronate (Actonel)</td>
<td>3-5 years normal mineralization</td>
</tr>
</tbody>
</table>


Table 14
Antibiotic regimens (Begin 1 to 2 days before dental treatment)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>500mg tds for 8 days</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>500mg tds for 8 days</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>150mg bds for 8 days</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>500mg tds for 8 days</td>
</tr>
<tr>
<td>Azithrocin</td>
<td>2 tabs stat, 1 tab od for 9 days*</td>
</tr>
</tbody>
</table>

*Wade and Suzuki (2007)

Table 15
Websites for bisphosphonate-associated osteonecrosis

<table>
<thead>
<tr>
<th>Website</th>
<th>URL</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Osteoporosis Foundation</td>
<td><a href="http://www.nof.org">www.nof.org</a></td>
</tr>
<tr>
<td>American Society for Bone and Mineral Research</td>
<td><a href="http://www.asbmr.org">www.asbmr.org</a></td>
</tr>
<tr>
<td>American Dental Association (Updated weekly)</td>
<td><a href="http://www.ada.org/prof/resources/topics/ostenecrosis.asp">www.ada.org/prof/resources/topics/ostenecrosis.asp</a></td>
</tr>
</tbody>
</table>
Clinical images of BON

Mild presentation of BON - image courtesy of John W. Hellstein and Hardin MD - University of Iowa

Presentation of BON with accompanied by an oro-antral fistula - image courtesy of John W. Hellstein and Dr M. D. Hardin from the University of Iowa - http://www.lib.uiowa.edu/hardin/md/ui/dent/osteonecrosis5.html
Severe presentation of BON - image courtesy of John W. Hellstein and Hardin MD University of Iowa - http://www.lib.uiowa.edu/hARDIN/MD/ui/dent/osteonecrosis6.html

Photograph courtesy of Dr. Sook-Bin Woo from Oral Medicine at the Brigham and Women's Hospital in Boston. The patient had myeloma and was on zolendronic acid. Exposed necrotic bone can be seen.
Case Report - Treatment and Outcome

The following case report is adapted from, “Issues related to diagnosis and treatment of bisphosphonate-induced osteonecrosis of the jaws” - Wade and Suzuki 2008 (Grand Rounds in Oral and Systemic Medicine). This case illustrates the experiences of a private practitioner’s caring for a cancer patient who was receiving IV bisphosphonate therapy. RD was a 67-year-old white male who presented in January 2005 on referral from his dentist for “exposed bone on the lingual mandible”. The patient had completed endodontic treatment on tooth LR6, six months previously, but the treatment did not relieve his pain.

He complained of increasingly severe pain in the right mandible that radiated anteriorly and of swelling and purulent discharge. He had been diagnosed with renal cell carcinoma and had undergone removal of his right kidney. The cancer had metastasized to his right hip and he had undergone a right total hip replacement. He was being treated with high dose pain medication and zolendronic acid. The dental examination (Figure 1) revealed a 2- to 3-mm-diameter area of exposed bone lingual to tooth LR6, with anterior swelling, erythema, and 2 draining fistulae over a large multilobulated, lingual torus.

Treatment consisted of clindamycin 300 mg every 6 hours for 10 days, along with a hydrogen peroxide rinse 4 times daily. Initially the situation improved but did not resolve. The patient returned in July 2005 with an enlarged area of exposed bone and a draining fistula over the torus. The medication was changed to penicillin V potassium 500 mg every 6 hours, along with metronidazole 500 mg every 6 hours. The patient was then lost to follow-up for several months as a result of a change in health insurance.

In June 2005 the patient returned, complaining of pain, swelling, and discharge. After debridement of a small amount of sequestered bone, the patient was prescribed the same penicillin V potassium–metronidazole regimen as earlier. Because of continued pain and mobility, tooth LR6 was extracted.

During the procedure, an abscess was noted and infected tissue was debrided; treatment with penicillin and metronidazole was continued and the patient’s pain resolved. He continued to struggle with poor oral hygiene in the area of the necrotic segment.

In July 2005 (Figure 2), a larger area of exposed bone was found lingual to tooth LR6. One month later, the necrotic bone was surgically debrided, and the antibiotic regimen was continued.

In March 2006, tooth UL1 also developed an abscess. To avoid extraction of the tooth and the possibility of additional necrotic bone, the crown of tooth was amputated, endodontic treatment was completed and the root was left in the bone. A small sequestrectomy was completed on the buccal bone of tooth LR6 and antibiotic maintenance was continued with Pen VK 500 mg every 6 hours.
When seen in May 2006 (Figure 3) the exposed bone remained but the patient was free of infection and on maintenance antibiotics.

In January 2007 (Figure 4) the patient presented once more with increasingly severe pain in the right mandible, with swelling and pus. The patient was treated with the PenVK/Metronidazole regimen and the infection resolved.

He died of renal cell carcinoma in March 2007. This litany of care is illustrative of the challenges facing clinicians who care for bisphosphonate patients.
References


