

1: Fleisher, Kenneth E.

osteomyelitis and osteoradionecrosis Osteomyelitis is an infectious, inflammatory process of bone marrow with involvement of the overlying cortical plates and periosteum. The marrow space provides a conduit and medium for spread of odontogenic pathogens from dental disease, dentoskeletal trauma, or both.

Cox, DDS, MBA; and Bahram Javid, DMD Abstract The key to appropriate treatment of odontogenic osteomyelitis or bisphosphonate-related osteonecrosis of the mandible in patients with autoimmune diseases lies in making the correct diagnosis based on meticulous review of signs and symptoms. As this complex case involving a patient with multiple comorbidities illustrates, diagnosis can be difficult, because these conditions may overlap or be mistaken for other conditions. However, prompt treatment is essential to limit the progression, which can be devastating for these medically complex patients. It is, therefore, important to understand local and systemic conditions that can weaken the immune system and predispose patients to chronic bone infection, meticulously go through signs and symptoms, and have a complete medical history, including patient medications. Chronic osteomyelitis CO is a rare infection of the medullary portion of the jawbone with purulent exudate. Of dental infectious origin, this condition often occurs in immunocompromised individuals. The infection then spreads both within the marrow and also through the cortical bone to the periosteum. The periosteum, with time, begins to form new bone the involucrum while the central necrotic bone is known to be called sequestrum. Both can be identified by x-ray after 6 to 8 weeks of the infectious process. Treatment of CO is surgical and includes excision of the soft-tissue sinuses, extraction of involved tooth or teeth, debridement of the intrabony abscess with removal of sequestra, and long-term antibiotic therapy usually at least 6 to 8 weeks based on the culture and sensitivity. An infectious disease consultation is often recommended. Bisphosphonate-related osteonecrosis of the jaws BRONJ is a relatively rare complication of treatment with nitrogen-containing bisphosphonates NBPs, which are taken for a variety of conditions ranging from osteoporosis to metastatic cancer, resulting in avascular necrosis of the jawbone and bone exposure in the oral cavity. The exposed bone can become infected from pathogenic oral bacterial organisms. All bones of the skeleton are affected. Relative ease of bone exposure after extraction of a tooth contributes to the development of bone infection and necrosis. Due to a generalized involvement, this condition can also be called osteochemonecrosis. The bisphosphonate medications tend to selectively target and destroy osteoclasts, altering the bone metabolism and allowing a unilateral osteoblast-mediated bone build-up. This results in a formation of dense and poorly vascularized bone. Due to the involvement of the entire jaw, BRONJ cases tend to be treated more conservatively than cases of osteomyelitis or osteoradionecrosis, where surgical debridement is important. Both CO and BRONJ can have similar signs and symptoms, are most commonly found in the posterior mandible, and result in the formation of necrotic bone in the jaws. Although there is no data on the interplay of multiple factors in these conditions, immunocompromised patients on long-term treatment with NBPs, who concurrently have an advanced dental disease, need to be evaluated for CO so an accurate diagnosis can be established and a targeted treatment plan implemented. In this report, the authors describe a challenging case involving a patient who developed jawbone necrosis. It emphasizes the importance of a proper differential diagnosis including BRONJ and CO while accurately determining the final diagnosis so that the proper therapy can be instituted. The authors followed the guidelines of the Helsinki Declaration for this study. This article was exempt from the institutional review board approval. In addition, the patient had hypertension, right total hip replacement surgery without complications 3 years prior, and was allergic to penicillin. On examination, the patient had a decayed remaining lower right third molar root with associated mild swelling and erythema of the surrounding tissue. A panoramic radiograph showed a small portion of the third molar root mainly in the soft tissue above the alveolar bone level Figure 1. The day after presentation, the patient underwent extraction of the root of the lower right third molar without complications. One hour prior to her surgery, the patient took mg of clindamycin, and she continued on mg of clindamycin three times daily for the next 5 days. The patient returned for follow-up examination 1 week postoperatively and demonstrated normal healing for this

timeframe. One month later, the patient called to report swelling and pain in the area of the extraction site. On examination, swelling was evident in the posterior mandible in the area of extraction, extending to the buccal vestibule and masseteric region, with limited mouth opening to about 15 mm, and purulent discharge behind the second molar. Given that this condition had existed for 6 to 8 weeks, the preliminary diagnosis of CO was made, and the patient consented to indicated treatment, which consisted of debridement of the wound and extraction of the second molar. The procedure was performed on the same day under local anesthesia; mg of clindamycin was given just prior to the surgery. A buccal full-thickness flap in the second-third molar area was raised, and multiple small bony sequestra with granulations tissue were visualized and removed until fresh bleeding bone was seen; the involved second molar was also removed with copious irrigation after debridement. The patient was placed on clindamycin mg four times daily and was followed weekly. Four weeks later, the wound remained open with purulent discharge. A second, wider bone debridement procedure was performed, with removal of a few more necrotic bone fragments. The agreed upon approach was to discontinue the alendronate and to decrease the dosage of prednisone from There was a temporary improvement in her jaw symptoms, but after 5 to 7 days, infection with purulent discharge returned. Follow-up imaging, including a panoramic radiograph Figure 3 , showed persistent mottled, mixed irregular radiolucent-radiopaque appearance, slightly more extensive than that seen on the previous panoramic image. The third debridement of the wound was performed 10 weeks after extraction of the root of the third molar, which was 6 weeks after the first debridement and 3. A large amount of granulation tissue and multiple sequestra of devitalized bone were curetted out down to vital-appearing bleeding bone. A second culture and sensitivity test did not reveal the presence of microorganisms. Because of concerns for mandibular osteomyelitis and possibly actinomycosis , the ID physician discontinued oral clindamycin, and the patient was placed on a 6-week course of intravenous ceftriaxone 2 gm, once a day through the peripherally inserted central catheter PICC line. In 48 to 72 hours, the patient reported much improvement in symptoms. Granulation tissue began to fill the wound, negating the need for further debridement. After 6 weeks of ceftriaxone, complete closure of the wound was occurring, and a panoramic radiograph demonstrated significant remodeling of the bone without a mottled appearance or evidence of sequestration. Although the patient subsequently developed diabetes mellitus DM type 2 and was placed on insulin, it did not complicate the wound healing Figure 5. Upon discontinuation of ceftriaxone, the ID physician returned the patient back to a 3-week course of oral clindamycin mg, three times a day. The last panoramic radiograph taken on this patient was 5 months after the initial presentation and 3 months after the last debridement. It demonstrated partial fill of the mandibular defect and bone remodeling without evidence of necrosis Figure 6. A few oral conditions can present as non-vital necrotic bone in the jaws, including: Although any of these processes can develop in the immunocompetent individual, they can initiate much earlier and progress much more quickly in an immunocompromised patient or one with autoimmune disease on immunosuppressive medications, such as the patient in the described case report. The patient in this case report had RA—a systemic chronic inflammatory autoimmune disease that usually occurs in middle-aged women and affects mainly joints and other tissues and organs lungs, pericardium, sclera, etc. It typically leads to symmetrical small-joint destruction articular cartilage and often ankylosis with functional compromise. Vasculitis compromising peripheral blood supply of tissues has an important role in pathophysiology of this condition. Treatment of RA includes anti-rheumatic drugs Imuran or azathioprine, others , anti-inflammatory medications glucocorticoids, NSAIDs , and analgesics opioids, etc. This medication is known to suppress the bone marrow, causing increased susceptibility of patients to infections. In the presented case, the patient developed necrotic bone with sequestration in the proximity of the decayed tooth. The tooth was eventually removed, but the infection spread deeper into the bone, resulting in the formation of necrotic bone and multiple sequestra. At this stage, the patient was diagnosed with chronic osteomyelitis. The term osteomyelitis has been used to describe a wide variety of pathological conditions, including acute and chronic bacterial suppurative , diffuse sclerosing, focal sclerosing condensing osteitis , osteomyelitis with proliferative periostitis, and others. A prolonged course of oral and intravenous antibiotics is usually required to treat this condition. Later into the case—when it became known that the patient had been on alendronate nitrogen-containing bisphosphonate Fosamax for the

previous 3 years” the differential diagnosis included BRONJ. BRONJ is considered a risk for oral and especially intravenous bisphosphonate therapy. Duration of bisphosphonate therapy plays an important role and the mandible appears to be a favorite location for this condition. There was 1 an obvious infection of the medullary bone of the posterior mandible with purulent discharge of a long duration associated with a decayed infected tooth; 2 the presence of multiple sequestra; 3 the need for multiple bone debridement procedures; and 4 a long course of oral and intravenous antibiotic treatment that was necessary to control infection. The clinical dilemma in cases such as these” which is clear from the title of this article” is to formulate the proper diagnosis. Making the Diagnosis The authors believe that in this particular case, the proper diagnosis tends to point towards osteomyelitis, with BRONJ playing the secondary role. There are several subtle clinical indicators that were important in the learning process and that led to this conclusion. This is common for jaw osteomyelitis of odontogenic origin from the infected tooth of a long duration and not common for BRONJ, where the dentoalveolar surgery is usually the initiating factor a major risk factor, according to the AAOMS Position Paper. This was seen in the described case Figure 4. Presence of a vital surrounding bone was also confirmed clinically every time the debridement procedure was performed. BRONJ treatment often does not show signs of remodeling and separation due to presence of permanently affected avascular bone in the entire jaw. In BRONJ cases, the entire skeleton is affected by the drug-related condition often called chemonecrosis. The morning fasting serum C-terminal cross-linking telopeptide CTX , an index of bone turnover that can help to identify the degree of BRONJ, was not tested in the presented case. It may slowly improve with a conservative superficial debridement of just exposed portions of necrotic bone. That was not the approach that was used in the presented case. Fourth, targeted antibiotic therapy is extremely helpful in treatment of CO. In the presented case, although oral clindamycin was not effective initially, the patient dramatically improved as soon as targeted intravenous ceftriaxone therapy was initiated. Due to the avascular state of the surrounding bone and a decrease in bone turnover, an antibiotic may not always get to the affected jaw area and a topical rinses use of chlorhexidine is often more practical. Finally, the association between an immunocompromised systemic condition and development of osteomyelitis is strong. Osteomyelitis of the jaw is often accompanied by regional or systemic compromise of the immune response. Although it is rare to see CO of the jaws in developed countries, it has been described in patients with immune comorbidities. Saia et al²⁰ reported BRONJ cases as a rare outcome in high-risk nitrogen-containing bisphosphonate users who underwent surgical extraction where baseline osteomyelitis was a strong risk factor for BRONJ development. In conclusion, the authors believe that it is extremely important for oral and maxillofacial surgeons to understand local and systemic conditions that can weaken the immune system and predispose dental patients to chronic bone infection. Acknowledgment The authors thank Stephen E. Follansbee, MD, an infectious disease specialist, for review of the article and thoughtful recommendations. Managing the care of patients receiving antiresorptive therapy for prevention and treatment of osteoporosis: J Am Dent Assoc. Marx RE, Stern D, eds. Oral and Maxillofacial Pathology: A Rationale for Diagnosis and Treatment. Single-dose intravenous therapy wpamidronate for the treatment of hypercalcemia of malignancy: Comparison of , , and mg dosages. Zoledronic acid is superior to pamidronate in the treatment of hypercalcemia of malignancy: A pooled analysis of two randomized, controlled, clinical trials.

2: Osteomyelitis - Wikipedia

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Few studies with the same objectives were found in a recent review of the literature; 1 , 3 , 10 , 11 but more information was needed in order to clarify histological differences between the diseases. Since the information was retrieved from the files of an oral pathology service, the number of cases was not identical, but all cases were maintained in the study, thus avoiding the significant reduction of sample size to a minimum. Another important aspect refers to OMJ. It is true that MRONJ and ORNJ can easily evolve into osteomyelitis once secondary infection occurs, 12 which can hinder the final diagnosis as well as the comprehension of the etiological process of each disease. The analysis of the histological criteria was based on their presence or not, and no morphometric method was used to quantify cells or structures, as this is not a routine practice for the analyzed diseases. Nevertheless, most of the analyzed criteria did not reveal significant differences, but it was clear that some of them were more prevalent in one or other disease. These aspects will also be discussed in order to elucidate some subtleties of each disease. Also, regarding the methodology, the morphometric analysis was not performed mainly due to the large variability in sample size, since the study was performed with biopsy specimens from different patients performed by different surgeons. The presence of necrotic bone was fairly common among the clinical diseases. Although these characteristics were individually analyzed in our study, they were also taken as characteristics that compounded the general picture of bone necrosis. Although there was no significant difference in the presence of osteoclasts among the three clinical diseases, it was clear that they were lower in MRONJ specimens than in the other diseases, possibly due to the mechanism of action of the drug involved in the osteonecrotic process. The same occurred in reactive bone and osteoblastic coating. Despite the lack of significant difference among the diseases, OMJ specimens showed larger amounts of both criteria. When inflammation was assessed, more than 75 of the samples revealed presence of some kind of leukocytes, and neutrophils were more frequent in OMJ. When the diseases were compared, no significant differences were detected. Hyperemia and thrombosis predominated in ORNJ. In OMJ, microorganisms were observed in 50 of the samples, compared to Microorganisms of the genus *Actinomyces* have been found in these diseases by several authors, 6 , 13 , 14 , 15 , 16 including by Marx and Tursun 2 The microorganisms were detected on trabecular bone surfaces in 76 of MRONJ and in 58 of ORNJ cases. In OMJ samples, these microorganisms were found in medullary spaces. It is important to emphasize that only 6 OMJ samples were evaluated in the present study. Pathologists who work with diagnoses and know the three entities know that anamnesis is crucial for the diagnosis, given that clinical and radiographic features are very similar. With regard to the first research question, the blinded evaluation by two oral pathologists confirmed the hypothesis that it is not possible to establish a final diagnosis only by way of microscopic analysis. The diagnoses of the diseases mentioned above tended to be quite similar microscopically, as unanimously endorsed by experts. Clinical management of suppurative osteomyelitis, bisphosphonate-related osteonecrosis, and osteoradionecrosis: Marx RE, Tursun R. Suppurative osteomyelitis, bisphosphonate induced osteonecrosis, osteoradionecrosis: *Int J Oral Maxillofac Surg. Int J Clin Exp Pathol. J Oral Maxillofac Surg. American Association of Oral and Maxillofacial Surgeons position paper on medication-related osteonecrosis of the jaw: Image findings of bisphosphonate related osteonecrosis of jaws comparing with osteoradionecrosis. Radiographic findings in patients with medication-related osteonecrosis of the jaw. Histopathologic and histomorphometric analysis of irradiation injury in bone and the surrounding soft tissues of the jaws. Osteonecrosis of the jaws in patients treated with bisphosphonates - histomorphologic analysis in comparison with infected osteoradionecrosis. J Oral Pathol Med. Bisphosphonate associated osteomyelitis of the jaw in patients with bony exposure: J Appl Oral Sci. Bisphosphonate related osteonecrosis of the jaw: Important aspects regarding the role of microorganisms in bisphosphonate-related osteonecrosis of the jaws. Opportunistic actinomycosis in osteoradionecrosis of the jaws in patients affected by head and neck cancer: September 19, ; Revised: January 31, ; Accepted: February 16, Corresponding Author: Camila Lopes Cardoso,*

E-mail: The authors certify that they have no commercial or associative interest that represents a conflict of interest in connection with the manuscript. This is an Open Access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

3: Osteoradionecrosis / Osteomyelitis - University of Maryland, Baltimore

Currently, more common osteomyelitis variants are seen, namely, osteoradionecrosis (ORN) and bisphosphonate-related osteonecrosis of the jaws (BRONJ). Osteomyelitis, ORN, and BRONJ can present with similar symptoms, signs, and radiographic findings.

Osteomyelitis of the jaws: A year perspective, J Oral Maxillofac Surg

Fistulization is more commonly seen with purulent long-standing osteomyelitic infection and can harbor neoplastic change from inflammatory metaplasia cultures of sinus tracts, which usually show auras and are of little value. Necrotic bone and non-healing hard and soft tissue wound may be in evidence. Paresthesia is a symptom to which the clinician should pay greater attention because not only does it speak to increased intermedullary inflammation, swelling, and pressure, but it may have a terminal end result creating permanent nerve injury and subsequent neuropathic pain, which may be the more prevalent clinical problem faced in chronic osteomyelitis. This neuropathy will be discussed further later in this chapter. Positive laboratory findings are usually typical of those seen with any infectious inflammatory process such as elevated white cell counts. All of these assays could also be elevated by dehydration and poor oral fluid intake as a result of the infection being located in the jaw and the upper alimentary tract. Greater attention needs to be focused on the systemic sequela of local and regional oral infection and the infectious inflammatory process influence that has now been directly implicated in such distant organs as myocardium and colon as well as being associated with pre-term birth and lowbirth-weight infants. This would include not only periodontal and pericoronal infection, but also osteomyelitis, especially of the chronic variety. Cultures of wound prior to antibiotic therapy coupled with blood cultures taken at appropriate times. Many of these organisms are very fastidious or delicate so cultures must be maintained beyond the usual 3-day lab interval to identify the fragile pathogens. Occasionally there will be unusual pathogens including viruses like HIV or CMV or metastatic embolic infection to teeth-bearing areas of bone because of its unusual intermedullary vascular configuration as identified in case reports, but these are unusual. Radiographic evaluation of infectious inflammatory disease is usually in the form of scout film or orthopantomogram. This radiograph is more likely to identify risk or causative factors than the disease process itself, especially in the acute phase. Lytic radiolucent areas may be seen; however, the classic radiopaque reaction to infectious inflammatory disease processes is usually not appreciated until later in the more non-acute phase of the disease process. Figure CT and MRI both are helpful, with CT imaging giving more resolution to the lytic areas and MRI identifying loss of marrow signal associated with infection, swelling, and inflammation with possible necrosis. Figures and Triphasic bone scanning includes a flow phase of technetium bone scanning, which identifies areas of osteoplastic-induced bone turnover once this is ongoing, and indium or gallium scanning, which identifies actual infectious inflammatory leukocytic processes, although poor in resolution. Figure PET CT with the fluoride isotope is much more sensitive to bone turnover and metabolic change with marked improvement in resolution over old PET scanning, but it is somewhat cost prohibitive. Figures to Recently cone beam CT has shown possible benefit in the radiologic evaluation and cost analysis. Note loss of signal in the medullary compartment of the right mandible. Note poor resolution of margins of bony lesion. Note that bony lesion margin resolution is better than that in a ^{99m}Tc MDP scan but still poor as a surgical guideline. Surgical disruption of the infectious foci and organized abscess along with debridement of necrotic tissue and foreign bodies is paramount. As with most typical infectious processes, there is localized immunoregulatory effect by the host to wall off the infectious foci. This is augmented to some degree by the infection itself. Disruption of this infectious architecture is necessary if other adjunctive measures such as antimicrobial therapy are to have a chance to aid in resolution. Several types of surgical intervention recruit and create a heightened inflammatory phase, which allows reperfusion or hyperemia. Hyperemic conditions allow the host immune response to be augmented by antibiotics and to develop therapeutic thresholds in the infection site. Table

SURGERY MEDICINE and VOLUME 16 NUMBER 3 MAECH, PATHOLOGY OPERATIVE ORAL SURGERY OSTEOMYELITIS AND OSTEORADIONECROSIS Report of Two Cases Thomas J. Cook, D.D.S., Miami, Fla. Jackson Memorial Hospital PYOGENic osteomyelitis is an inflammatory process in the bone marrow.*

Received Aug 10; Accepted Sep The general surgeon who undertook the procedure was recommended to me by the family general practitioner GP , not an ear, nose and throat ENT specialist surgeon. The surgery was completed without the use of a drain, with radiotherapy strongly recommended. After surgery, I had a fluid-filled lump, pain, swelling, slight palsy and, following the removal of the stitches, a salivary leak developed. The surgeon removed some of the fluid from the lump and recommended over the following weeks increasing doses of hysocine butyl bromide, universally recommended to dry saliva over the following weeks. He did not think I should be prescribed antibiotics. My local GP, however, prescribed 2 courses of cephalexin. During this time, I had to increase my pain medication, taramadol hydrochloride, to counteract the increasing pain and swelling. As neither the GP nor the surgeon were investigating my slow recovery and suspected infection, an obstetrician friend from Brisbane and a pain management specialist in Sydney expressed that I should have recovered within 2 to 3 weeks as the surgeon had advised. Four weeks later, following 6 appointments to both surgeon and GP and an outpatient visit to the local hospital the latter two stating that I should re-consult the surgeon , I finally sought a third opinion from another local GP, also a respected surgeon, who is now my family doctor. He immediately took a swab; the results indicated that *Enterobacter aerogenes*, a bowel bacterium, was infecting the surgical site and inhibiting recovery. A double course of ciprofloxacin and raberprazole, to counteract the hysocine butyl bromide, was prescribed. In response to the antibiotics, the wound closed and the redness and pain subsided considerably. Thankfully, the salivary leak ceased on 18 October, though I still had overnight discharges. By the end of October, about to commence 27 treatments of radiotherapy, I suffered a week of severe dizziness and vertigo; this was relieved with metaclopramide. Less than two weeks into radiotherapy my ear discharged an extremely smelly yellow thick mucus. He did not, at the time, believe the infection was serious. The oncologist and resident hospital doctor prescribed 5 courses of oral nystatin for the developing fungal infection in my mouth area. When I returned home the left side of my face was severely burnt from the radiation treatment and my ear was continuing to discharge. My GP eventually relieved the discomfort by syringing my ear and prescribing amphotericin B, a stronger anti-fungal treatment. In January , my ear leaked the same yellowish mucus as during my radiotherapy. After my consultation in February , I finally felt I was receiving appropriate medical attention for my ear infection which had plagued me since October and which was now diagnosed as chronic otitis media, the severest form of ear infection. Tests confirmed the presence of both *Pseudomonas aeruginosa* and *Candida parapsilosis* in my ear. A grommet was inserted and a central line for an assortment of intravenous IV antibiotics which included tazocin, gentamicin and meropenem combined with oral fluconazole, an even stronger anti-fungal than previously prescribed. Following the insertion of the grommet, my ear leaked for several days with the same fluid as post-surgery. It was several days after the grommet surgery before the ENT registrar advised me to wear ear plugs to keep the ear dry during bathing to reduce infection. I continue to do this using a special swimming silicone ear plug in my left ear only. After 9 days in hospital, my head specialist of infectious diseases and microbiology explained I had soft tissue infection and possibly bone infection. Following my discharge, I was prescribed multiple courses of Ciprofloxacin and Fluconazole. I returned to Sydney several times throughout for follow up appointments with my head specialist. On 2 August , eleven months after my initial surgery, I finally returned to work, but with greatly reduced hours. On a website I discovered that severe otitis media leading to bone infection is a third world disease which is relatively unheard of in the western world. My condition was further complicated by radiotherapy. Internet research led to the discovery of a more potent anti-fungal, Caspofungin, successful in treating *Candida parapsilosis*. Consequently my head specialist organised hospital admission in November to receive Caspofungin medication and further IV antibiotics. About 2 months before my admission, I had suffered from another

Candida ear infection. However these drops blocked the grommet; it was subsequently removed leaving a hole in my eardrum. The diagnosis at this time described my condition as osteomyelitis temporal bone , osteoradionecrosis, mastoiditis and prone to recurrent ear infections. Although my ear continues to discharge intermittently, rather than seek medical treatment I just deal with the discomfort and symptoms, hoping it will not develop into another infection. My local ENT referred me to a professor of otology, who dismissed my diagnosis saying I only had temporomandibular joint TMJ problems, even though I explained that I had been using a dental retainer for years. When I touched the triangular area in front of my ear it felt and sounded like a moist sponge; now it only feels spongy when the swelling worsens. I believe the pressure from the swelling surrounding the surgical site intensifies my muscle and jaw soreness. Sometimes my jaw sounds like a creaky door. In January , I wrote to my head specialist requesting hyperbaric oxygen therapy HBOT , for osteomyelitis and osteoradionecrosis researched via the Internet. He referred me to the Prince of Wales Diving and Hyperbaric Unit, Randwick, sadly the sole hospital facility in New South Wales, only able to treat a maximum of 20 patients per day. The HBOT was conducted in both the multiplace and the monoplace chambers. The treatment was initially a very frightening experience but the compression and decompression fortunately did not affect my ear as much as I thought it would. The monoplace chamber seemed to be the most comfortable method for me. The conclusion was that significant improvement had occurred following HBOT although opacification or fluid was still noted. During , a neurologist noted that the anvil and hammer in my left ear appeared distorted. He also noted that my eyes correct the imbalances caused by vertigo and, as a consequence, I frequently suffer from sore and tired eyes. I continue to experience speech difficulties: I also continue to experience intermittent tingling and numbness around my mouth, tongue and lips. I often suffer from nausea similar to that of all-day morning sickness. I recommend HBOT for others suffering similar medical complications. To relieve my symptoms I undertake complementary therapies: She attributes the recent improved quality of her life to this treatment.

5: Pathology Outlines - Osteomyelitis: osteoradionecrosis (ORN)

Osteoradionecrosis (ORN) is considered a late effect of a radiation induced fibroatrophic process, but is not considered as primary osteomyelitis. It is more similar to aseptic / avascular necrosis of bone than primary infection of bone, although infection or bacterial colonization can occur.

Fleisher is a fellow of the American College of Surgeons, an association with rigorous qualifications for membership. He is a nationally known specialist in oral and maxillofacial surgery, whose areas of expertise include necrotic bone disease such as osteomyelitis, osteoradionecrosis and medication-related osteonecrosis of the jaw MRONJ. His other areas of specialization include surgical management of obstructive sleep apnea, jaw reconstruction, implant surgery, temporomandibular joint TMJ surgery and trauma. Fleisher is an attending in the department of Plastic Surgery at NYU Langone Medical Center and participates in training predoctoral students, international students and postgraduate residents in the oral and maxillofacial surgery training program at NYU College of Dentistry. Fleisher also participates in training postgraduate general dental residents at Bellevue Hospital Center and Gouverneur Hospital. Fleisher is the principle investigator of a study designed to understand the pathogenesis of Osteonecrosis of the Jaw ONJ. What is Osteonecrosis of the Jaw? Osteonecrosis of the jaw, often referred to as "ONJ", refers to an area of dead bone in the jaw. How do I know if I have Medication-Related osteonecrosis of the jaw? An oral health care specialist can typically make this diagnosis after a taking a thorough medical history and performing a careful examination. There are many risk factors for MRONJ that include antiresorptive therapy ie, bisphosphonates, denosumab , chemotherapy, poor oral hygiene, and infection. How is osteonecrosis of the jaw treated? For more information about ONJ, please contact Dr. Does fluorodeoxyglucose positron emission tomography with computed tomography facilitate treatment of medication-related osteonecrosis of the jaw? J Oral Maxillofac Surg ; Oral microbiota and host innate immune response in bisphosphonate-related osteonecrosis of the jaw. Int J Oral Science ; Metastatic cancer identified in osteonecrosis of the jaws in patients taking intravenous bisphosphonate medications. Antibiotic effects on bacterial profile in osteonecrosis of the jaw. Oral Diseases ; Concentration dependent effects of tobacco particulates from different types of cigarettes on expression of drug metabolizing proteins, and benzo a pyrene metabolism in primary normal human oral epithelial cells. Food and Chemical Toxicology ; Predicting risk for bisphosphonate-related osteonecrosis of the jaws: CTX versus radiographic markers. Bisphosphonate-related Osteonecrosis of the Jaws: A Year Book Quarterly ; 20 2: Fleisher KE, Krieger A. J Oral Maxillofacial Surg ; Am J Neuroradiology ; US Respiratory Disease ; 2 2: Experimental and Molecular Pathology ; Report of a case. Compendium ; 16

6: New approach for the treatment of osteoradionecrosis with pentoxifylline and tocopherol

Irradiation osteomyelitis of the jaws, a chronic infection of the maxilla or mandible after irradiation therapy for cancer of the oral cavity, is a major complication of irradiation therapy. Its etiology, pathology, and treatment are described with reference to 10 cases occurring among irradiated patients.

It is important to understand that the role of the Office is to appraise the scientific evidence only, and not to be involved in actual policy development. Assessments are performed in response to requests from the public sector such as hospitals, physicians, professional associations, regional districts, government; private sector groups such as manufacturers; and individuals from the general public. One or more of the following criteria are used to determine the priority of an assessment and the level of analysis: The collection of information for assessment is done in a systematic way to get all information from traditional sources such as libraries as well as fugitive information from other sources. A comprehensive search of the literature is done through the U. The evaluation of a health technology is based upon the analysis of the information for quality of the evidence and strength of the findings. Logical and defensible conclusions about the technology are formulated. A document is then prepared in a predetermined format. The documents are then sent out to one of a team of experts from a variety of academic or clinical disciplines for external review. Comments and suggestions are considered by the Steering Committee and incorporated into the paper. Distribution of the paper is by request from the Office or through inclusion on the BCOHTA mailing list; summary versions appear in the quarterly newsletter.

V6T 2B5; Kathryn D. Thus, the VGH felt it would be useful to obtain an overview of the available scientific evidence on the efficacy and effectiveness of HBO for these two conditions. The literature was systematically searched, as per the B. Relevant additional papers from prior years were obtained from the reference lists of the papers identified and were reviewed in depth. This process yielded approximately 40 papers on the two topics of interest. With two exceptions, all the papers identified were either review articles, case series, case reports, or animal studies. Animal studies and case reports are not included in this assessment of the literature. Most reviews comment on the lack of prospective trials, although some go to great lengths to justify the absence of trials by pointing out how difficult they would be to carry out. The two controlled trials were: These negative results must be viewed with caution since the power of the study to detect meaningful differences is low; and 2 Marx et. Data from case series is difficult to interpret because of poor descriptions of methodology e. Moreover, cost data were provided and these are discussed in the report. In summary, for COM there is neither evidence that HBO clearly makes a difference in the outcome nor support to expand the use of HBO, although, as noted before, the literature is so poor that a definitive assessment is impossible. With regard to ORN, although the data are equally poor, the complex nature of the condition, the results reported in the case series, and the single randomized trial suggest that there may be stronger indications for HBO use than is the case with COM, although the trial was limited to the evaluation of prophylactic HBO in the context of tooth extraction for the prevention of ORN. One conclusion is clear: HBO is regarded by virtually all authors as an ac!. For ORN, differential success with and without HBO appears to be greater and although primary management is surgery and appropriate antibiotics, the complexity of the tissue injury in ORN particularly of the mandible the site most often studied suggests that HBO may be efficacious and effective. However, as noted above, L. On the one hand, HBO use for several conditions e. Thus, while the impact of expanding the use of HBO for COM and ORN has definite cost implications, these are relatively small compared with the basic and substantial total management cost associated with these conditions including multiple hospitalization, multiple surgery, antibiotics, etc. Conclusions regarding the value of HBO, in terms of costs versus benefits, are currently not possible since these relationships for COM and ORN are complex and no formal economic evaluations were found in the literature. The first International Conference on the use of HBO was held a century later, in , with eight subsequent conferences up to including one in Vancouver in . Over the last thirty years interest in, and knowledge about this form of therapeutic intervention has increased geometrically. This paper reviews the evidence for the use of HBO in chronic osteomyelitis COM , also known as refractory osteomyelitis, and osteoradionecrosis ORN , a common condition seen after radiation

therapy, especially of the mandible. The pathophysiology of these conditions is similar in that both involve significant bone infection associated with severe tissue hypoxia, hence the use of HBO. These are of two types: The latter effect is of less importance since it is variable depending on the organism, the amount of pressure used, and other conditions. For example, aerobic bacteria show a biphasic response to O_2 with growth enhancement at 0. Moreover, the killing action is time dependent. Thus, indirect action through leukocyte function is of primary importance; direct action on bacteria is said not to be a factor since HBO used prophylactically to prevent infection does not seem to work. In addition, optimal oxygenation of the infected bone enhances osteogenesis, collagen formation and neovascularization, which are critical in filling dead space and enhancing the entry of leukocytes and antibiotics into affected bone 2,3. With regard to ORN, radiation therapy not only produces the direct effects of disrupting mitotic activity the effect more pronounced in proportion to the mitotic activity of the target cells and surrounding tissue, but there is also a late effect: HBO appears to work by two mechanisms. First by counteracting the anoxic effects of obliterative endarteritis with HBO, although it produces vasoconstriction, pO_2 levels actually increase and initial vasoconstriction is followed by vasodilatation; and second, prolonged treatment with HBO produces neovascularization and collagen formation, the same beneficial effect seen in COM. This difference is the basis for evidence to suggest that HBO is useful prophylactically in ORN of the mandible see below. Pressure is measured in atmospheres absolute ATA. One ATA is equivalent to the air pressure at sea level. During a "dive" the pressure gauge is set to 0, and thus a chamber pressurized to HBO is said to be well tolerated at 1. However, O_2 is a toxic agent for multiple organs. In addition, Vitamin E is often used prior to HBO, presumably to reduce the tissue damage by free oxygen radicals. Specific toxic reactions to HBO include, oxygen seizures, otic barotrauma, pulmonary barotrauma, and myopia. Moreover, there is a long list of contraindications to its use, including: The indications for use of HBO include: There has been a steady increase in use since the chamber was installed: For the year, most patients were treated for osteonecrosis unrelated to radiation therapy, decompression sickness, CO poisoning-IS. No data are provided regarding ranges or number of treatments by diagnosis. These costs do not include physician fees. These are, of course, average costs and thus do not reflect variation across treatment groups which undoubtedly exists. One issue not clear from these data is whether the chamber costs vary by the length or depth of the dive; i. The relevance of these variables to costs are discussed below. The VGH data fail to provide any estimates of denominators. In addition, total management costs for COM or ORN also include hospitalization, surgery, antibiotics, and other direct patient care costs not to mention indirect costs. Thus the figures cited in the VGH report are only a fraction of overall patient management costs. In addition, the relevant sections of the Handbook 2 and Problem Wounds 3 were reviewed to identify additional relevant citations published prior to This process yielded a total of 61 papers which were sorted regarding type- of study: Twenty papers or abstracts met the selection criteria although not all papers were available locally or through inter-library loan, and thus 14 papers were available for in-depth review, and six abstracts were assessed. The 41 papers and abstracts not discussed in this review, aside from being case reports and animal studies, reported data on clinical conditions other than COM and ORN such as: Of the 20 recent papers or abstracts reviewed here: Notwithstanding the approach taken for this paper, several case series published prior to and thus not included in our search process are briefly cited to enable the reader to get a more complete "feel" for the quality of this literature and the basis upon which clinical impressions of effectiveness have been formed. Proponents of its use therefore view HBO as an adjunct to the primary therapy described above. Since surgical and antibiotic therapy. However, the proportion of these patients who might benefit from HBO is not clear. Since none of the clinicians currently actively involved in research on HBO consider it to be other than an adjunct to standard therapy, the key question for this review is whether HBO produces significant clinical improvement compared with standard therapy. While there are considerable animal and basic science data to suggest a positive therapeutic effect, studies in humans -are-less numerous and, with the exceptions noted above, are generally restricted to case reports, case series, or reviews. Being reviews, however, little is to be gained by describing them in detail since they provide no primary data. While the consistency of opinion is clear, it should be noted that three of the four reviews 5,7,8 are from the same institution the University of Texas Medical Branch at Galveston and, not surprisingly, these three reviews have

at least two authors in common, thus the independence of opinion is rather limited. The fourth review 6 is from the University of Chicago. On occasion, different papers which are supposed to be original articles, use previously published data. Despite this, the preface to a recent textbook 3 makes the following statement: Remaining questions are whether or not perfusion of a given wound is adequate to achieve therapeutic P_{O2} within safe limits of oxygen breathing and then to determine the optimal dose. They also review a number of case series, noting in the first section "Clinical Series" that: Thus Kelly 9 for example, in a study of closed irrigation and suction, compared 40 patients who had this modality with 35 who did not. Davis and Heckman 5, although providing few details about this study, claim that it has many methodological flaws which, unfortunately, they do not detail. In addition, they cite three additional case series which are briefly considered below. They also discuss and criticize the only trial in the literature. However, in the two review articles citing this paper, no details on subject selection, number of treatments, or time to clinical improvement are provided. Again, no details are provided regarding patient selection other than they all failed to respond to conventional therapy, intensity of HBO treatment, or other patient characteristics. Details regarding HBO treatment are not described nor is prior therapy described in detail. Davis and Hunt 18 reviewed 70 patients with chronic osteomyelitis in various sites spine, pelvis, chest wall, skull, etc. The average duration of COM was 30 months range 67 months to 23 years. All patients had contiguous focus, as opposed to hematogenous, disease. Treatment, in addition to HBO which was used in all patients, included antibiotics and careful surgical debridement all patients, autogenous bone grafting in 7 patients and soft tissue grafts in 7 patients. These patients received an average of 42 HBO treatments range . The average number of treatments in patients without recurrence was 39 range , while for patients with recurrence it was 78 range . Recurrence rate was not correlated with the number of treatments. Further analysis presented by these authors 20 with extended follow-up average 8. Eltorai 21 reported on the treatment of 44 patients, with HBO at 2 ATA for an average number of 50 sessions, who had COM resulting from spinal cord injuries, and pressure sores around the pelvis.

7: Pathology Outlines - Osteomyelitis: medication related osteonecrosis of the jaw (MRONJ)

We present an extremely rare case of osteomyelitis post cobalt radiotherapy. To our knowledge, this is the first case to be reported of osteoradionecrosis and osteomyelitis developing as a chronic complication post radical mastectomy and cobalt radiotherapy.

Wu Received Aug 26; Accepted Sep This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. Abstract In the past, osteomyelitis was frequent and characterized by a prolonged course, treatment response uncertainty, and occasional disfigurement. Today, the disease is less common; it is believed that the decline in prevalence may be attributed to increased availability of antibiotics and improvement of overall health patterns. However, each condition is a separate entity, with different treatment approaches. Thus, accurate diagnosis is essential for adequate management and improved patient prognosis. The aim of this paper is to report three cases of inflammatory lesions of the jaws—osteomyelitis, ORN, and BRONJ—and to discuss their etiology, clinical aspects, radiographic findings, histopathological features, treatment options, and preventive measures. Introduction The osteomyelitis is an inflammatory condition of the bone, which generally begins as an infection of the marrow cavity, rapidly involves the Haversian canals, and eventually extends to the periosteum [1]. In the past, osteomyelitis was frequent and characterized by a prolonged course, treatment response uncertainty, and occasional disfigurement due to loss of bone and teeth and resulting facial scars. Today, the disease is less common, and it is believed that the decline in prevalence may be attributed to the increased availability of antibiotics and improvement of overall health patterns [2]. Nonetheless, osteomyelitis remains a challenging disease for both clinicians and patients. Currently, more common osteomyelitis variants are seen. ORN is one of the most serious complications in the treatment of head and neck malignancies and is defined as the ischemic necrosis of the irradiated bone, which becomes hypovascular, hypocellular, and hypoxic [3 , 4]. BRONJ is one of the more recently reported serious adverse effects of bisphosphonates treatment, which are used to manage oncologic patients and to prevent fractures in osteoporosis [5 , 6]. However, each condition is a separate entity, with different management approaches [7]. Thus, the aim of this paper is to report three cases of inflammatory lesions of the jaws—osteomyelitis, ORN, and BRONJ—and to discuss their etiology, clinical aspects, radiographic findings, histopathological features, treatment options, and preventive measures. Written informed consent was obtained from all the patients. A drainage point with purulent material was also present Figure 1 a. Radiographic examination revealed osteolysis and bone sequestration on the mandibular alveolar ridge Figure 1 b. Based on clinical and radiographic findings, a provisional diagnosis of osteomyelitis was rendered. The material was submitted to histopathological examination which revealed nonviable bone and a mixed inflammatory infiltrate of lymphocytes and plasma cells, confirming the diagnosis of chronic suppurative osteomyelitis. The area healed appropriately within one month Figures 3 a and 3 b. The patient has been under follow-up for 5 years with no signs of recurrence.

8: Hyperbaric oxygen for osteomyelitis and osteoradionecrosis - UBC Library Open Collections

Osteoradionecrosis / Osteomyelitis. Infections within the jaw bones (mandible and maxilla) may occur as a result of dental infection, exposure to radiation for treatment of a head and neck cancer (osteoradionecrosis-ORN) or as a result of exposure to a bisphosphonate medication (MRONJ).

In adults, the vertebrae and the pelvis are most commonly affected. Acute osteomyelitis almost invariably occurs in children because of rich blood supply to the growing bones. When adults are affected, it may be because of compromised host resistance due to debilitation, intravenous drug abuse, infectious root-canaled teeth, or other disease or drugs. In some subpopulations, including intravenous drug users and splenectomized patients, Gram-negative bacteria, including enteric bacteria, are significant pathogens. *Staphylococcus aureus* is the most common organism seen in osteomyelitis, seeded from areas of contiguous infection. But anaerobes and Gram-negative organisms, including *Pseudomonas aeruginosa*, *E. coli*. Mixed infections are the rule rather than the exception. The two most common are *Blastomyces dermatitidis* and *Coccidioides immitis*. In osteomyelitis involving the vertebral bodies, about half the cases are due to *S. aureus*. The *Burkholderia cepacia* complex has been implicated in vertebral osteomyelitis in intravenous drug users. The resulting new bone is often called an involucrum. Osteomyelitis is an infective process that encompasses all of the bone osseous components, including the bone marrow. When it is chronic, it can lead to bone sclerosis and deformity. Chronic osteomyelitis may be due to the presence of intracellular bacteria inside bone cells. Intracellular existence of bacteria in osteomyelitis is likely an unrecognized contributing factor to its chronic form. In infants, the infection can spread to a joint and cause arthritis. In children, large subperiosteal abscesses can form because the periosteum is loosely attached to the surface of the bone. Many infections are caused by *Staphylococcus aureus*, a member of the normal flora found on the skin and mucous membranes. In patients with sickle cell disease, the most common causative agent is *Salmonella*, with a relative incidence more than twice that of *S. aureus*. Computed tomography scan of the right lower extremity of a year-old patient, showing abscess formation adjacent to nonunion of a right femur fracture. Extensive osteomyelitis of the forefoot Osteomyelitis in both feet as seen on bone scan The diagnosis of osteomyelitis is complex and relies on a combination of clinical suspicion and indirect laboratory markers such as a high white blood cell count and fever, although confirmation of clinical and laboratory suspicion with imaging is usually necessary. They can show the cortical destruction of advanced osteomyelitis, but can miss nascent or indolent diagnoses. The presence of edema, diagnosed as increased signal on T2 sequences, is sensitive, but not specific, as edema can occur in reaction to adjacent cellulitis. Confirmation of bony marrow and cortical destruction by viewing the T1 sequences significantly increases specificity. The administration of intravenous gadolinium-based contrast enhances specificity further. In certain situations, such as severe Charcot arthropathy, diagnosis with MRI is still difficult. Generally a triple phase technetium 99 based scan will show increased uptake on all three phases. Traditionally, the length of time the infection has been present and whether there is suppuration pus formation or sclerosis increased density of bone is used to arbitrarily classify OM. Chronic OM is often defined as OM that has been present for more than one month. In reality, there are no distinct subtypes; instead there is a spectrum of pathologic features that reflect balance between the type and severity of the cause of the inflammation, the immune system and local and systemic predisposing factors.

9: OSTEOMYELITIS AND OSTEORADIONECROSIS | Pocket Dentistry

Medication-related osteonecrosis of the jaw, osteoradionecrosis, and osteomyelitis: A comparative histopathological study that these are quite distinct clinical pathologies with.

U.S. participation in African Development Fund. Tumor and host endothelial cell selective interactions and modulation by microenvironmental chemokines: t Smoke on the Water Kaplan Nursing School Entrance Exam Footloose in Cornish folklore Itl Integrated Total Language Private rights and public illusions Questions about angels Life studies and for the union dead Part II: Biologic and molecular basis of regenerative medicine Bombos vs. Everything Volume 1 Matting and framing made easy The thrill of the hunt LVII. In Nat. Sanctorum Comeli et Cypriani 199 Best-selling guide to dream interpretation Gaze or contemplation? Womanly dominion deceitfully assaulted The new warrior class revisited Ralph Peters Layout Optimization in VLSI Design (Network Theory and Applications) Scott foresman ing street 5th grade practice book frinde The Leadership Lessons of the U.S. Navy SEALS Hates his parents The Road to Forgiveness Post gazette as Electronics pocket handbook Beware of turning hobbies into jobs The third creation of the world Why Johnny cant sing hymns Watcher and the watched From Galileo to Gell-Mann Riding high on the Cass Railroad Max meets Manny and Sal Characterization of Natural Organic Matter in Drinking Water Welcome to the Planet! The Andes regions Statistical analysis of data James C. Boyd The possibility of the impossible Sweet Ebony Blues Of Lodz and Love (Library of Modern Jewish Literature) Getting to maybe