# Clinical Concepts of Dry Socket

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Dry socket is one of the most studied complications in dentistry, and a great number of studies have searched for an effective and safe method for its prevention and treatment. One of the great clinical challenges since the first case was reported has been the inconsistency and differences in the various definitions of dry socket and the criteria used for diagnosis. The pathophysiology, etiology, prevention, and treatment of dry socket are very important in the practice of oral surgery. The aim of the present report was to review and discuss each aspect.

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Dry socket is the most common postoperative complication after tooth extraction, with an onset at 2 to 4 days after surgery.[1-5] It was first described by Crawford[6] in 1876. It has also been referred to as alveolar osteitis, localized osteitis, alveolalgia, alveolitis sicca dolorosa, septic socket, necrotic socket, localized osteomyelitis, fibrinolytic alveolitis, and others.[1] The incidence of dry socket has ranged from 1% to 4% of extractions, reaching 45% for mandibular third molars.[1,7] It is one of the most studied complications in dentistry, and a great number of studies have searched for an effective and safe method for its prevention and treatment. One of the great clinical challenges since the first case was reported has been the inconsistency and differences in the various definitions of dry socket and the criteria used for diagnosis. The pathophysiology, etiology, prevention, and treatment of dry socket are very important in the practice of oral surgery. The aim of the present report is to review and discuss each aspect.

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## Clinical Concepts and Pathophysiology

Dry socket was first described as a complication of disintegration of the intra-alveolar blood clot, with an onset 2 to 4 days after extraction.[1-6] According to Fazakerlev and Field,[7] the alveolus empties, the osseous surroundings are denuded and covered by a yellow-gray necrotic tissue layer, and the surrounding mucosa usually becomes erythematous. It is clinically characterized by a putrid odor and intense pain that radiates to the ear and neck.[8] Pain is considered the most important symptom of dry socket. It can vary in frequency and intensity, and other symptoms, such as headache, insomnia, and dizziness, can be present.[9] Calhoun[10] in 1971 also reported trismus as a frequent symptom that develops 10 to 40 days after extraction, if the infection does not spread. Regional lymphadenopathy can be present on the affected side, and fever is infrequent. Dry socket is commonly observed in patients 40 to 45 years old.[11,12] Published data have reported an incidence of 1% to 4% after teeth extraction, with an incidence 10 times greater for lower teeth than for upper teeth[13] and reaching 45% for mandibular third molars.[1,3-5,7,14,15]

Hansen[16] in 1960 described alveolitis simplex, featured by accidental loss of the clot and the absence of pain, in addition to alveolitis sicca dolorosa and granulomatous alveolitis. Hermesch et al[17] classified this complication into 3 types: superficial alveolitis marginal, suppurative alveolitis, and dry socket. In marginal alveolitis, the perialveolar mucosa becomes inflamed and partially covered by granulomatous tissue and is painful during mastication. In suppurative alveolitis, the clot becomes infected and is covered by a green-grayish membrane and can contain dental fragments or osseous sequestrum. It causes medium in-

tensity pain, and fever can also be present. In dry socket, the alveolar osseous walls are exposed, with total or partial clot loss, dark coloration, and a fetid odor. Continuous, intense, and frequently radiating pain is present that is not relieved by analgesics. Local hyperthermia and lymphadenopathy can also occur with this type of alveolitis.

Oikarinen[18] in 1989 classified this complication as real alveolitis and nonspecific alveolitis. Real alveolitis results in the typical symptoms of dry socket and requires professional follow-up. In contrast, nonspecific alveolitis, with an onset 3 to 4 days after extraction, is more common and does not require professional care despite the painful symptoms.

Recently, investigators have suggested the following definition for dry socket: postoperative pain surrounding the alveolus that increases in severity for some period from 1 and 3 days after extraction, followed by partial or total clot loss in the interior of the alveolus, with or without halitosis.[1,19]

Microscopically, dry socket is characterized by the presence of inflammatory cellular infiltrate, including numerous phagocytes and giant cells in the remaining blood clot, associated with the presence of bacteria and necrosis of the lamina dura.[20] In 1973, Birn[21] reported that the inflammatory process can extend to the medullar spaces and sometimes the periosteum, resulting in connective tissue inflammation of the contiguous mucosa, with microscopic features typical of osteomyelitis. Degradation of the blood clot in association with dissolution of erythrocytes and fibrinolysis, deposits of hemosiderin, and the absence of organized granulation tissue have also been described in histopathologic investigation of dry socket.[22]

Many denominations, classifications, and descriptions of dry socket have been reported. However, despite the controversies, in general, dry socket has been characterized as an inflammation in the alveolus of recently extracted teeth, for which pain and the period of onset are specific clinical signs indicative of proper diagnosis.

## Etiology

The exact etiology of dry socket has not yet been defined. However, several local and systemic factors are known to contribute and have been described in published studies.

Real dry socket is characterized by the partial or total premature loss of the blood clot that forms in the interior of the alveolus after extraction. This must be distinguished from other conditions, such as hypovascularization of the alveolar bone, caused by vascular and hematologic impairment; osteonecrosis induced by radiotherapy; osteopetrosis; Paget's disease; cement-osseous dysplasia, and so forth, in which the clot forms in the interior of the alveolus.[1,23]

Clinical and experimental studies have described an increased local fibrinolytic activity as a principal factor for the etiology of dry socket.[21,24-26] Birn[21] observed an increase in fibrinolytic activity in the alveolus with dry socket compared with a regular alveolus. He reinforced that the partial or total lyse and destruction of the clot is caused by mediators released during inflammation by direct or indirect activation of plasminogen into the blood.[21] When mediators are released by the cells of the alveolar bone after trauma, the plasminogen is converted into plasmin, causing clot rupture by disintegration of fibrin. This conversion occurs in the presence of cellular or plasmatic proactivators and other activators. Those activators have recently been classified as direct (physiologic) and indirect (nonphysiologic) and have also been subclassified according to their origins as intrinsic or extrinsic activators.[23] The intrinsic activators originate from the components of plasma, such as activator factor XII-dependent or factor Hageman-dependent and urokinase. In contrast, direct extrinsic activators originate outside the plasma and include activators of tissue and endothelial plasminogen. The activators of tissue plasminogen are found in most mammalian tissues, including the alveolar bone.[21] The indirect activators include streptokinase and staphylokinase, substances produced by bacteria that interact with plasminogen and form an activator complex that converts plasminogen into plasmin.[21]

The characteristic pain associated with dry socket has been attributed to the formation of kinins in the alveolus. The kinins activate the primary afferent nerve terminations, which could have been sensitized previously by other inflammatory mediators and other allogeneic substances, which in concentrations of 1 ng/mL cause intense pain.[1,21] Plasmin is also involved in the conversion of kallikrein into kinins in the osseous alveolar marrow. Thus, the presence of plasmin might be a possible explanation for both significant aspects of dry socket (ie, neuralgic pain and clot disintegration).

Although all the theories reported of the etiopathology of dry socket still need to be established, some evidence has suggested that an interaction exists between excessive local trauma and bacterial invasion. This association results in the formation of plasmin and, consequently, fibrinolysis inside the socket.[1,27] In 1989, Catellani[28] stated that the pyrogens secreted by the bacteria are indirect activators of fibrinolysis in vivo. Catellani[28] studied the effectiveness of those pyrogens on the treatment of thromboembolic disease, injecting the products intravenously. An interesting fact is that dry socket does not occur until after the first postoperative day. The explanation is that the

blood clot contains antiplasmin, which must be consumed by the plasmin before disorganization of the clot.[1]

Surgical extraction that includes the presence of flaps and sectioning of the tooth with an osteotomy level have also been referred to as factors contributing to dry socket.[29] Birn[21] considered that the trauma resulting from extraction, as well as aggressive curettage, might harm the alveolar bone cells, causing inflammation of the alveolar osseous medulla and release of cell mediators to the alveolus, where they cause fibrinolytic activity, increasing the risk of dry socket. This has been highlighted by studies in which less-experienced surgeons had a greater incidence of complications after the extraction of nonerupted third molars compared with more experienced surgeons.[30-32] Also, dry socket was the most common complication observed in these studies.[30-32] Investigators have studied the relationship between the reason for extraction and the incidence of dry socket. They found a 21.9% incidence of dry socket when the extraction was considered therapeutic (presence of infection and caries) compared with 7.1% for prophylactic extractions (without any symptoms).[3]

The presence of dental and osseous remains within the socket has also been considered a possible cause of dry socket.[21,33] In 1969, Simpson[33] demonstrated through microscopic studies of monkeys that those fragments are commonly observed in any extraction and do not necessarily cause problems, although they might cause inflammation and some delay in the chronology of the alveolar repair. Bone and dentin components such as sialoprotein and phosphoprotein have been reported to trigger leukocyte chemoattraction and the production of inflammatory cytokines, which characteristically upregulate bone resorption and downregulate bone formation.[34-37]

Vasoconstrictors, which are present in local anesthetics, have also been considered contributing factors for the etiopathogeny of dry socket. This affirmation was contested, however, because patients undergoing extraction with local anesthesia without local infiltration have also developed dry socket.[1] Other investigators have also observed that patients who underwent intraligamentary anesthesia did not present with a greater incidence of dry socket compared with patients who had undergone anesthesia exclusively by regional anesthesia.[38,39]

Poor oral hygiene and consequent alveolar contamination is also an important factor for the onset of dry socket. This relationship was supported by reports of this complication in patients with poor oral hygiene and/or pre-existing local infection, such as pericoronitis and severe periodontal disease.[11,39]

Concerning the involvement of bacteria in the pathogenesis of dry socket, investigators have observed the presence of *Streptococcus* $\alpha$ and *$\beta$-hemolíticus* in material collected from human dental alveolus.[40] Others have found 70% aerobic micro-organisms and only 30% anaerobic, which are a part of the buccal flora.[41] In contrast, in 1977, Ingham et al[42] observed that the anaerobes exceeded the aerobic flora, which were equivalent to 72% of the total bacteria isolated in several parts of the mouth. A series of bacteria, which included *Enterococcus, Streptococcus viridians, Streptococcus, Bacillus coryneform, Proteus vulgaris*, *Pseudomonas aeruginosa*, *Citrobacter freundii,* and *Escherichia coli* were identified in the biologic material within the alveolus in experimental dry socket models.[43] Also, in accordance with the potential role of bacteria in dry socket development, the inoculation of *Actinomyces viscosus* and *Streptococcus mutans* in animal sockets was reported to delay the chronology of alveolar repair.[44] In 1978, Nitzan et al[45] demonstrated a possible relationship between the presence of aerobic micro-organisms and the etiology of dry socket. They also reported high fibrinolytic activity in the cultures of anaerobic *Treponema denticola*, which is found in periodontal disease.[45] Dry socket rarely occurs during childhood, a period in which this micro-organism is usually not detected in the oral environment. In 1986, Mitchell[46] identified periodontal pathogen bacteria that produce enzymes with fibrinolytic activity, such as *Porphyromonas gingivalis* and *Fusobacterium nucleatum*. In 1989, Awang,[47] although agreeing with the role of anaerobic bacteria in the development of dry socket, considered inconsistent the relationship between the clinical aspects of dry socket and the typical activity pattern of these microorganisms, such as redness, edema, fever, and pus. He believed that the clinical characteristics of dry socket most commonly observed constitute indirect action of those bacteria.[47] These findings reinforce the theory about the participation of the micro-organisms in the development of dry socket. In addition, bacteria can elicit changes in the clotting process through phagocyte activation and the generation of inflammatory mediators, such as tumor necrosis factor-$\alpha$ and interleukin-1, inflammatory cytokines known to interfere in the repair process. Similarly, osseous or teeth fragments in the alveolus can result in leukocyte chemoattraction and activation and release of inflammatory cytokines.[34,35,37] Tumor necrosis factor-$\alpha$ and interleukin-1 increase the action of the activator of plasminogen type urokinase and the inhibitor of activation of type 1 plasminogen.[48] Thus, lyse of the clot will occur by activation of plasminogen activator of plasminogen type urokinase-dependent and dislocation of vitronectin inhibitor of activation of type 1 plasminogen-dependent from its receptor of activator of plasminogen type urokinase, which weakens the interaction between macrophages and the fibrin ma-

trix, fundamental to the initial organization of the granulation tissue inside the alveolus.

In addition to the putative influence of microbial and inflammatory factors, endocrine mediators can also interfere in the repair process after extraction and predispose to dry socket onset. Estrogens, as well as pyrogens and some drugs, indirectly activate the fibrinolytic system. It is believed that those hormones contribute to the onset of dry socket, because they increase the blood clot lyse.[28] These investigators have also reported that fibrinolytic activity seemed to be lower from the 23rd to 28th day of the menstrual cycle. However, for women who did not use oral contraceptives, a greater or lower tendency to dry socket was not found, independent of the phases of the menstrual cycle. The use of oral contraceptives has shown a direct relationship to the incidence of dry socket in studies conducted before 1960 and after 1970. After 1970, the popularization of oral contraceptive intake and a greater incidence of dry socket were observed among women.[49-52] An interesting prospective, controlled, and randomized study demonstrated a greater incidence of dry socket in women who took an oral contraceptive.[53] Garcia et al,[54] in 2003, observed that after extraction of third lower molars in women aged 17 to 45 years, 11% of those taking oral contraceptives and 4% who were not developed dry socket. Another study reported the increase of some clotting factors, including factor II, VII, VIII, and X and plasminogen in women who took oral contraceptives.[55]

An additional contributing factor to the onset of dry socket is smoking. In a interesting clinical study, the investigators showed that of 400 third molars extracted, the patients who smoked 10 cigarettes daily had a 4 to 5 times greater risk of dry socket compared with nonsmokers (12% versus 2.6%).[56] This incidence increased an additional 20% if the patient smoked 20 cigarettes daily and an additional 40% for those who had smoked on the day of the surgery or the first postoperative day.[56]

Monaco et al,[57] in 1999, observed a statistically significant difference between harmful habits such as smoking and drinking alcoholic beverages and postoperative complications such as pain and fever. In addition, they observed a greater incidence of dry socket in patients aged 18 years or older. They considered the increase in age a predisposing factor, which has also been observed by other investigators.[58] Smoking can cause the introduction of harmful substances that might act as contaminators to the surgical wound. Nicotine, cotinine, carbon monoxide, among others, are cytotoxins for several types of cells and consequently inhibit the healing process.[59] Nicotine, the active drug in tobacco, increases platelet aggregation, increasing the risk of microvascular thromboses and peripheral ischemia.[60] In addition, it inhibits the proliferation of fibroblasts and macrophages.[60] Carbon monoxide forms carboxyhemoglobin in the blood, causing a decrease in oxygen transportation and alterations in vascular endothelium.[61] Also, the release of endogenous catecholamine leads to a decrease in perfusion to the tissues.[62]

The heat generated by the burn of tobacco does not seem to be a significant factor in the etiopathogeny of dry socket. An analysis of narguile use, a type of pipe in which the smoke is chilled by passing through water or special fluids before being inhaled, did not reveal significant differences in relation to the incidence of dry socket compared with cigarette use.[63] It has been believed that the amount of contaminators, varying according to the type of tobacco, source of flame, suction, and substances inhaled are the most important factors for the onset of dry socket.[58] The systemic alterations in the use of tobacco are the most significant aspects explaining the greater incidence of dry socket in smoking patients, as previously observed in other studies.[59-61]

## Preventive Methods

Dry socket prevention is determined by the medical and dental history of the patient, physical examination findings, pertinent laboratory examination results, and the presence of contributing factors. To avoid complications, strict guidelines for maintaining an aseptic field during the procedure and the correct indication and use of the surgical technique must be followed. In 2002, Blum[1] suggested that factors inherent to the patient must also be considered as risk factors for dry socket. These included a history of dry socket, deep osseous impaction of mandibular third molars, poor oral hygiene, a recent history of pericoronitis, ulcerative gingivitis or active illness associated with the tooth to be extracted, smoking (in particular >20 cigarettes daily), oral contraceptive use, and immunocompromised patients.[1]

In addition to avoiding these factors, the prevention of dry socket has been studied in relationship to some antifibrinolytics agents, antibiotics, analgesics, antiseptic agents, and combinations of these substances. The use of antifibrinolytics primarily aims to avoid blood clot lysing. The antifibrinolytic agent, ester propyl for hidroxy benzoic acid, topically applied to the alveolus significantly prevented dry socket (24% for the control group and 0% for the experimental group), with significant side effects.[64] In contrast, the use of oral tranexamic acid (0.5 mg) as a topic local antifibrinolytic did not reduce the incidence of dry socket (control group 23% and experimental group 22%).

The use of clot support agents, such as polyglactic acid, impairs the lyse, indicating its use for the pre-

vention of dry socket. In the initial studies, a 2% rate of dry socket was detected for the experimental group and 18.1% for the control group.[1,65] During subsequent studies, polylactic acid was combined with chlorhexidine, leading to a remarkable rate of 23.6% for the experimental group and 13.6% for the control group.[1,65]

Alveolus irrigation after extraction with varying amounts of physiologic saline revealed that increasing the amount of physiologic saline (25, 175, and 350 mL) progressively decreased the incidence of dry socket (10.9%, 5.7%, and 3.2%, respectively).[15,66] Analgesic dressings have also been used to prevent dry socket; however, most of such agents contain eugenol, a component that delays the healing process.[67]

Because of the potential involvement of bacteria in the pathogenesis of dry socket, the use of antibiotics in its prevention has also been studied. In 1939, Archer[68] sought to reduce the incidence of dry socket after 773 extractions of lower molars and premolars by applying tablets of sulfanilamide and sulfathiazole and obtained favorable outcomes. In 1989, Swanson[8] studied the intra-alveolar use of gel sponges with tetracycline, neomycin, and bacitracin after extraction of mandibular third molars. Compared with the control group (without treatment), he observed a reduction in the occurrence of dry socket from 37.5% to 3%.[8]

A double-blind study investigated the effects of achromycin impregnated in Gelfoam versus placebo in the prevention of dry socket after extraction of symmetrically positioned mandibular third molars. The incidence of dry socket was 7% for the experimental group and 19% for the control group.[69] Other investigators, using the same method, evaluated lincomycin-impregnated Gelfoam (Johnson & Johnson, Somerville, NJ), with an incidence of 1.1% for the treated group and 7.8% for the control group, revealing greater effectiveness compared with other agents used during that period.[70] In 1981, Davis et al[71] used tetracycline combined with granular gel after 860 extractions of mandibular third molars. They found that only 23 patients (2.67%) developed dry socket.[71] Julius et al,[72] in 1982, used Gelfoam saturated with ophthalmic solution, Terramycin (oxytetracycline HCl; Pfizer, New York, NY), and Cortril (hydrocortisone acetate, Pfizer) after extraction of mandibular third molars. They found a lower incidence of dry socket (6.6%) in the treated group compared with the controls (28.8%).[72] Accordingly, other investigators used the same method and the same medication protocol and obtained a rate of 1% for dry socket.[73]

Investigators have also compared the use of hydrochloric lincomycin (Lincocin, Pfizer) and Gelfoam, oxytetracycline combined with Terra-Cortril and Gelfoam, and Gelfoam and saline solution after extraction of mandibular third molars and observed a lower incidence of dry socket for the experimental groups, 11.4% and 12.9%, respectively, compared with 16.4% for the control group.[74] In another study, the use of Gelfoam saturated with topical clindamycin right after extraction was investigated, with positive outcomes similar to those found in other reports.[14] This reinforced the role of anaerobic bacteria as an etiologic factor of dry socket and the effectiveness of antimicrobial agents in reducing its incidence.

The prescription of metronidazole for the treatment of dry socket was elaborated in a study and demonstrated to be a simple and effective method for its prevention. Of the 555 patients who received 200 mg of metronidazole, only 6 (1%) developed dry socket. Of the 541 patients in the control group, who had received a placebo, 23 (4.2%) developed dry socket.[12] In 1987, Barclay[75] analyzed the use of metronidazole in patients at risk of pericoronitis. However, it did not have a significant effect compared with placebo for the prevention of pain and dry socket.[75] Different outcomes were observed in a clinical double-blind randomized study by Mitchell,[46] in 1986, in which tinidazole was compared with a control group for the prevention of postoperative infection. They found a significant reduction of infection in the group that received tinidazole. Mitchell[46] also approved the use of that antibiotic postoperatively for osseous impaction. The use of 400 mg metronidazole, 2 or 3 times daily for 5 days, as prophylaxis for postoperative infections, was analyzed after extraction of mandibular third molars.[76] The investigators did not observe any statistically significant difference between the 2 groups.[76] Another study reported a significant reduction in the infection indexes after extraction of third molars with osseous impaction when the patients had received preoperative antibiotic prophylaxis, although the same results were not achieved for teeth with soft tissue impaction.[77]

In contrast, Monaco et al,[57] in 1999, reported that the prescription of amoxicillin postoperatively did not have an important role in the prevention of dry socket. Other investigators did not observe favorable outcomes for the prevention of dry socket when they used amoxicillin combined with clavulanic acid or clindamycin postoperatively for mandibular third molars.[78]

The use of penicillin with clavulanate plus mouthwash with chlorhexidine 0.12%, preoperatively, perioperatively, and postoperatively favorably reduced the incidence of dry socket to 20.9% for the chlorhexidine group, 8.9% for the chlorhexidine combined with antibiotic group, and 23.7% for the control group using irrigation with physiologic saline.[79]

Mouthwash with chlorhexidine digluconate at 0.12% has been an efficient antiseptic for the prevention of dry socket. Some studies have shown important reductions in the incidence of dry socket after extraction of mandibular third molars.[80,81] Although some studies reported that this antiseptic eliminates almost 95% of all saliva bacteria, it was demonstrated that the remaining 5% are capable of causing infection.[82]

However, some investigators tested the effect of chlorhexidine 0.12% as a preoperative mouthwash and as immediate irrigation after extraction and did not find any advantages compared with the control group, which used physiologic saline.[83] That study was refuted by Larsen,[84] in 1990, who affirmed that the control group was improper and the conclusions were not valid, in addition to discussing the reliability of the method.

A meta-analysis review study on the use of chlorhexidine for the prevention of dry socket after extraction of mandibular third molars showed that use of a unique mouthwash, just before surgery, did not significantly reduce the incidence of this complication.[85] However, its use preoperatively on the day of surgery and for several days postoperatively significantly reduced the incidence of dry socket.[85]

Torres-Lagares et al,[86] in 2006, analyzed the effectiveness of the intra-alveolar application of a bioadhesive gel with chlorhexidine 0.2% to prevent dry socket after extraction of impacted third molars in a double-blind randomized study. The outcomes showed an incidence of dry socket of 11% in the experimental group, a statistically significant reduction compared with 30% in the control group.[86]

Hedström and Sjögren,[87] in 2007, made a systematic review study of the preventive methods for dry socket and found a large variation in the models and quality of the randomized studies; thus, the evidence of the efficacy of most preventive methods was inconclusive.[87] However, local treatment with tetracycline and chlorhexidine 0.12% mouthwash (preoperatively and postoperatively for 7 days) was clinically significant in preventing dry socket in mandibular third molar extractions. Nevertheless, the investigators also suggested careful use of tetracycline because some studies have reported hypersensitivity and systemic toxicity.[87,88]

## Treatment

Many possibilities for treating dry socket have been reported, including a variety of materials, irrigation solutions, and procedures within the alveolus. In 1929, investigators reported irrigation with heated saline solution, powdered sodium perborate, gauze with iodoform, the prescription of codeine, and subsequent irrigation with a concentrated solution of sodium perborate.[89] The use of a paste (composed of acetylsalicylic acid, Peru balsam, eugenol, sodium benzoate, and lanolin) for intra-alveolar application, with the use of gauze, was indicated by Pell[90] in 1934.

To treat hyperplastic alveolitis, Jensen,[91] in 1978, reported on the removal of intra-alveolar remains with curettage followed by suture for clot protection. For dry socket, Schofield et al[92] recommended treatment with glycerin or guaiacol eugenol or pastes from these compounds combined with zinc oxide introduced within the alveolus with the help of gauze to relieve the pain.[92] Other investigators suggested simple and palliative treatment, consisting of debridement, ablution with saline solution, followed by a dressing with gauze impregnated with 5% iodoform and eugenol.[93]

MacGregor,[93] in 1967, interviewed 127 physicians, asking them about the therapeutic agents used to treat dry socket. Most had adopted systemic antibiotic therapy (67 used penicillin) and made dressings with zinc oxide and eugenol or neomycin, among others. Mainous,[94] in 1974, reported a clinical case of a late and severe foreign body-type reaction owing to the application of a paste made of zinc oxide and eugenol for the treatment of dry socket.

However, because of its complex etiopathology, which is not yet completely known, a specific and effective treatment of dry socket has not yet been presented.[1] Although local treatment with antibiotics has been described as clinically significant in preventing dry socket,[87,88] the efficacy of such drugs in the treatment of dry socket has also been extensively investigated.[46,83,86,95] The regular bacterial microflora of the mouth comprises specially anaerobic bacteria; thus, a greater prevalence of these micro-organisms, such as *Streptococcus facultative*, *Porphyromonas, Prevotella*, *Peptostreptococos*, and *Fusobacterium,* are present in odontogenic infections.[96]

Metronidazole (2-metil-5-nitroimidazol-1-etanol) is a nitroimidazol that acts as a synthesis inhibitor and on the degradation of microbial DNA. It was initially used for the treatment of infections caused by *Trichomonas vaginalis* and for the treatment of infections caused by *Entamoeba histolytica* and *Giardia lamblia*.[97] Shinn,[98] in 1962, reported the recovery of a patient with ulcerative gingivitis vaginal trichomoniasis, who was treated with metronidazole. It was approved for treatment of dry socket because it is a medicine and its properties meet the necessary requirements for the control of anaerobic microorganisms, which are present in dry socket.[21,27] The systemic and topical use of antibiotics for the treatment of dry socket have been described. Rood and Danford[12] used metronidazole, 400 mg/day for 5 days, for the treatment of dry socket and obtained favorable outcomes, including the release of pain. However,

most studies have focused on the topical use of antibiotics to treat dry socket.

In 1984, Mitchell[99] investigated the effectiveness of a paste made of 10% metronidazole for the treatment of dry socket. Faster healing was observed when the paste was used. Two years later, Mitchell[100] defined the properties of the ideal dressing for dry socket as one that promotes fast and effective release of pain; does not irritate the surrounding tissues; is easily absorbed or incorporated; allows close contact with the osseous tissue; is antiseptic; is stable to mouth fluids; does not alter in volume in contact with blood and saliva; and is easily applied. In addition, the treatment should be made at a unique appointment and preferably be of low cost.[46] However, Mitchell[99] also investigated the treatment of dry socket with a paste of collagen (formula K) applied after irrigation with physiologic saline. Of 151 patients, 100 received the collagen paste and 51 received a paste of zinc oxide and eugenol. The outcomes were favorable for the collagen paste, with a decrease in pain from 1 to 4 days. In 1988, Mitchell[100] suggested the use of nitroimidazoles for the treatment and prevention of dry socket, because of the evident participation of anaerobic bacteria in the etiology of dry socket. He also suggested the use of this medicine as a powder, with reference to the use of tetracycline as a powder. However, Moore and Brekke,[101] in 1990, found some foreign body reactions when using powdered tetracycline with polylactic acid and attributed it to the insoluble microparticles of the medicine, in addition to the hydrophobic characteristics of the polymer. Thus, they recommended against the use of powdered antibiotics for recent extractions.

Poi,[102] in 1994 analyzed the paste used in humans by Mitchell[99] in 1984, after applying it to subcutaneous tissue of rats. In that trial, the composition studied was 10% metronidazole, 2% lidocaine, and carboximetilcelulose as the base and to provide a mint flavor. They concluded that the paste presented characteristics that indicated its topical use.[102] According to Poi,[102] the ideal dressing for filling the alveolus should be bactericidal, antifibrinolytic, and analgesic and should contribute to alveolar healing. A relevant factor was manipulation during treatment, because cleaning and dressing inevitably intensify the pain.[102] The investigators reported on the necessity of techniques for instrumentation of these osseous spaces with minimal discomfort, followed by immediate and long-lasting release of the pain. In such cases, they believed that 2% lidocaine gel could be useful, providing prompt analgesia for the nerve terminations, immediately after instrumentation without any side effects.[103]

Poi et al,[104] in 1998, studied the influence of paste composed of metronidazole and lidocaine for the recovery of the infected alveolus in rats. In the study, 5 groups were analyzed: group 1, noninfected alveolus; group 2, alveolus infected without treatment; group 3, infected alveolus treated with curettage and physiologic saline irrigation; group 4, infected alveolus treated with curettage, physiologic saline irrigation, and alveolus filling with paste composed of 10% metronidazole, 2% lidocaine, lanolin as the base, and mint; and group 5, infected alveolus treated with curettage, physiologic saline irrigation, and alveolus filling with carboximetilcelulose as the base and mint. The treatment for group 3 did not help the healing process compared with the other methods, because dry socket requires local treatment that inhibits bacteria proliferation and protection of the alveolar walls. This aspect has been previously discussed by other investigators.[105] Bresco-Salinas et al[96] stated that when contamination occurs, it is mandatory to surgically clean the area and provide antibiotics. Nevertheless, surgical cleaning has not been recommended by some investigators for fear of aggravating the infectious process.[106] The same paste used in group 4 was studied clinically by other investigators, who found it presented beneficial outcomes for the treatment of dry socket, with significant pain reduction and the absence of local and/or systemic side effects.[107]

Poi et al,[108] in 2000, studied a paste mainly composed of metronidazole, 2% lidocaine, carboximetilcelulose, and mint with 5% ascorbosilane C (ascorbyl methylsilanolpectinate). They found that it reduced free radicals, protected the cellular membrane, and regenerated cutaneous tissues, in addition to helping the synthesis of collagen and elastin. From these outcomes, they concluded that the paste was effective in the treatment of infection and did not interfere with the normal chronology of the healing process, in an experimental dental model of an infected alveolus in the rat.[108]

From these experiments, which have demonstrated the role of anaerobic bacteria in buccal infections, including dry socket, some topical antiseptic combinations capable of releasing a great amount of oxygen, seem to be effective in fighting such organisms. One example is sodium iodide and hydrogen peroxide. Hydrogen peroxide is an unstable composite that is easily dissociated in molecular oxygen and water. The solution used therapeutically is a 3% peroxide solution. When it comes in contact with tissue, oxygen is released, and the germicidal action occurs. It is this effervescence mechanism that induces wound cleaning and debris removal.

Mrzlikar,[109] in 1990, treated 122 patients with pain after extraction using 6% hydrogen peroxide and obtained pain relief for all the patients with 1 to 8 irrigation sessions. For some investigators, hydrogen peroxide presents harmful effects to bone, inhibiting glucose metabolism and bone collagen synthesis.[110]

These investigators discussed the necessity of studies analyzing different concentrations and periods of exposure, in addition to specific investigations in the buccal region.[110] Zied et al,[111] in 2005, microscopically evaluated the healing process in rats after covering with gauze immersed in 3% hydrogen peroxide for 2 minutes followed by suturing. They concluded that this type of treatment was a complicating factor for the alveolar healing process.[111]

The compounds made by iodine are still the most effective antiseptics used. Its germicide spectrum includes all forms of vegetative pathogens, bacteria, viruses, fungi, and protozoans. Even spores, in general, are eliminated when exposed to iodine for a long period. Iodides in general are not inhibited by the presence of organic compounds; they are not corrosive and contain low toxicity compared with their germicidal strength; and allergic reactions are very rare. Sodium iodide is a germicide agent that contains long-lasting antiseptic activity in contaminated wounds and, depending on its concentration and pH, the solution will be more or less effective against bacteria.[112] The concentration of iodide regulates the balance of iodine diluted in its free form and complex structure. Increasing the concentration of iodide results in a reduction in the amount of free iodine in the solution; the level of free iodine determines its antiseptic function.

The combination of iodine-based substances with hydrogen peroxide might be advantageous. The combination of PVP-I and hydrogen peroxide exerted synergistic bactericidal effects against periodontal pathogens,[113-115] allowing Maruniak et al,[116] in 1992, to conclude that a significant reduction effect occurs against dental plaque and gingivitis using the combination of iodine and hydrogen peroxide.

Although most investigators agree prevention is better than treatment, none of the isolated preventive methods has been successful or achieved total acceptance. Most physicians still use their own methods, which are usually the topical antimicrobial agents used for other maxillofacial infections, usually without any scientific studies to confirm the effectiveness for the treatment of dry socket.[1] One example is the use of irrigation with 2% sodium iodide plus 3% hydrogen peroxide for the treatment of patients hospitalized with osteoradionecrosis caused by radiotherapy, which resulted in the best clinical outcomes compared with other treatments, including surgical debridement.[117,118] This irrigation solution, because of its antianaerobic property, was effective in the areas infected by these microorganisms.[119] It also physically removes debris and necrotic remains, eliminating the necessity for clinical cleaning of the area.[117]

## Current Recommendations for Dry Socket Prevention and Treatment at Department of Oral Surgery—Bauru School of Dentistry, University of São Paulo

Dry socket is a complication that occurs frequently after tooth extraction, causing discomfort to the patient, pain, and a fetid odor. Additionally, because a specific etiology has not yet been determined, it is necessary to follow preventive methods in the daily practice of tooth extraction starting with the patient's medical history. From the published data, it was not possible to determine an ideal or consensual treatment protocol. Each institution has adopted a different protocol; thus, despite the many studies and publications, additional investigations are still required to establish the best method to treat dry socket. At our department, the medical and dental background of the patient, pertinent physical examination, and laboratory examination findings are considered as the basic guidelines for undergoing surgery. Our clinical experience supports the published findings that indicate a greater risk of disease or complications must be analyzed. It is necessary to be careful when planning tooth extraction in patients at risk of dry socket including those with poor oral hygiene, older than 40 years of age, those with debilitating systemic problems, women who take oral contraceptives, patients with a history of pericoronitis, patients receiving corticotherapy, and smokers. Another approach to prevent dry socket is to be careful to cause less damage to the bone. In view of the relatively low incidence of dry socket in our patients (about 0.97%), we believe that our prevention procedures have been effective in clinical practice. In addition to prevention, it is fundamental to cure this complication; thus, a patient who presents with dry socket must be examined daily, and the alveolus must be slightly irrigated with bactericidal solutions to remove food remains, osseous and dental remains, or foreign bodies that could interfere with the clotting process and/or facilitate infection. Our institution has adopted the following protocol: irrigation of the alveolus with 3% hydrogen peroxide and 2% sodium iodide, at a 1:1 proportion followed by superficial curettage of the debris. From our clinical experience, we believe that aggressive curettage could cause greater trauma to the osseous alveolar tissues and bacteremia. In addition to local procedures, 0.12% chlorhexidine is prescribed as a mouthwash, 3 times daily for 14 days. If clinical signs of infection, such as fever, suppuration, and pain are present, we have prescribed amoxicillin 1,500 mg/day; for patients allergic to amoxicillin, we have prescribed clindamycin 1,200 mg/day. Analgesics can be prescribed for the pain. Daily follow-up examinations

must be done until the symptoms have resolved. The use of these protocols and preventive methods by our team has resulted in very few complications and has led to total treatment success.

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