ODONTOGENIC INFECTIONS

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Preface

Infections originating from teeth or their supporting structures, known as odontogenic infections, are among the most common diseases in the oral and maxillofacial region. The source of odontogenic infections is commonly bacteria that colonize the oral cavity. These bacteria, when given the appropriate circumstances, can become pathogens. As a rule, odontogenic infections are polymicrobial with a large percentage being primarily anaerobic infections. Caries, periodontal disease, and pericoronitis are the initiating infections that can spread beyond teeth to the investing bone. Once the infection is in the bone, it will usually follow a path of least resistance until reaching a plate of cortical bone where it erodes through the cortex into the soft tissues. Once in the soft tissue, the infection spreads via diffuse cellulitis, then into an abscess. Head and neck anatomy are complex, with many contiguous spaces, and thus infections in one anatomic region may easily spread to other regions. Spread continues along the fascial planes extending along the superficial cervical neck fascia into the deep cervical neck fascia. The degree of infection depends on the virulence of the infecting bacteria, the immune status of the patient, and the anatomy of the infected region. The incidence of an odontogenic infection will vary with the population studied. Those individuals with poor dental hygiene and those who are immunosuppressed are most susceptible. Clinical manifestations depend on the spaces involved, and include pain, fever, malaise, fatigue, swelling, odynophagia, dysphagia, trismus, dysphonia, otalgia, and dyspnea.

Most patients with odontogenic infections are managed in an outpatient setting with incision and drainage and tooth extraction, and supportive medical therapy that includes antibiotic administration. However, the practitioner must constantly bear in

mind that these infections occasionally become severe and life threatening within a short time. For this, dental practitioners must have detailed knowledge of the presentation, etiology, investigations, and access to appropriate medical and surgical interventions. Early recognition and correct management of severe infections can be lifesaving, especially in medically compromised patients and in those who present late in the infectious disease process. The three keys to successful management of deep neck infections are protection and control of the airway, antibiotic therapy, and surgical drainage.

The primary goal of the present book is to produce a comprehensive text that fully integrates the latest concepts and techniques in management of odontogenic infections. The main aim is to provide the readers with an update information regarding pathophysiology, clinical and radiographic presentation, microbiology, diagnosis, management, and complications of odontogenic infections. Accordingly, the text has been divided into six chapters. Chapter one is concerned with oral microbiology and immunology. Chapter two is dealing with the pathophysiology of odontogenic infections. In chapter three, management of odontogenic infections is presented. In chapter four, antibiotic therapy of odontogenic infections is given. Chapter five deals with life-threatening complications. In chapter six osteomyelitis of the jaws is discussed.

I would like to acknowledge my friends, the staff members of the department, young colleagues, residents, and students. Without their end-less support and input, this textbook, would not have been possible. Also, I want to express my appreciation to my grandson Ziad Marei for designing the cover artwork of this book. For that, I am deeply grateful.

Ahmed M. Adawy

Dedication

In the memory of my beloved wife Ahlam,
and to my daughters; Heba and Maha, for their inspiration, patience, and support.

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Chapter 1: Oral microbiology and immunology

Oral microbiome

Microorganisms found in the human oral cavity have been referred to as the oral microflora, oral microbiota, or more recently as the oral microbiome (1). The oral cavity harbors at least six billion bacteria representing more than 700 species, as well as other types of microorganisms including viruses, protozoa, fungi, and archaea (2). Traditionally, culture-based identification has been the "gold standard" for the detection of most bacterial and fungal infections (3). The specimen is grown on a solid, semi-solid or liquid medium under aerobic, microaerophilic, or anaerobic conditions. Then organisms are presumptively identified based on colony morphology and staining properties. Culture of microorganisms is also important for the determination of antimicrobial sensitivity. Furthermore, the virulence attributes of an organism and their expression patterns could only be studied after successful isolation of the organism in vitro. A major limitation of conventional culture methods is that approximately 60% of the oral microbiome, for example, are not yet culturable by available methods. Therefore, a large proportion of the species found in each specimen may not be identified. Another limitation of conventional culture method is the time required for identification of pathogens. Often, species identification cannot be made until 7 days or more after sampling. By this time, the patient's clinical course has usually either improved or deteriorated dramatically. Antibiotic sensitivity testing may require up to another 7 days in the case of slow-growing organisms. New molecular methods, which identify the infecting species by their genetic makeup, have the ability to identify organisms that are not readily

recovered by bacterial culture and to gather information on large numbers of different bacteria from a single specimen (4). Specimens for microbiological diagnosis include pus (aspirated being ideal), scrapings from mucosal lesions, brushings, discharges and supra and sub-gingival plaque. However, given the fact that many oral infections are polymicrobial, it is possible that not all the causative organisms in each niche are identified through this approach. With the advent of ribosomal RNA gene sequencing, several unknown aspects of the oral microbiome have been revealed. Furthermore, this has enabled the prediction of yet undiscovered species in the oral microbiome and, it has been conservatively estimated that at present, nearly 40% of the species are yet to be characterized (5).

Microbiome of the oral cavity is not uniform, and it is now known that there are different population of bacterial species could inhabit different oral niches. The oral cavity includes several distinct microbial habitats, such as teeth, gingival sulcus, attached gingiva, tongue, cheek, lip, hard palate, and soft palate. Studies have documented that different oral structures and tissues are colonized by distinct microbial communities (1). Microorganisms on different oral niches do not occur as free-floating organisms, but rather are organized as a structured community of bacterial cells enclosed in a self-produced polymeric matrix; the so-called “bacterial biofilm”. Biofilms are described as matrix-embedded microbial populations, adherent to each other and/or to surfaces or interfaces (6). This ability to attach to a surface is an important bacterial survival mechanism that contributes to antimicrobials resistant (7). However, such relatively “stable” bacterial biofilm communities are subjected to change by factors such as age, diet and underlying systemic health (8). These changes can be manifested during the first few months of life as the mouth at this time consists only of mucosal surfaces for microbial colonization. Another change will happen when hard non-shedding surfaces appear with the eruption of the primary dentition, providing a unique surface in the body

for microbial colonization. The eruption of teeth also generates an additional major nutrient source via the gingival crevicular fluid. In addition, ecological conditions within the mouth will also be affected by the loss of teeth, in edentulous person the microbiome will shift towards aerobic status. The insertion of prostheses will create new environment for colonization of anaerobic bacteria again (9). Further fluctuations in the stability of the ecosystem can be induced by external factors including the types of food ingested, periods of antibiotic therapy, and variations in the composition and rate of flow of saliva. The growth of oral microorganisms depends on temperature, pH, oxidation reduction potential, availability of nutrients and water, morphology of oral structures, flow of saliva and the presence of antimicrobial compounds. Each of these factors puts a selection pressure on the oral ecosystem and helps to maintain balance between populations of microorganisms. In addition, there is significant variation across different individuals examining bacterial populations at the same anatomic site. Different physiologic states and behaviors have profound effects on the commensal flora of the individual presumably by altering the microenvironment for bacterial growth in favor of certain organisms at the expense of others. For example, smoking alters the microflora of the oral cavity, with increased numbers of potentially pathogenic bacteria present compared with the oral flora of nonsmokers (10). The host's diet can also influence the oral microbial flora. This diet provides a readily accessible nutritional supply to the microorganisms and can influence the numbers and types of organisms present in the oral cavity. Most microorganisms prefer a diet high in carbohydrates. A high-protein diet rather than high-carbohydrates diet tends to cause a reduction of acidogenic flora such as Lactobacillus.

The National Institutes of Health recently established the Human Microbiome Project to document the different populations of bacteria that colonize the human body, including areas of the head and neck, to explore how differences in colonizing

bacterial flora impact human health. Data produced from this project have led to a renewed thinking about how infectious processes are likely due to the complex interactions between the host immune system, pathogenic bacteria, and the resident commensal microbes (11). Through these studies and others, bacterial populations of different regions of the head and neck are currently being characterized for both healthy and diseased populations.

Classification of bacteria

Most bacteria can be divided into two categories, either gram positive or gram negative, based upon a differential staining technique. The Gram stain reveals a major structural difference between the two major groups of bacteria based upon the thickness and degree of cross-linking of the cell wall. The thick layer of peptidoglycan in gram-positive cell wall stain purple, while the thin wall of gram-negative cell appears as pink. Among the bacteria, there are also organisms that cannot appropriately be classified based on Gram staining, such as Mycobacterium tuberculosis. Instead of Gram staining, mycobacteria can be stained by the Ziehl-Neelsen staining technique, which is also called acid-fast staining. Most bacteria are about 1 to 5 μm across the largest dimension of the cell. A bacterial colony of roughly 3 mm in diameter that forms on an agar plate can contain upward of 100 million organisms. Bacteria also come in a wide variety of shapes: coccoid or spherical; bacillary or rod shaped; fusiform or long, thin rods that taper at the ends; curved; irregular; or a combination of shapes, fig (1). Bacteria are further classified by their growth pattern to aerobic, anaerobic, and facultative metabolism, and by their pattern of haemolysis. Odontogenic infections are characterized as a combination of aerobic and anaerobic bacteria. Microorganisms which are isolated from orofacial infections include Gram-positive aerobic cocci, α-haemolytic streptococci, peptostreptococci and Gram-negative anaerobes. Some of the common bacterial pathogens of odontogenic infection (12), are listed in Table (1).

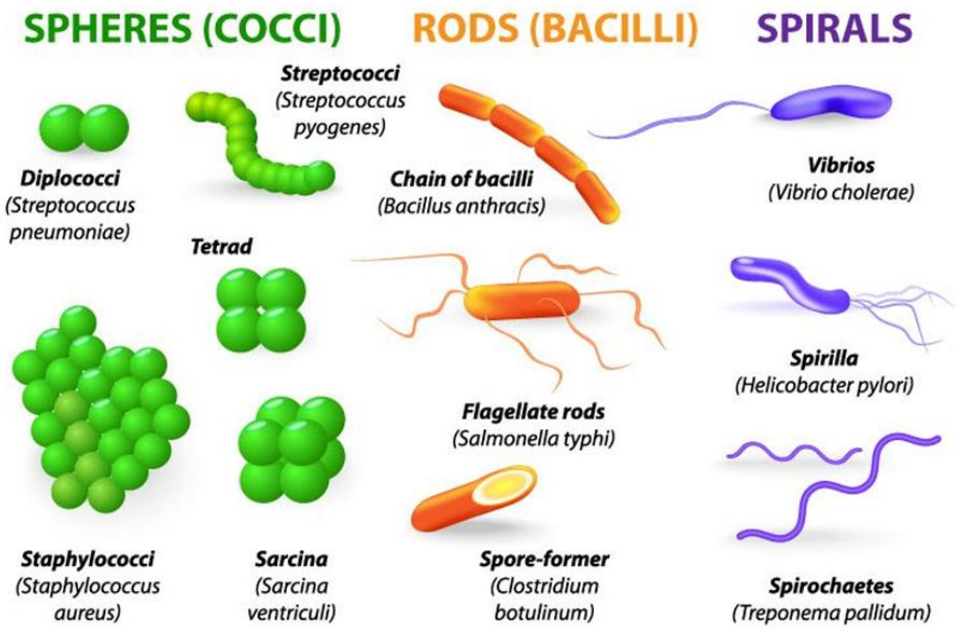

Fig. (1): Bacterial shapes

Common bacterial pathogens of odontogenic infection

Gram-positive cocci

Viridans Group Streptococci.

Streptococcal species are gram positive and display α−hemolysis, resulting in a green color around the colonies that gives rise to the name (*viridis* is Latin for "green"). Viridans streptococci are predominantly found in the oral cavity and are divided into four subspecies. These are mitis, mutans, salivarius, and anginosus (13). This group of organisms tends to be more pathogenic in patients who are immunocompromised. Viridans streptococci are implicated in the formation of dental caries and are pathogenic when introduced into fascial planes of the head and neck forming abscesses. In addition, viridans streptococci bacteremia is a known cause of subacute native and prosthetic valve endocarditis. Current literature has not fully elucidated the features that enable viridans streptococcus to behave as a

commensal pathogen in some hosts and host locations and as a pathogen in other hosts or locations. However, the different virulence factors of *S. mutans* help to explain its diversity as a pathogen.

Gram-negative cocci.

Veillonella organisms are anaerobic and can be located on the tongue and in the saliva. The most common of these are V parvula, V atypia, and V dispar.

Gram-positive rods and filaments.

The Actinomyces organisms are branched filamentous facultative anaerobes gram-positive rods that usually inhabit the oral cavity. They include: A israelii, A viscosus, A naeslundii, and A odontolyticus. Actinomyces species are pathogenic locally in the oral cavity or through direct extension into fascial planes as abscesses. Infection can spread when normal mucosal barriers are disrupted, leading to abscesses with connecting sinus tracts. These abscesses are most found in the face and neck as cervicofacial actinomycosis, but they can also occur throughout the thorax, abdomen, pelvis, and central nervous system.

Gram-negative rods and filaments.

Bacteroides, Fusobacterium, Prevotella, Capnocytophaga, Campylobacter, Eikenella, Actinobacillus, Selenomonas, and Porphyromonas (13) are gram negative facultative rods and filaments.

Spirochetes.

Treponema is the predominant genus that occupies the oral cavity. It is usually found in the gingival crevice and is responsible for acute necrotizing ulcerative gingivitis (14).

Table (1): Common bacterial pathogens of odontogenic infection.

Gram-positive bacteria	Gram-negative bacteria
Streptococcus mutans	*Fusobacterium nucleatum*
S. sanguinis	*F. periodonticum*
S. oralis	*Haemophilus parainfluenzae*
S. mitis	*Porphyromonas gingivalis*
S. gordonii	*P. endodontalis*
S. parasanguinis	*Prevotella intermedia*
S. salivarius	*P. loescheii*
S. anginosus	*P. melaninogenica*
Gemella morbillorum	*P. denticola*
Rothia dentocariosa	*P. nigrescens*
Actinomyces naeslundii	*Tannerella forsythia*
A. gerencseriae	*Bacteroides odontolyticus*
A. odontolyticus	*Neisseria subflava*
A. oris	*Veillonella parvula*
Filifactor alocis	*Aggregatibacter*
Lactobacillus salivarius	*actinomycetemcomitans*
L. fermentum	*Capnocytophaga ochracea*
L. plantarum	*C. gingivalis*
Bifidobacterium dentium	*Campylobacter rectus*
Eubacterium nodatum	*C. ureolyticus*
Parvimonas micra	*Treponema denticola*
Peptostreptococcus anaerobius	*T. socranskii*
Propionibacterium acnes	*T. vincentii*

Pathogenicity of oral microbiome

Bacteria that cause odontogenic infections are part of the oral microbiome; those that comprise the bacteria of plaque, those found on mucosal surfaces, and those found in the gingival sulcus without causing disease. When there is disruption of the balance between host and microbes because of a change in the host or bacterial population, certain bacteria (e.g., *Streptococcus aureus, S. pneumoniae*) behave as pathogens that cause invasive infection and clinical symptoms. These bacteria are

primarily aerobic gram-positive cocci, anaerobic gram-positive cocci, and anaerobic gram-negative rods. These bacteria cause a variety of common diseases such as dental caries, gingivitis, and periodontitis. When these bacteria gain access to deeper underlying tissues, as through a necrotic dental pulp or through a deep periodontal pocket, they cause odontogenic infections. As the infection progresses more deeply, different members of the infecting flora can find better growth conditions and begin to outnumber the previously dominant species.

Local factors

Several factors can influence the pathogenicity of these microbiome. These include saliva, diet, changes in the local microenvironment, and the presence of other microorganisms. Saliva is an important factor that influences the microbiome flora in the oral cavity. Changes in the pH, temperature, flow, and dietary content (e.g., minerals, vitamins, proteins) of the saliva influence the number and type of microorganisms present in the oral cavity and surrounding tissues, which affect how the body responds to infection. The minerals in the saliva, which regulate pH, provide a buffer and act as cofactor to the salivary enzymes. The organic components of the saliva include vitamin C, amino acids, carbohydrates, proteins, and glycoproteins. These components serve as nutrients to the local microorganisms, add viscosity, and impact adherence and aggregation (15).

Infection

Infections may arise when a change occurs in the intrinsic microbiome flora. Such change can be caused by invasion of the host cell by pathologic microorganisms or another form of disruption in the immune system. The infectious process occurs in four distinct steps: 1. Adherence, 2. Colonization, 3. Multiplication, and 4. Penetration.

Adherence is the initial step in the process, which occurs when the host is exposed to the microbe and the microbe adheres itself to the host cell. The major mechanism

of adherence seems to be recognition of specific receptors on the host cell surface by the microbe (16). Pili and other microbial cell structures assist the microorganism in adhering to the cell. The ability of a microorganism to colonize and cause disease depends on their cell surface components which helps them in attaching to the tissue surface, further on metabolic activity and utilization of nutrients (17). The next step in the infectious process is colonization of the host by the microbe. The microorganism seems to rely on this process for survival and thus must overcome the host's natural resistance. Colonization can occur without infection. The third step in the infectious process is multiplication. To further survive, the microbe must be able to reproduce within the host. The microbe does this by avoiding phagocytosis. Extracellular pathogens avoid phagocytosis by producing capsules, fimbriae, or pili. Other pathogens avoid this phagocytic process by producing lytic enzymes and antioxidants (e.g., catalase in staphylococci) (18). During multiplication, the nutritional needs of the microbes are extremely high. They seek nutrients from several sources, including extracellular enzymes like kinases, nucleases, and proteases. Other microorganisms produce specific compounds that stimulate nutritional support; for example, E coli produces a porphyrin-like substance that binds iron for nutritional growth and stimulation. The fourth and final stage of the infectious process is penetration. This step occurs when the microorganism invades the host-cell tissues by attaching to the mucous membrane and crossing the epithelial cell layer. The host responds to this invasion through a series of cell-signaling events designed to identify and destroy pathogens.

Immune response to infection

There are two kinds of immunological defense:

1. Natural or innate immunity, comprising mainly pre-existing antigen-nonspecific defenses. Innate immunity does not require prior exposure to the microorganism to respond to it.
2. Adaptive or acquired immunity, on initial exposure to a pathogen, requires 3 to 7 days for a response to occur. With multiple exposures to the pathogen over time, either naturally or through immunization, there is a decrease in the lag time and an increase in the magnitude and efficacy of the adaptive immune response. The adaptive immunity is sometimes called specific immunity because it can develop new responses that are highly specific to molecular components of infectious agents, called antigens. These encounters trigger the development of new cellular responses and production of circulating antibody, which have a component of memory if the invader returns. During which the adaptive immune system responds in an antigen-specific manner to neutralize the threat efficiently and retains a memory of the threat so that any future encounter with the same threat will result in an accelerated and heightened protective response.

The primary effectors of both innate and adaptive immunity components are cells that are part of the white blood cell series derived from hematopoietic stem cells in the bone marrow. It is important to note that these aspects of immune functioning do not operate in isolation; indeed, there is close functional integration between the innate and adaptive arms of the immune response (19). Innate immunity serves to provide the first line of defense in preventing infection. It includes physical barriers such as the skin and mucous membrane, phagocytic cells (e.g., neutrophils, macrophages), specialized receptors that bind and detect classes of macromolecules associated with pathogens, and molecules that promote inflammation, chemotaxis, opsonization, and the action of circulating glycoproteins such as complement. Mechanical barriers physically inhibit micro-organisms from attaching to and penetrating the host cells. These barriers include the skin, hair, mucous membranes,

and other physiologic secretions. The skin is the primary physical barrier to infection. Penetration through this layer is almost impossible for many microorganisms. The hair protects the skin from the invading microbes. The mucous coating provides another mechanical barrier against the microorganisms. Specialized epithelial ciliated cells help remove microbes from the upper respiratory tract. Other physiologic functions that assist the mechanical barrier include sneezing, coughing, and vomiting. Organisms that can pass the mucosa encounter a population of cells with the ability to engulf and destroy them. These include poly-morphonuclear leukocytes (polymorphs) and macrophages. The former are short-lived circulating cells, which can invade the tissues, while the latter are the mature, tissue-resident stage of circulating monocytes. These cells are activated by factors of the complement system, as in C5a, C3a and C4a for example, release mediators which, when combined with the complement proteins, attract leukocytes to the site of aggression and contribute to the passage of these cells from the vessels to the tissues. Apart from its phagocytic activity, eosinophils may destroy microorganisms by means of releasing proteins with microbicid activity. Within these cells, enzymes like myeloperoxidase having microbicid properties also exist. In addition, body fluids contain chemical agents such as complement, which can directly injure the microbe. In most cases, infectious agents are eliminated by innate immunity. When the innate immunity is not sufficient to prevent infection, the invading microorganism is successful in replicating within the host, and a productive infection ensues. Once this occurs, many of the elements of innate immunity are still active, but an adaptive immune response occurs over time (20).

Lymphocytes are the main cells of the adaptive immunity. Immature lymphocytes produced from stem cells in the bone marrow may continue their development within the bone marrow to form B lymphocytes or migrate to the thymus and develop into T lymphocytes. ‘Education’ within the primary lymphoid organs ensures that

emerging lymphocytes can discriminate self from non-self. Mature lymphoid cells continuously circulate between the blood, lymph, lymphoid organs, and tissues until they encounter an antigen, which will cause them to become activated effector cells of the immune response. The immune system recognizes and distinguishes a variety of structural features of self and non-self-components. The latter include almost everything but self: for example, bacteria, viruses, toxins, pollens, chemicals, transplanted organs, and even tumor cells derived from self-tissue. To this end the immune system recruits different kinds of immune cells, such as B and T lymphocytes, natural killer (NK) cells, dendritic cells, and macrophages. These cells have specific functions and are equipped with distinctive sets of receptors to recognize self and/or non-self-components. The main function of B cells is to make antibodies against specific antigens, the so-called humoral immunity. Humoral immunity is host defense provided by antibodies that are produced by B-lymphocytes against specific antigenic components of the affecting microorganism. Antibodies, also known as immunoglobulins, are proteins that attach themselves to pathogens. Initially, IgM antibodies respond to the infection, followed by IgG. IgM activates the byproducts of the classical pathway of complement C3a, which acts as an opsonin, and C5a, which acts as an anaphylatoxin. This activation facilitates phagocytosis through the C3a receptor of the phagocytic cell and enhances leukocyte migration to the site of infection. IgG acts as an opsonin by binding to the microorganism at the antibody-combining site. Circulating secretory IgA acts locally to impair microbial colonization and invasion at the mucosal surface. The antibodies may perform their inhibitory action in three ways: 1) opsonization, 2) activating the complement system, and, 3) promoting the neutralization of bacteria or its products. Antibodies often bind to bacteria- produced toxins and neutralize the action of these products.

Humoral and cell-mediated immunity (21) are the two factors of concern in adaptive immunity. In most infectious diseases, the host response depends on processing of antigens by the macrophage antigen–presenting cells. This response may be dominated by a humoral response in which opsonizing antibody specific to the pathogenic organism facilitates phagocytosis and clearance of the microorganism and its toxins, or it may be dominated by a cellular response, the so-called cell-mediated immunity in which cytokines, phagocytes, or cytolytic T cells eliminate infected host cells to clear the pathogen. Some T cells kill pathogens and infected cells. Other T cells help control the adaptive immune response. T lymphocytes are divided into two major subsets: T-helper cells, and T-cytotoxic cells. The T-helper cells are required for activating the effector function of B cells, other T cells, natural killer cells and macrophages. They do this by transmitting signals via cell-to-cell contact interactions and/or via soluble hormone-like factors called lymphokines. The T-cytotoxic cells kill target cells such as virus-infected host cells. Another functional property of some T lymphocytes is to down regulate immune responses.

Adaptive immune response is slower than the innate response but is better able to target specific pathogens. It takes time for T and B cells to respond to the new antigens. Once exposed to the pathogen, these cells develop a memory for the pathogen so that they are ready for the next infection. As part of the adaptive immune response, some T and B cells change into memory cells. Memory cells mostly stay in the lymph nodes and the spleen and “remember” particular antigens. If a person becomes infected with the same pathogen again, these cells can quickly and vigorously begin fighting the infection.

After entering a host, the pathologic microorganism, or its major antigens, is taken up by macrophages. The antigen is then expressed on the macrophage surface with the major histocompatibility complex proteins and is presented to T lymphocytes. When the body is exposed to an infection it responds peripherally and

systematically. The classic signs and symptoms of the host peripheral response to infection are the well-known inflammatory response that is presented as rubor (redness), calor (hotness), tumor (swelling or edema), dolor (pain), and functio laesa (loss of function). Systematically the response may consist of fever, chills, rigors, headaches, and anorexia. The peripheral and systematic responses are caused by the complement pathway activation by the microbial pathogens. This reaction is protective and aims at limiting or eliminating the irritant.

Several medical conditions may increase the risk for infections by affecting their immunocompetence. This compromised immunocompetence may be seen in elderly patients, malnutrition states, alcoholism, cirrhosis, diabetes, renal failure, dialysis, corticosteroid use, and drug abuse. Numerous studies, for example, have indicated that the correlation between facial cellulitis and diabetes mellitus patients was confirmed and diabetic patients are more susceptible to facial cellulitis and deep neck infections caused by odontogenic infections (22,23). In fact, life-threatening head and neck infections are encountered commonly in patients with compromised host defense mechanisms. Immunodeficiency disorders cause a breakdown of the physical barriers to infection, which are the first line of defense, and cause immunologic cell dysfunction (24).

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Chapter 2: Pathophysiology of odontogenic infections

Pathophysiology of odontogenic infections

Most odontogenic infections are related to dental pulp necrosis and periodontal disease (1). Necrosis of the pulp is the result of deep caries of a tooth, to which the pulp responds with a typical inflammatory reaction. Vasodilatation and edema cause pressure in the tooth and severe pain as the rigid walls of the tooth prevent swelling. If left untreated, the pressure leads to strangulation of the blood supply to the tooth through the apex and consequent necrosis. This is followed by bacterial invasion through the pulp chamber and into the deeper tissues. In comparison, periodontal infections may initiate following bacterial invasion within the tissues adjacent to periodontal pocket (2). However, serious odontogenic infection is more commonly the result of pulpal infection than of periodontal infection. Another cause of odontogenic infections is pericoronitis. Pericoronitis is inflammation of the tissues surrounding the crown of a partially erupted tooth, most commonly a mandibular third molar (3). This occurs due to trauma from the opposing maxillary third molar, or entrapment of debris and associated microorganisms underneath the operculum, the lid of gingival tissue covering the erupting tooth. Pericoronitis most commonly affects young adults and is associated with horizontal impaction of third molars. Patients with pericoronitis typically present with pain, swelling and trismus. Whatever the cause, infection then proceeds until the bacteria invades the periapical tissues (4). Fig. (1), represents illustration of an apical abscess. Once infection

extends past the apex of the tooth, the pathophysiological course of a given infectious process can vary, depending on the number and virulence of the organism, host resistance, and anatomy of the involved area. Infection can localize as an abscess or spread through soft tissue as cellulitis, or both. In common clinical usage, these terms are often confused. An abscess is collection of purulent material containing pus formed of necrotic tissue, bacteria, and dead white blood cells, whereas cellulitis is an acute disorder associated with warm, diffuse, painful, indurated swelling of soft tissues that also may present with erythema. Next, the indurated swelling begins to soften as an abscess develops represented by localized area fluctuance.

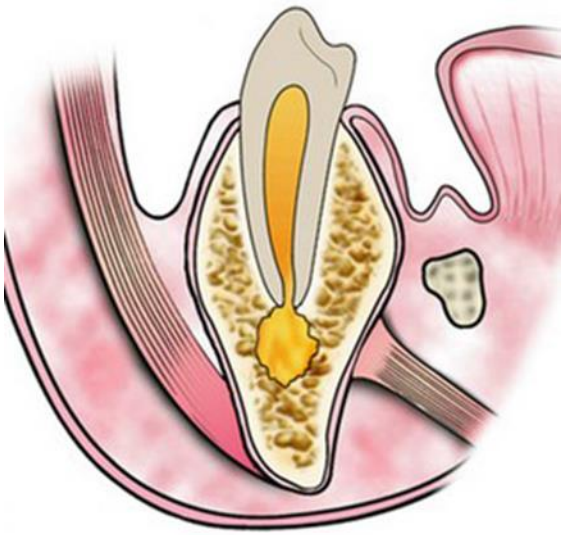

Fig (1): Pus is formed in the cancellous bone, and spreads in various directions by way of the tissues presenting the least resistance until a cortical plate is encountered.

Differentiating between cellulitis and abscess is based on duration, pain, size, localization, palpation, presence of pus, degree of seriousness, and type of bacteria (Table 1). During an infection, cellulitis is considered the initial phase, with an abscess forming in the later stage of the infection. An acute apical abscess is characterized by throbbing pain of rapid onset, which is exacerbated by biting.

Further, the presence of oedema within the apical region can produce the sensation that the tooth is in supraocclusion. The affected tooth is often highly sensitive to pressure and percussion. Erythema and swelling of associated tissues are common clinical findings (5). Swelling can occur intra-or extraorally, or both, depending on the relative amount of inflammatory infiltrate, oedema and pus formation, and the spread of these through the connective tissue spaces. Pain is often severe in the initial stages of abscess formation, however upon perforation of the periosteum and spread of infectious products into the loose connective tissue spaces, pain will often dissipate. Radiographic presentation may be variable. In acute form changes in bone density may not be noticeable (you have to wait for approximately 10 days to detect bone rarefaction), widening of the periodontal ligament may be seen, but frank apical radiolucency is unusual unless the situation represents a flare-up of a chronic apical abscess.

Table (1): Differences between cellulitis and abscess.

Characteristic	Abscess	Cellulitis
Duration	Acute	Chronic
Pain	Severe, generalized	Localized
Size	Large	Small
Localization	Diffuse borders	Well-circumscribe
Palpation	Doughy-indurated	Fluctuant
Presence of pus	No	Yes
Seriousness	Greater	Lesser
Bacteria	Aerobic	Anaerobic

Under certain circumstances, an acute infection is not completely resolved despite an aggressive immune response with or without antimicrobial therapy, and chronic infection results. Pus usually ruptures and a sinus tract is established, fig (2). At this

point pain is relieved. However, if the tooth continues to be neglected, one of several possibilities can occur. Slowly over time the bone involvement with the abscess can increase with more dissolution, possibly involving adjacent teeth. Frequently, sufficient destruction of bone develops to create an ill-defined radiolucency observable on dental radiographs. The patient may develop the classic “gum boil”, fig (3), which is the body’s attempt at healing the sinus tract with ever-increasing amounts of granulation tissue. Occasionally the tract becomes congested and the pain and swelling may briefly return, until the built-up pressure causes release and relief. This cycle may repeat many times. The one meaningful consequence of continued neglect is development of an osteomyelitis, which may be more severe and more difficult to eradicate. Another unusual possibility is the development of an orocutaneous fistula (fig. 4), which is much more common when it occurs in a longstanding mandibular infection.

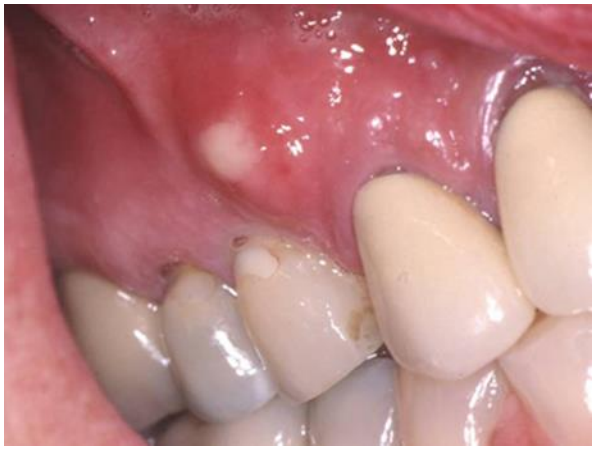

Fig. (2): Chronic sinus tract.

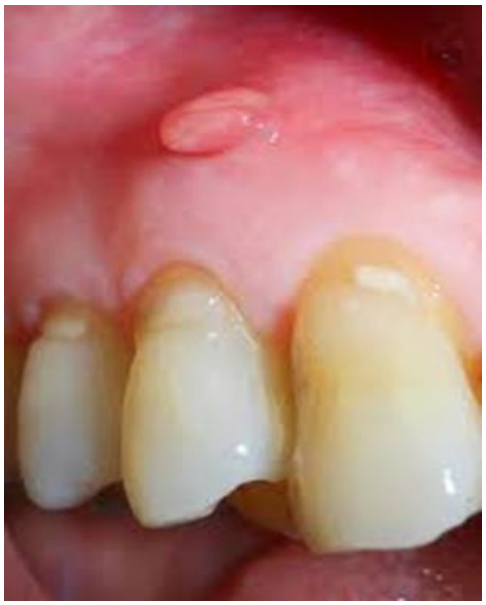

Fig. (3): Gum boil or fistula.

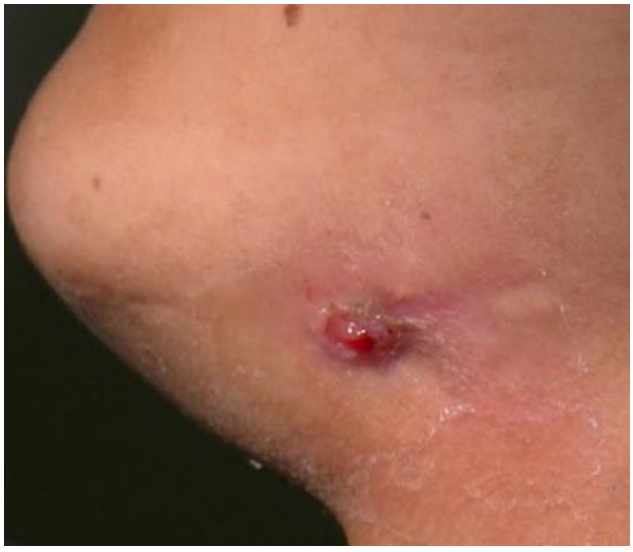

Fig. (4): Orocutaneous fistula.

A second alternative is that the purulent exudate formed in response to periapical infection spreads through the medullary bone to perforate the cortical bone and discharge into the submucous or subcutaneous soft tissue. In many cases, swelling develops only intraorally (6), in the form of vestibular abscess, fig. (5).

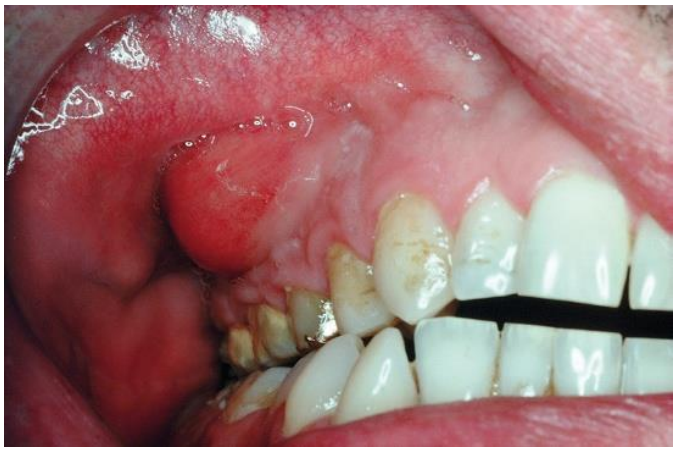

Fig. (5): Vestibular abscess presenting as a fluctuant swelling in the buccal sulcus.

Spread of localized infections

The routes by which the infections can spread are as follows:

1. By direct continuity through the tissues.

2. By lymphatics to the regional lymph nodes and eventually into the blood stream. The spread of infection from the lymph nodes into the tissues results in secondary areas of cellulitis or tissue space abscess.

3. By the bloodstream: Rarely, local thrombophlebitis may propagate along the veins, entering the cranial cavity via emissary veins to produce cavernous sinus thrombophlebitis.

Usually, odontogenic infections spread by direct continuity from the bony structures through the cortical bone along the path of least resistance. In the maxilla, acute apical abscesses drain through the buccal or palatal bone into the oral cavity (fig. 6), or occasionally into the maxillary sinus or the nasal cavity.

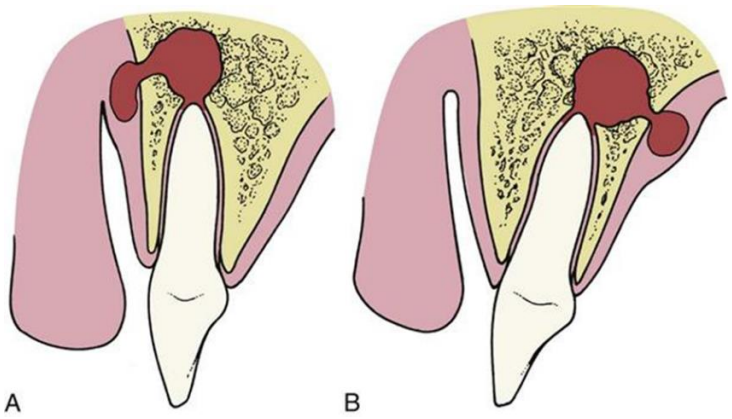

Fig. (6): Whether the pus spreads buccally (A), or palatally (B) depends mainly on the position of the tooth in the dental arch, the thickness of the bone, and the distance it must travel.

Apical abscesses of mandibular teeth may drain through the buccal or lingual bone into the oral cavity. However, the infectious process may also extend into fascial spaces of the head and neck and result in cellulitis and systemic signs and symptoms, with consequent complications. Based on the relationship between the point at which the infection erodes through alveolar bone and surrounding muscle attachments, infections arising from any maxillary or mandibular tooth can cause vestibular, buccal, or subcutaneous space infections. The buccinator muscle inserts superiorly into the alveolus of the maxilla and inferiorly in the alveolus of the mandible. Periapical infection may pass through the bony cortical plate superior to the attachment of the buccinator muscle to form a buccal space abscess. If the perforation is on the inferior side of the buccinator muscle, then the infection will spread into the vestibular space, fig. (7).

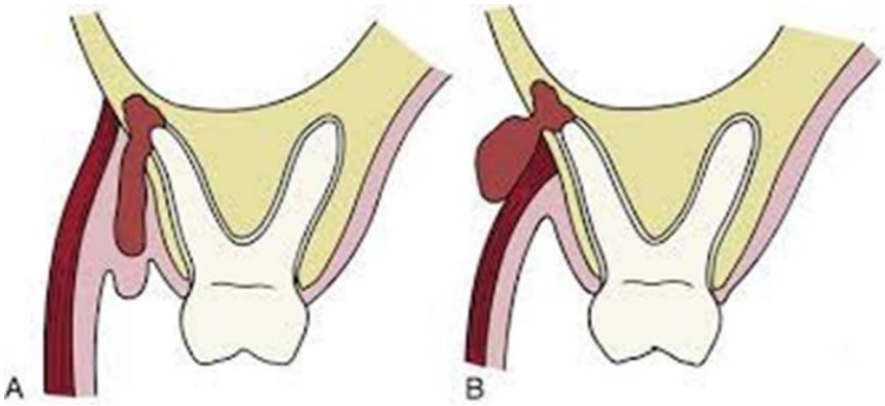

Fig. (7): The length of the root and the relationship between the apex and the attachments of various muscles play a significant role in the spread of pus: (A) vestibular abscess, (B) buccal space abscess.

Infections arising from maxillary teeth also tend to spread into the infraorbital, palatal, orbital, and infratemporal spaces, and the maxillary sinus. Mandibular dental infections tend to spread into the submandibular, sublingual, submental, and vestibular spaces. The mylohyoid muscle's origin is from the mylohyoid line of the mandible. For example, if a mandibular molar is affected and its root apices lie closer to the lingual cortical plate and above the attachment of the mylohyoid muscle, the purulent exudate can break through the lingual cortical plate into the sublingual space. If the root apices instead lie below the attachment of the mylohyoid muscle, the infection can spread into the submandibular space. The roots of the mandibular second and third molars lie below the mylohyoid muscle. Infectious spread of these teeth through the lingual plate forms submandibular space infections. The roots of the mandibular premolars and first molars lie above the mylohyoid and, therefore, infectious spread lingually associated with these teeth create sublingual space infections. The spaces that are primarily affected by odontogenic infections are located adjacent to the origin. Facial spaces have been classified as either primary or secondary spaces infection (7).

Primary maxillary spaces

- Canine
- Buccal
- Infratemporal

Primary mandibular spaces

- Submental
- Buccal
- Submandibular
- Sublingual

Secondary fascial spaces

- Masseteric
- Pterygomandibular
- Superficial and deep temporal
- Lateral pharyngeal
- Retropharyngeal
- Prevertebral

Anatomical consideration

Most odontogenic infections penetrate the bone in such a way that they become vestibular abscesses. On occasion they erode into fascial spaces directly, which causes a fascial space infection. Fascial spaces are fascia-lined areas that can be eroded or distended by purulent exudate. These areas are potential spaces that do not exist in healthy people but become filled during infections. The term ‘‘spaces’’ is inappropriate. Most spaces in the body are in fact either “potential spaces” (8), or “compartments” (9). Some contain named neurovascular structures and are known as compartments; others, which are filled with loose areolar connective tissue, are known as clefts. The spaces in the head and neck can be roughly divided into cranial (related to the skull and face) and cervical (related to the cervical spine), although these distinctions are not absolute.

The spaces that are involved directly are known as the fascial spaces of primary involvement. The principal maxillary primary spaces are the canine, buccal, and

infratemporal. The principal mandibular primary spaces are the submental, buccal, submandibular, and sublingual spaces. Infections can extend beyond these primary spaces into additional fascial spaces, or secondary spaces.

Primary maxillary spaces

Upper lip

Infection at the base of the upper lip, fig. (8), typically originates from the upper anterior teeth. It spreads to the orbicularis muscle, from the labial sulcus between the levator labii superioris muscle and the levator angularis oris muscle (10).

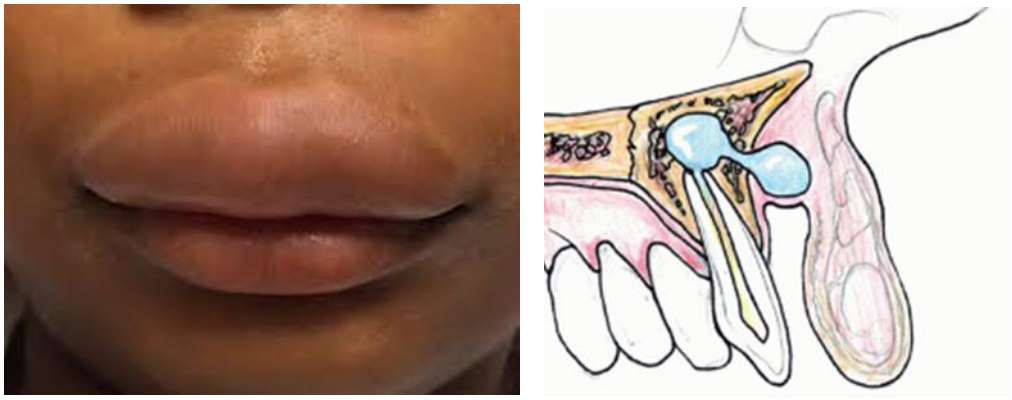

Fig. (8): Cellulitis of the upper lip.

Canine space

The canine space is located between the bony attachments of levator anguli oris and the levator labii superioris muscles. Spread of infection to the canine fossa, fig. (9), usually originates from maxillary canine or upper premolar teeth, often presenting above the buccinator muscle attachment. These swellings usually obliterate the nasolabial fold and may extend to the lower eyelid. Direct surgical access is achieved via incision through the maxillary vestibular mucosa above the mucogingival junction.

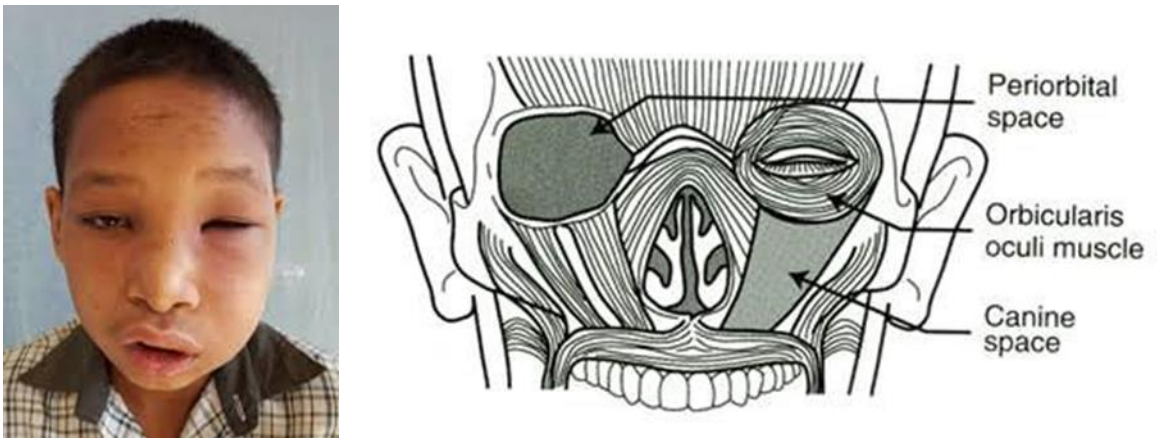

Fig. (9): Canine (infraorbital) and periorbital space infection.

Palate

The palate is usually involved in infections originating from the maxillary lateral incisor or the palatal root of a posterior tooth, usually, the first molar. The infection spreads from the apices of these teeth, perforating the palatal alveolar bone, and pus accumulates below the palatal mucoperiosteum, fig. (10).

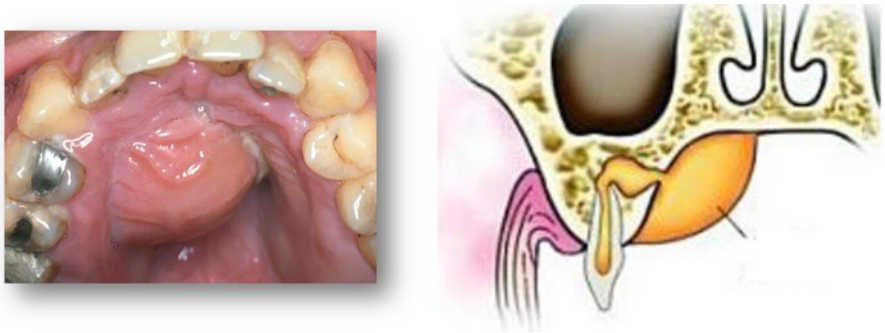

Fig. (10) Palatal abscess arising from the root of a maxillary lateral incisor.

Buccal space

Originally described as the space occupied by the buccal fat pad anterior to the masseter muscle. The buccal space, fig. (11), is bordered anterolaterally by subcutaneous tissue and the zygomaticus major, minor, and risorius muscles, medially by the buccinator, and posteriorly by the mandible, masseter, pterygoid muscles, and the parotid gland. The buccal space frequently communicates posteriorly with the masticator space and infection in this region is mostly spread

into the parotid, temporal, and submandibular spaces occurs with disease progression (11). Surgical access to the buccal space infections may be easily accomplished through the intraoral approach. More complicated infections, directed by location within the buccal space, may require a preauricular and/or submandibular approach.

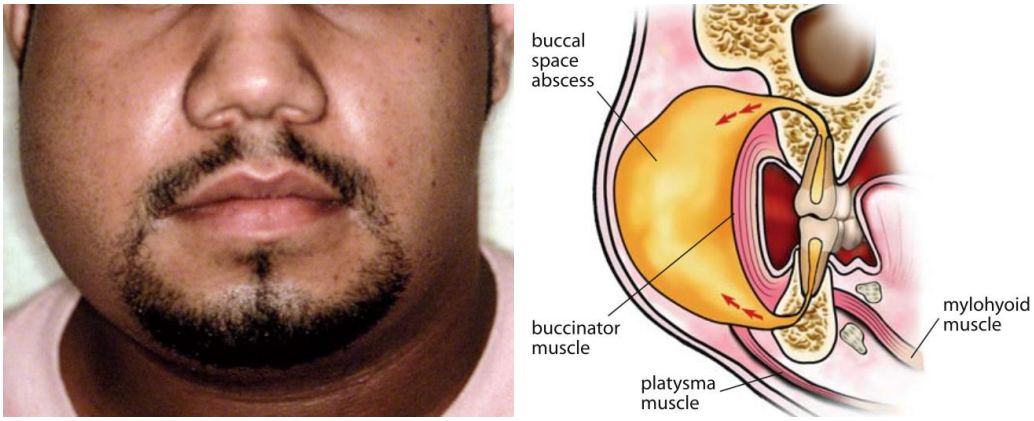

Fig. (11): Buccal space lies between buccinator muscle and overlying skin and superficial fascia.

Infratemporal space

Extension of infection from maxillary molars can pass into the infratemporal space. The space is located behind the zygomatic bone posterior to the maxilla and medial to the insertion of the medial pterygoid muscle inferior to the zygomatic arch. The infratemporal space is bounded superiorly by the greater wing of the sphenoid and is close to the inferior orbital fissure, with a possible risk of spread of infection to the orbit. Infection may ascend into the cavernous sinus through venous plexus in the ovale and spinosum foramen (12).

Primary mandibular spaces

Submental space

The submental space lies between the two anterior bellies of the digastric muscle. Anteriorly and laterally this space is bounded by the body of the mandible. It is contained, superficially, by the platysma muscle and, deeply and superiorly, by the mylohyoid muscle. Infection of this space usually arises from mandibular anterior teeth, where the infection perforates the lingual cortex (13). Clinically, submental infection is presented as a firm swelling below the chin, fig. (12), and the patient experiences considerable pain and difficulty with swallowing. Treatment is by surgical incision and drainage, with the incision running transversely in a skin crease behind the chin.

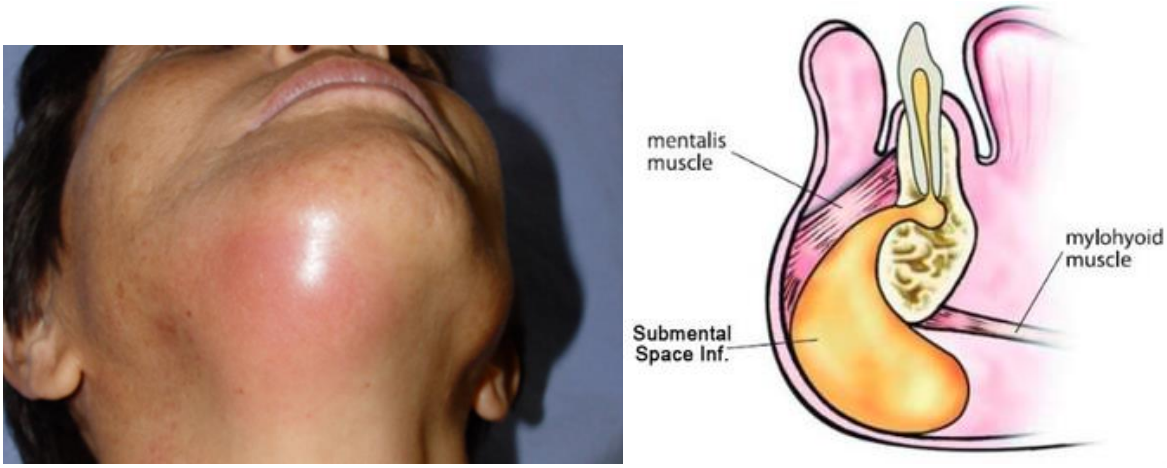

Fig. (12): Submental space infection.

Sublingual space

The sublingual space, fig. (13), is the potential anatomic area between the oral mucosa of the floor of the mouth superiorly and the mylohyoid muscle inferiorly. The genioglossus and geniohyoid muscles form the medial boundary. The lateral boundaries of the space are the lingual surfaces of the mandible. The source of infection is any mandibular tooth in which the purulent exudate breaks through the

lingual cortical plate, and the apex or apices of the tooth lie above the attachment of the mylohyoid muscle (13). Infection in this space will raise the floor of the mouth and displace the tongue, medially and posteriorly. Such tongue displacement may compromise the airway and immediate intervention may be required. Dysphagia and difficulty with speech are also common.

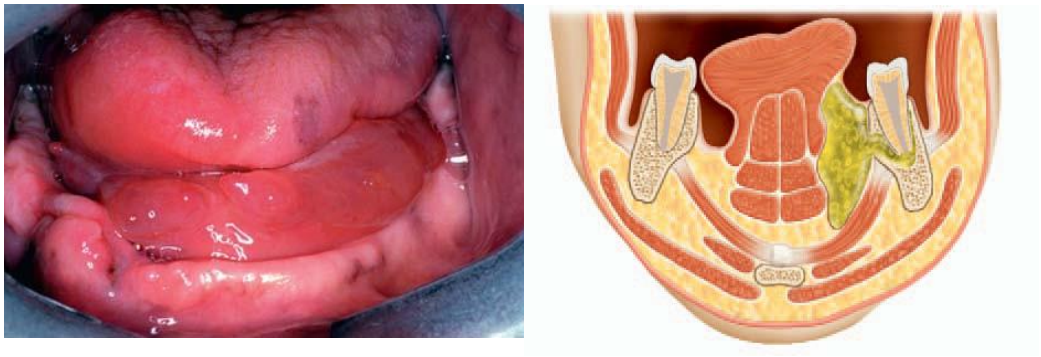

Fig. (13): Sublingual space infection causes elevation of the floor of the mouth.

Submandibular space

The submandibular space, fig. (14), is the potential space between the mylohyoid muscle superiorly and the platysma muscle inferiorly. The source of infection is a posterior tooth, usually a molar, in which the purulent exudate breaks through the lingual cortical plate, and the apices of the tooth lie below the attachment of the mylohyoid muscle. Involvement of the submandibular space causes severe symptoms such as neck rigidity, trismus, dysphagia, respiratory distress, sialorrhea, and pyrexia (14). The submandibular space freely communicates with the sublingual space, since there is no fascia separating these spaces at the posterior margin of the mylohyoid muscle and infection of one space readily spreads to involve the other space (15). Infection originating in the anterior teeth would initially extend to the sublingual space and subsequently spread directly or through the mylohyoid muscle into the submandibular space.

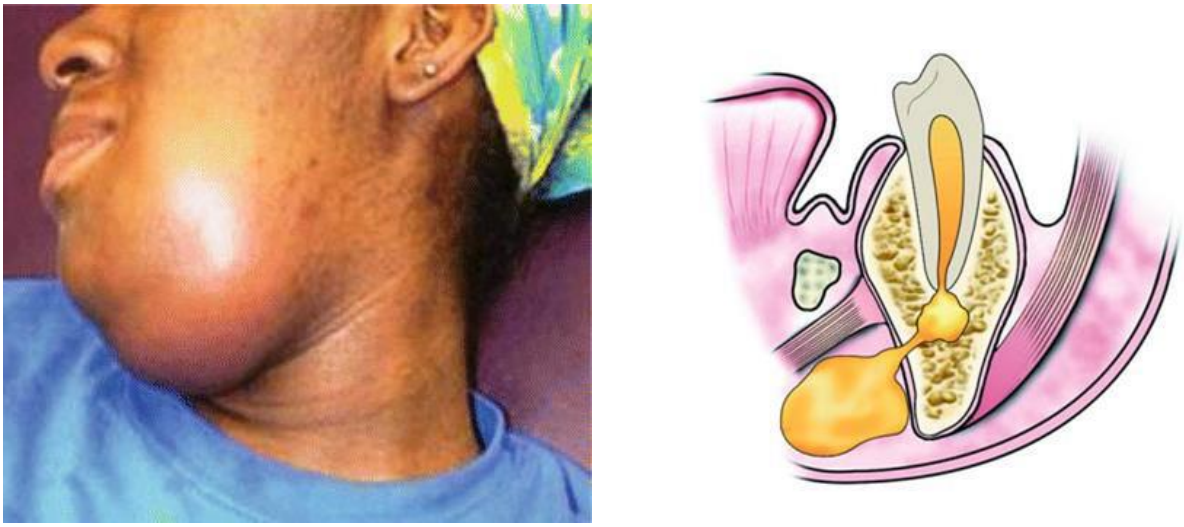

Fig. (15): Submandibular space infection.

Numerous studies have indicated that the submandibular space was the most common location for a single space abscess (16,17). Further, the submandibular space was the most frequently involved in patients with multispace infections (18). In their study on 103 patients with head and neck space infections of odontogenic origin, Rega et al. reported that the submandibular space was the most common location in the multiple space abscesses (19). Moreover, the submandibular space is regarded as a space through which inflammation spreads to the parapharyngeal space. If the infection spreads into the parapharyngeal space, rapid and critical airway obstruction may occur (20).

After infection spreads to primary spaces, they can progress to include secondary spaces. Because the spaces communicate through fascial planes, infection spreads by continuity rather by lymphatics or blood vessels (21). Secondary spaces include pterygomandibular, masseteric, lateral pharyngeal, superficial, and deep temporal, masticator, retropharyngeal, and prevertebral. From there, such infections can spread into the danger space and the mediastinum. In addition, infections can rise superiorly through the sinuses or vascular structures to invade the brain or the intracranial dural sinuses such as the cavernous sinus.

Secondary fascial spaces infection

Pterygomandibular space

Infection in this space is manifested by trismus, due to the involvement of the pterygoid muscles. This space, fig. (16), is bounded medially and inferiorly by the medial pterygoid muscle and laterally by the medial surface of the mandibular ramus. Posteriorly, parotid glandular tissue curves medially around the back of the mandibular ramus to form a posterior border, while anteriorly the buccinator and superior constrictor muscles come together to form a fibrous junction, the pterygomandibular raphe (22). The lateral pterygoid muscle forms the roof of this space.

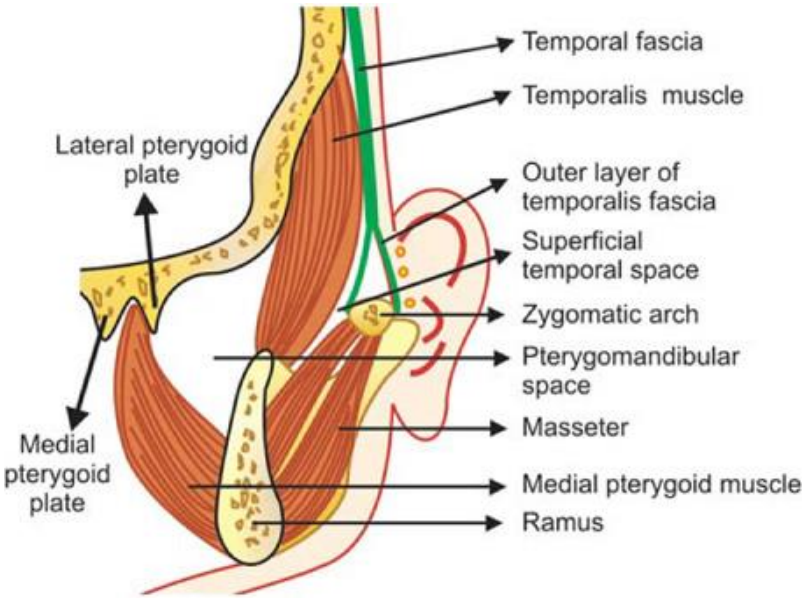

Fig. (16): Pterygomandibular space.

Masticator space

The masticator space was originally described as four compartments space: submasseteric, pterygomandibular, superficial temporal, deep temporal. The most common source of infection in the submasseteric space is from lower third molar pericoronitis. This space, fig. (17), is bound laterally by the masseter muscle and

medially by the outer surface of the ramus of the mandible (23). It is in direct communication with the lateral pharyngeal space posteriorly. Severe trismus due to spasm of the masseter muscle is a characteristic feature of involvement of the submasseteric space. Temporal space is divided by the temporalis muscle into superficial and deep temporal space. The superficial temporal space is the space between the temporal fascia covering the temporalis and the temporoparietal fascia. It extends superiorly to the pericranium, lateral to the temporalis muscle and medial to the temporoparietal fascia. Inferiorly, this space is continuous with the masseteric space. The deep temporal space lies between the temporalis, the periosteum of the temporal bone, and the lateral pterygoid muscle. It extends superiorly to the attachment of the temporalis muscle to the inferior temporal crest, lateral to the temporal bone and deep to the temporalis muscle. Inferiorly, this space is continuous with the infratemporal space (24). Both spaces freely communicate anteriorly, and the deep temporal space communicates with the masticator space, fig. (18).

Fig. (17): Submasseteric space infection.

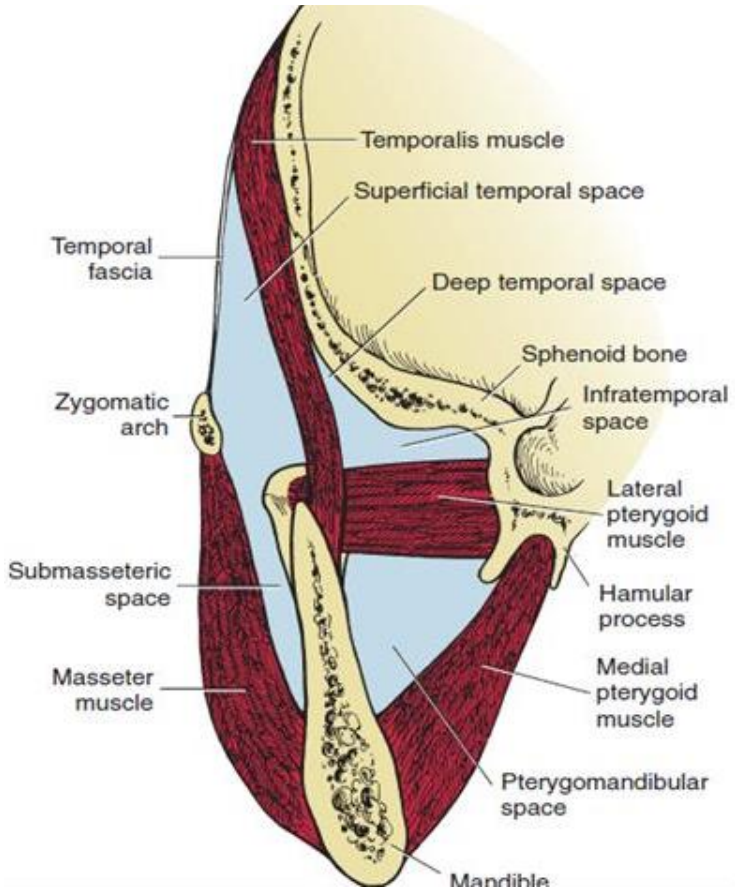

Fig. (18): The four compartments of the masticator space. Superficial temporal space, deep temporal space, submasseteric space, and pterygomandibular space. Note the approximate location of infratemporal space.

Parotid space

The term parotid "space" is used almost exclusively to describe the potential space created by the fascia that encloses the parotid gland (25). The deep lobe of the parotid gland extends posteromedial to the mandible and forms a lateral border of the parapharyngeal space. Although anatomic studies suggest that the fascia covering this aspect of the parotid is complete, the spread of infection from the parotid to the parapharyngeal space noted in the clinical literature indicates that it does not provide a functional barrier.

The parapharyngeal spaces

The parapharyngeal spaces is commonly described as an inverted pyramid, cone, funnel, or triangle with the skull base superiorly and the greater cornu of the hyoid bone or mandible inferiorly (26). Laterally, it is bordered by the medial pterygoid muscle and parotid gland, posteriorly by the prevertebral muscles or carotid sheath (depending on the definition), and medially by the visceral fascia covering the pharyngeal muscles. The parapharyngeal spaces comprise the lateral pharyngeal and retropharyngeal spaces (Fig. 19). The lateral pharyngeal space is located on the lateral side of the neck, bounded medially by the superior constrictor muscle of the pharynx and posterolaterally by the parotid space. The superior and inferior margins of the space are the base of the skull and the hyoid bone, respectively. The lateral pharyngeal space contains the carotid sheath, which contains the common carotid artery, internal jugular vein, and the vagus nerve, glossopharyngeal nerve, accessory nerve, and the hypoglossal nerve, as well as the sympathetic trunk. Thus, spread of infection into this space carries a significant danger of spreading into a descending neck infection and involvement of the mediastinum. Clinically, stiffness of the neck, swelling of the lateral wall of the pharynx, medial displacement of the tonsils, dysphagia, and trismus are among the characteristic clinical features of involvement of this space. Anatomically, the retropharyngeal space is located between the anterior surface of the prevertebral fascia and the posterior surface of the superior constrictor muscle of the pharynx and extends inferiorly into the retro-esophageal space, which extends into the posterior compartment of the mediastinum. It has the same characteristic clinical features as infection of the lateral pharyngeal space and carries a significant complication risk of a descending neck infection.

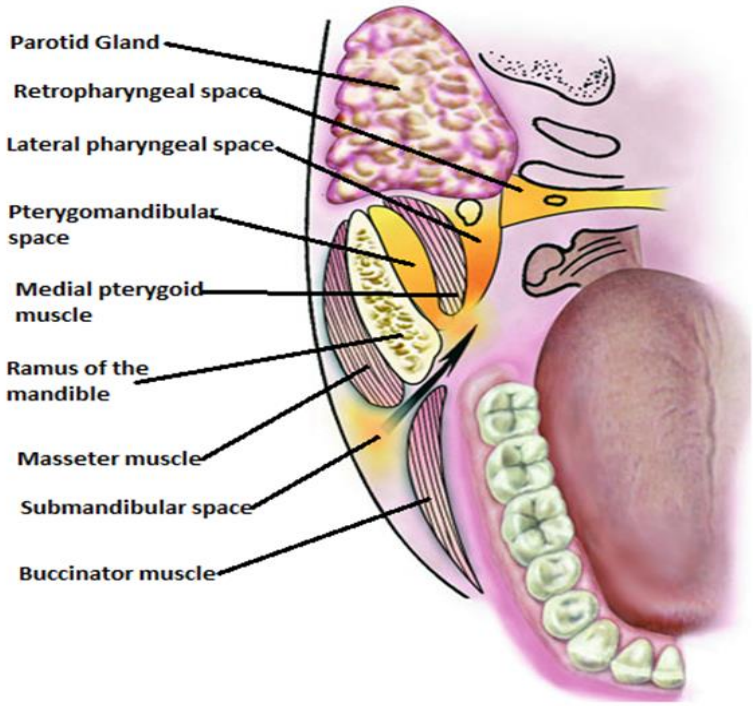

Fig. (19): Parapharyngeal spaces.

Cervical spaces

The deep layer of the deep cervical fascia, fig. (20), separates into a posterior prevertebral division and an anterior alar division (27). The prevertebral division is adherent to the anterior aspect of the vertebral bodies from the base of the skull down the spine extending from the 1st cervical vertebra to the coccyx. It extends posteriorly around the spine and the muscles of the deep neck, the vertebral muscles, muscles of the posterior triangle, and the scalene muscles. It envelops the brachial plexus and subclavian vessels, extending laterally into the axillary sheath. The alar division is located between the visceral division of the middle layer and the prevertebral division of the deep layer. The deep layer corresponds to the posterior boundary of the retropharyngeal space, extending down to the level of the 2nd thoracic vertebrae, where it fuses with the visceral fascia. Thus, the deep layer of the deep cervical fascia is important in providing the posterior boundary for extension

of infection to the mediastinum. The danger space (28) is the potential space between the alar and prevertebral fascia. Because this space is composed of loose connective tissue, it is considered an actual anatomic space extending from the base of the skull into the posterior compartment of the mediastinum to a level corresponding to the diaphragm. The retropharyngeal fascia fuses with the alar fascia at a variable level between the 6th cervical and 4th thoracic vertebrae, forming the bottom of the retropharyngeal space. When an infectious process contacts this anatomic barrier, it may rupture through the alar fascia and enter the danger space.

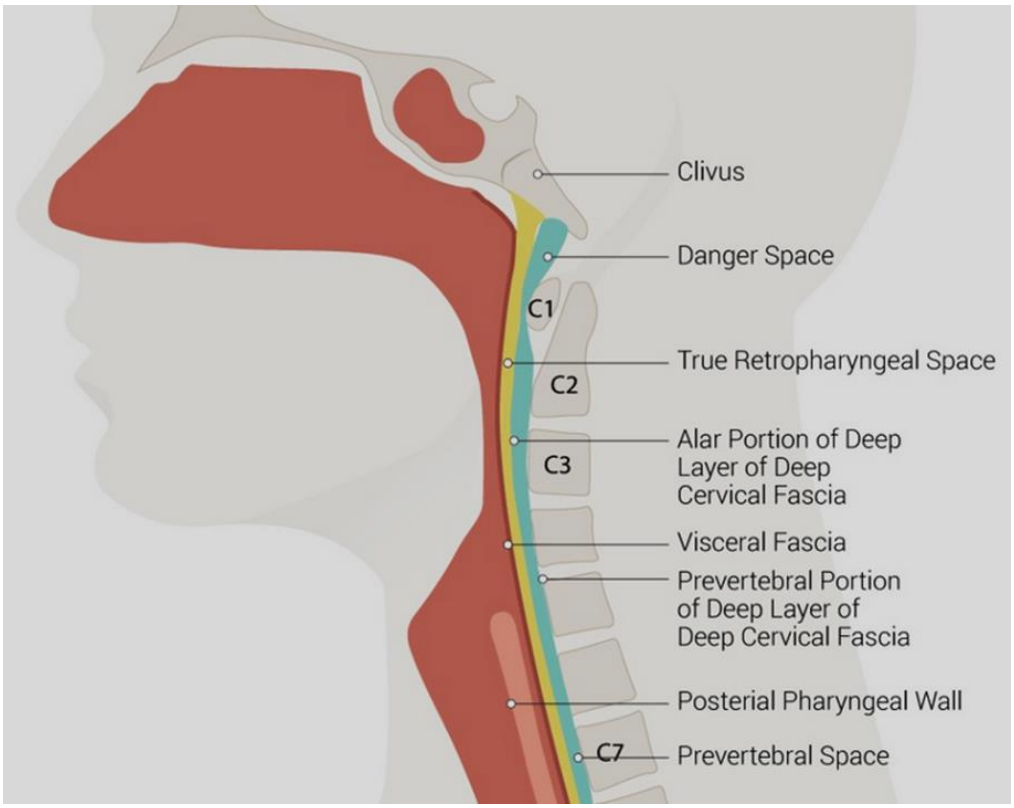

Fig. (20): Prevertebral fascia and danger space. Note the proximity of retropharyngeal space to the danger space through the alar fascia.

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Chapter 3: Management of odontogenic infections

Management of odontogenic infections

Odontogenic infections represent a wide spectrum of conditions, from simple localized abscesses to deep neck space infections. The initial assessment of the patients requires considerable clinical skill and experience and determines the need for further airway management or emergent surgical therapy. Knowledge of head and neck fascial space anatomy is essential in diagnosing, understanding spread, and surgically managing these infections. The primary goal of surgical management for odontogenic infections is to drain the pus collections and to remove the source of infection, usually by extracting the offending tooth. Supportive medical therapy that includes antibiotic administration should be considered.

Examination and assessment

Thorough patient examination is a critical component of treatment of odontogenic infections. Patient evaluation begins with a comprehensive history and physical examination followed by an assessment of the pertinent findings. The first step in the physical examination is to obtain the patient's vital signs, including temperature, blood pressure, pulse rate, and respiratory rate. The need for evaluation of temperature is obvious. Patients who have systemic involvement of infection usually have elevated temperatures. Patients with severe infections have temperatures elevated to 38°C or higher. The patient's pulse rate increases as the patient's temperature increases. Pulse rates of up to 100 beats per minute are not uncommon in patients with infections. If pulse rates increase to greater than 100 beats/min, the patient may have a severe infection and should be treated more aggressively. The vital sign that varies the least with infection is the patient's blood pressure. Only if the patient has significant pain and anxiety will an elevation occur in systolic blood

pressure. However, septic shock results in hypotension. Finally, the patient's respiratory rate should be closely observed. The normal respiratory rate is 14 to 16 breaths per minute. Patients with mild to moderate infections may have elevated respiratory rates greater than 18 breaths/min. Patients who have abnormal vital signs with elevation of temperature, pulse rate, and respiratory rate are more likely to have serious infection and require more intensive therapy and evaluation by an oral-maxillofacial specialist. One of the major considerations in odontogenic infections is the potential for partial or complete upper airway obstruction because of extension of the infection into the deep fascial spaces of the neck. As respirations are monitored, the operator should carefully check to ensure that the upper airway is clear and that the patient is able to breathe without difficulty. Airway assessment is a critical component of this examination. It allows for assessment of the necessity for emergent referral.

A patient history includes attaining information regarding the symptoms, onset, and duration of the present illness. This information helps to form an understanding of the severity of the patient's infection. The common presenting signs and symptoms were pain, swelling, lymphadenopathy and trismus. Patients will often present with systemic signs and symptoms of disease, such as fever, chills, malaise, pain on swallowing, and loss of appetite. Because these are general symptoms, more localizing symptoms such as odynophagia (pain when swallowing), dysphagia (difficulty in swallowing), trismus (reduced opening of the jaws), odontalgia (toothache, also known as dental pain), and dysphonia (hoarse voice) are often present. Mayor and coworkers (2) showed that the most common clinical presentation of deep neck space infections was odynophagia in 84% of patients, followed by dysphagia (71%), fever (68%) neck pain (55%), neck swelling (45%), trismus (39%), and respiratory distress (10%). Similar symptoms have been shown in other series as well (3-4). Signs include neck swelling, elevation of the floor of the

mouth, drooling (flow of saliva outside the mouth), diaphoresis (perspiration, also known as sweating), elevated temperature, and bulging of the lingual aspect of the mandible or pharyngeal wall.

The patient's medical history and current medications are key in assessing the patient's ability to fight infection as well as providing insight to potential drug interactions. Delineation of those medical conditions that may result in decreased host defenses is important. These compromises allow more bacteria to enter the tissues or to be more active, or they prevent the humoral or cellular defenses from exerting their full effect. Several specific conditions may compromise patients' defenses. Some of the more common are uncontrolled diabetes mellitus, chronic hepatitis, uremia or chronic renal failure, and relative immune-suppressed states such as HIV/ AIDS or in patients on chemotherapy (5). These conditions result in decreased function of leukocytes, including decreased chemotaxis, phagocytosis, and bacterial killing. Moreover, they require thorough workup and monitoring because they can be exacerbated by the infection and can also lead to more severe infections. Diabetes requires strict management, and control of blood sugar below 200 mg/dL is imperative for good control of infection (6). In fact, hyperglycemia correlates directly with lowered resistance to all types of infections. Diabetic individuals have also been shown to develop complications from abscesses more frequently and to have a longer duration of hospital stay than nondiabetics (7). The second major group of immunocompromising diseases includes those that interfere with host defense mechanisms, for example, leukemias, lymphomas, and many types of cancer. These diseases result in decreased white cell function and decreased antibody synthesis and production.

The patient should be inspected for any evidence of swelling and overlying erythema. Palpation, percussion, and thorough visual examination of the extraoral and intraoral swellings provide necessary information for identifying the source and

location of the infection. Physical examination should include intraoral evaluation with focus on the floor of mouth and dentition, and oropharyngeal region. Potential initiating factors such as dental problems, dental interventions, recent upper respiratory infection, recent surgery, or trauma need to be assessed. Attention should also be directed to the size of swelling, tongue position, floor of the mouth swelling or elevation, visual disturbances, voice changes, vestibules, and uvula position. Areas of swelling must be examined by palpation, checked for tenderness, amount of local warmth or heat, and the consistency of the swelling. The consistency of the swelling may vary from very soft and almost normal to a firmer, fleshy swelling (described as "doughy") to an even firmer or hard swelling (described as "indurated"). An indurated swelling has similar firmness to a tightened muscle. Another characteristic consistency is fluctuance. Fluctuance feels like a fluid-filled balloon. Fluctuant swelling almost always indicates an accumulation of liquid pus in the center of an indurated area. In all odontogenic infections, examination usually reveals the presence of deep caries, periodontal inflammation, or impacted or fractured teeth as the cause. Bone fractures or gingival trauma should not be overlooked in the search for the causative factors of abscesses or cellulitis.

Although observation and palpation can elicit the presence of superficial dentoalveolar and fascial space infections (i.e., buccal, canine, submental spaces), the presence of deep infections must always be a suspicion. Inasmuch as the presence of or even surgical drainage of superficial infection may obscure a concomitant or secondary deep space involvement. Radiological diagnosis is fundamental in determining the location, extension, and possible complications of these lesions. The role of diagnostic imaging is to define the location of the infection and to explore for possible spread of the disease beyond the site of origin (8). Dental panoramic radiography is particularly useful to identify the cause of infection (fig. 1) by providing good visualization of maxillary and mandibular dental structures but

provides little information about the severity of the infection. Computed tomography (CT), including cone-beam CT (CBCT) plays an important role in detecting bony changes and periosteal reactions. However, CT is superior to CBCT in the assessment of soft tissue spread of infections. Contrast-enhanced CT is considered the most accurate and widely used imaging modality in the evaluation of deep neck infections. Early reports on the accuracy of contrast-enhanced CT scans in diagnosing deep neck infections were favorable, with published reports of 100% accuracy. It provides the exact picture of abscess or gas formation and the location and possible spread of infection to distant regions. In a study by Kirse and Roberson (9), ring enhancement and irregularity (scalloping) of the collection wall (Fig.2,3) were analyzed for their value in predicting the presence of pus. Based on these data, it can be inferred that the presence of scalloping of the abscess wall is a late development in abscess progression. The literature also clearly demonstrates that the combination of clinical examination and contrast enhanced CT have the strongest accuracy, sensitivity, and specificity in diagnosing deep neck infections and in identifying a drainable collection (10). However, to limit the over utilization in the emergency setting, a CT was determined to be unnecessary if the subjects presented without “red flag” signs on physical exam, which included voice change, elevated floor of mouth, signs of inflammation of deep fascial spaces, periorbital edema, nonpalpable inferior border of the mandible, dyspnea, dysphagia/odynophagia, and trismus (11). Recent studies, however, have focused on the ability to diagnose abscesses using imaging studies that limit the patient exposure to radiation, including the use of ultrasound, magnetic resonance imaging (MRI) and low-voltage CT scanning. Magnetic resonance imaging (MRI) produces better soft tissue detail then CT. In 2001, Munoz et al. (12) compared MRI versus CT in the initial evaluation of acute infections involving the neck in 47 patients. They found MRI superior when looking at lesion conspicuity, number of spaces involved, extension and source of

infection. Ultrasonography has been suggested as a possible modality for imaging of infections (fig.4); it is becoming increasingly available in outpatient settings, its noninvasive nature, lack of radiation and low cost, makes it an attractive option, Use of ultrasound gives reliable determination of abscess versus cellulitis. Further, ultrasound is that it is transportable to the patient, can be used to direct an aspirating needle, and involves no radiation (13). However, so far it has not been successful in detecting deep fascial space infections.

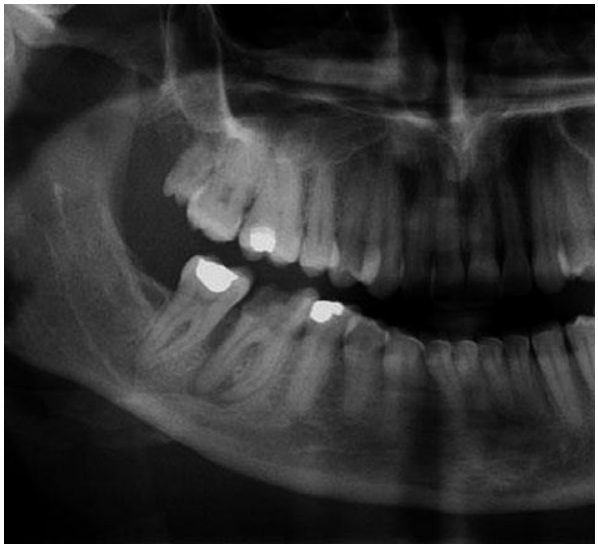

Fig. (1): Orthopantomogram showing grossly carious lower right first molar with associated periapical radiolucency.

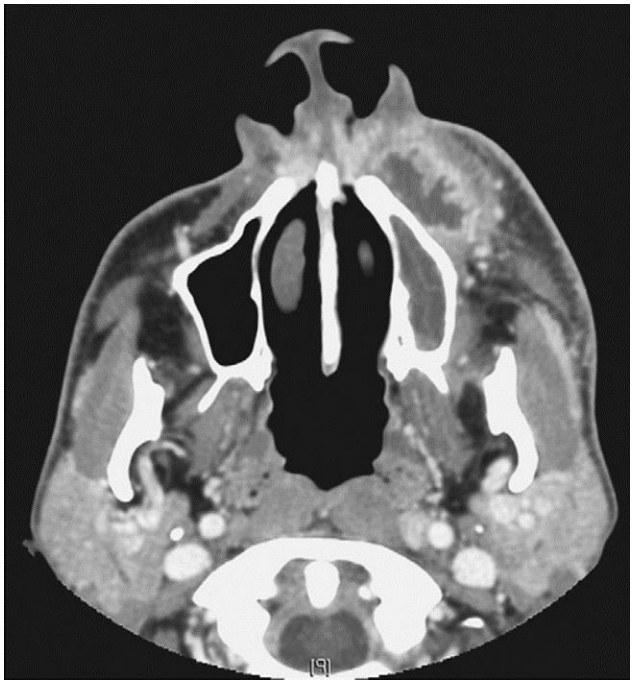

Fig. (2): Contrast-enhanced CT scan of a focal, ring-enhancing infraorbital abscess with an irregular (scalloped) contour of the abscess wall.

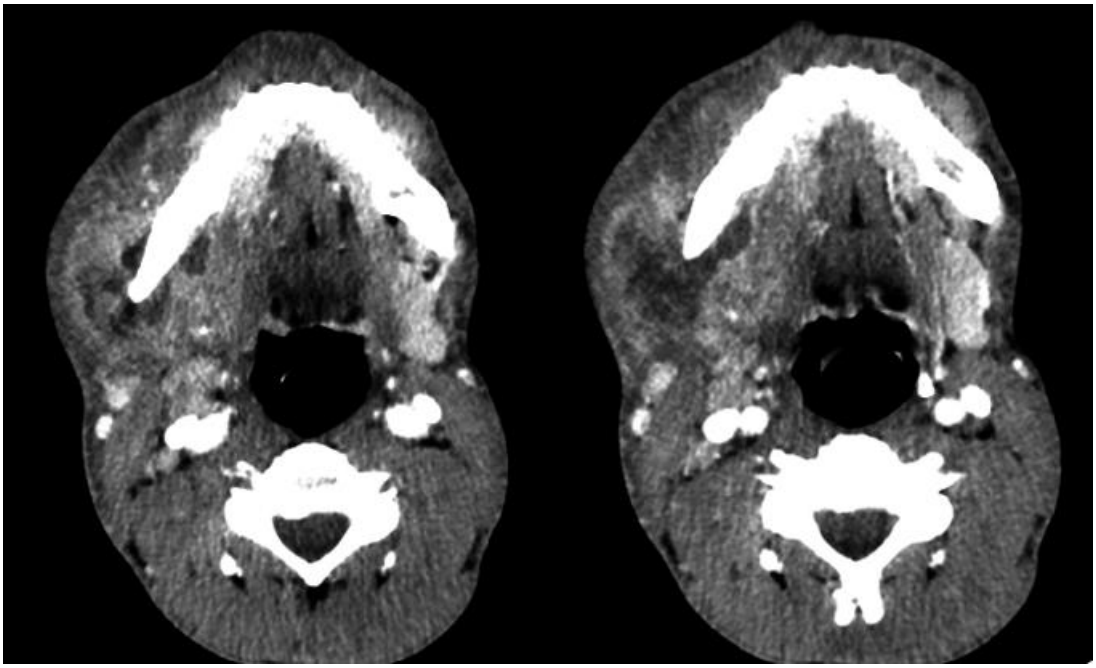

Fig. (3): Axial CT scans demonstrating acute odontogenic infections occupying the Rt. submasseteric and pterygomandibular spaces.

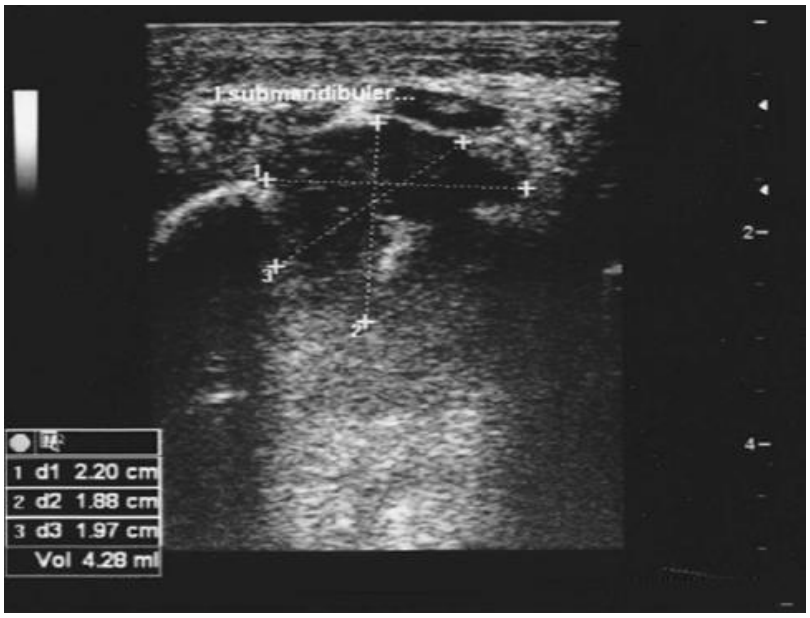

Fig. (4): Sonogram showing the submandibular space abscess.

The role of the laboratory in diagnosing odontogenic infections in routine practice in dentist's offices is controversial. Blood tests that should be carried out include a full blood count, with a differential white cell count and inflammatory markers such as C-reactive protein. Blood cultures are not routine, unless the patient is febrile, and sepsis is of concern. Although conventional measures to estimate infections such as white blood cell count (WBC), erythrocyte sedimentation rate (ESR), and complement reacting protein (CRP) values are valuable in determining state of patient at testing time, the predictability of these is worth limited. Numerous studies have concluded that white blood cells count, and C-reactive protein are effective markers for determining severity of infection, efficacy of treatment regime for patients with fascial space infections of odontogenic origin (14,15). Some attempts have been made to utilize CRP levels as an inflammatory prognostic factor in management of infections of odontogenic origin, its rapid rise and falls makes it a much more sensitive predictor than ESR and WBC count (16).

Severity score

Determining the severity of an infection requires assessment of three main factors: (1) airway patency, (2) anatomic location, and (3) rate of progression (17,18). The severity score for a given subject is the sum of the severity scores for all of the spaces involved by cellulitis or abscess, based on clinical and radiographic examination. Severity score 1; low grade severity, includes the buccal, vestibular and subperiosteal spaces as they do not compromise vital structures or air way. Severity score 2; moderate grade severity, includes the masticatory spaces which can be further subclassified to submasseteric, pterygomandibular and superficial and deep temporal spaces, and perimandibular spaces which can be further subclassified to submandibular, submental and sublingual spaces, those account to a moderate severity due to their access to airway and trismus potential. Severity score 3; high grade severity includes spaces in which swelling can directly obstruct or deviate the airway or endanger vital structures, this group includes lateral and retro pharyngeal spaces, pretracheal space, danger space, and mediastinum space, and intracranial infection. Another scoring system (19) has been developed that can predict the morbidity of the infection by the use of different predictor variables, including; S (space of infection), P (symptoms on presentation), L (leukocytosis), D (existing immunocompromised disease). The authors believe that this severity score system will empower a more appropriate and aggressive initial treatment for odontogenic infections, hence decreasing the morbidity rate.

Criteria for admission

The decision regarding whether to treat odontogenic infections in an ambulatory, out-patient setting, or inpatient environment is multifactorial and depends on well-recognized criteria, although educated and experienced surgical judgment remains a

flexible influence. The criteria for admission with one or more deep space infections include:

1. Airway obstruction or an impending threat to airway patency based on clinical examination, including dyspnea, dysphagia, tongue displacement, uvular deviation, and severe trismus (CT scan confirmation of a narrowed airway is obligatory for planning therapy, including anesthesia. Inability to swallow oral antibiotics may tilt the judgmental balance toward admission.)
2. Severe dehydration or electrolyte imbalance
3. Comorbid medical issues (i.e., loss of glycemic control)
4. Body temperature <36.0°C and/or >38.0°C
5. Elevated white cell count >12,000/cumm,
6. CRP levels greater than 10 mg/l
7. Necrotizing fasciitis
8. Descending mediastinitis or ascending orbital-cerebral infection
9. Altered or obtruded state of consciousness
10. Social or psychiatric issues (e.g., homelessness, psychosis) or the potential for noncompliance with outpatient therapy.

In general, admission criteria were swelling of the face or neck area suggesting an abscess or a cellulitis and one or more of the following: temperature above 38.3˚C, white blood cell (WBC) count greater than 10.8 × 103/L, CRP levels greater than 10 mg/l, airway compromise, trismus, lower eye-lid involvement and dysphagia. Antecubital venous blood was drawn on admission and on the day of release. Body temperature was measured orally at least twice daily, mean values and standard deviations of the laboratory values were calculated. In one study of 100 consecutive patients with odontogenic infections, Ylijoki et al (20) found that fever and a high level of CRP was a good indicator for the need for intensive care unit treatment and thus for the course of the infection. Flynn and coworkers (17) showed that fever,

swelling, dysphagia and trismus were the symptoms most observed in patients hospitalized for odontogenic infection. It has also been demonstrated that elevated white blood cell count and elevated C reactive protein (CRP) are key findings in the decision to admit patients with odontogenic infection. The combined presence of these symptoms and inflammatory markers is a classical criterion indicating the need for admission to ensure clinical surveillance and treatment.

Airway management

Airway compromise is the most immediate and life-threatening of the complications encountered in management of deep neck infections. Proper management of the airway can be a lifesaving measure in certain patients and should be of primary focus. There are three options for airway management: close clinical observation, endotracheal intubation (fiberoptic or direct), or surgical airway. There are different advantages and disadvantages to each. Observation of the airway is adequate if initial evaluation reveals no impending airway compromise but does require close evaluation. The main complications of observation without mechanical intervention are unrecognized impending airway loss, risk of over sedation with loss of airway, or extension of infection and edema leading to asphyxiation. The benefit is that there is no mechanical intervention, which carries inherent risk. The advantages of endotracheal intubation include the speed with which airway control can be achieved, and that it is a nonsurgical procedure. Disadvantages include the potential for failed intubation, inability to bypass upper airway obstruction, requirement for mechanical ventilation, and subglottic stenosis, and endotracheal tube displacement/unintentional extubation. Tracheotomy, on the other hand, allows for the bypass of upper airway obstruction. It is a very secure airway, there is less need for sedation and mechanical ventilation, and it allows for earlier transfer out of critical care units (21). Tracheotomy is a surgical procedure with inherent risks such as pneumothorax, bleeding, subglottic stenosis, or tracheoesophageal fistula, as well

as unsightly scar. Training with airway management procedures, as well as available hospital resources such as anesthesiology, fiberoptic equipment, and critical care resources, also have an impact. The decision to observe the airway, perform intubation, or tracheotomy must be made on an individual basis, considering the advantages and disadvantages of each (21). Airway security alone is not sufficient because most deep fascial space infections of the head and neck, especially odontogenic ones, are caused by inherently abscess-forming bacteria. Surgical drainage of deep fascial spaces involved by abscess or cellulitis prevents further spread of the infection into deeper anatomic spaces and hastens resolution.

Surgical management

Treatment of odontogenic infections involves early recognition and correct diagnosis, prompt initiation of antibiotic therapy, removal of potential source of infection with or without surgical intervention. The aim of operative treatment performed in the management of acute apical abscess is to relieve pressure by establishing drainage. This is usually done by extraction of the affected tooth or by gaining access to the pulp chamber. In case of limited drainage through the apical foramen, the tooth should be extracted as soon as possible. Extraction provides complete removal of the cause of the infection and drainage of the accumulated periapical pus and debris. Controversy exists as to whether exodontia should be performed in the presence of acute infection (22). However, a literature review has confirmed that immediate extraction results in faster resolution, decreased pain, and earlier return of function and oral intake, whilst the risk of seeding the infection into deeper tissues is low (23). If an abscess is present, it should be incised to establish drainage. As a rule, “never let the sun go down on undrained pus” (24). Incision of the abscess allows removal of the accumulated pus and bacteria from the underlying tissue. Evacuation of the abscess cavity dramatically decreases the load of bacteria and necrotic debris. Evacuation also reduces the hydrostatic pressure in the region

by decompressing tissues, which improves the local blood supply and increases the delivery of host defenses and antibiotics to the infected area. Further, incision and drainage serve to prevent the spread of the infection into deeper anatomic spaces.

Incision and drainage

Whenever an abscess is diagnosed, it must be drained. For intraoral vestibular abscess, the technique of incision and drainage (fig.5) is simple and usually conducted under regional anaesthesia in an out-patient setting. The preferred site for intraoral incision is directly over the site of maximum swelling and inflammation. However, it is important to avoid incising across a frenum or the path of the mental nerve in the lower premolar region. The surface mucosa is disinfected with povidone-iodine (Betadine) and dried with sterile gauze. Obtaining a pus specimen for culture and sensitivity testing must be considered. A large gauge needle, usually 18 gauge, fitted on small plastic syringe is used for specimen collection, fig. (6). The specimen is then inoculated directly into aerobic and anaerobic culturettes. Aerobic bacterial infections is most often associated with acute cellulitis. Anaerobic bacteria is often isolated from sites with chronic abscess formation (25). Once the culture specimen is obtained, stab incision is made through the mucosa and submucosa into the abscess cavity. A closed curved hemostat is then inserted through the incision deep into the cavity. The hemostat is opened in several directions to break up any small cavities of pus that have not been opened by the initial incision. Pus is aspirated and a small drain is inserted to maintain the opening. The most commonly used drain for intraoral abscesses is a quarter inch sterile Penrose drain, fig. (7). The drain is then sutured to one edge of the incision with a non-resorbable suture, fig. (8), and kept in place until all the drainage has stopped, usually for 2 to 5 days.

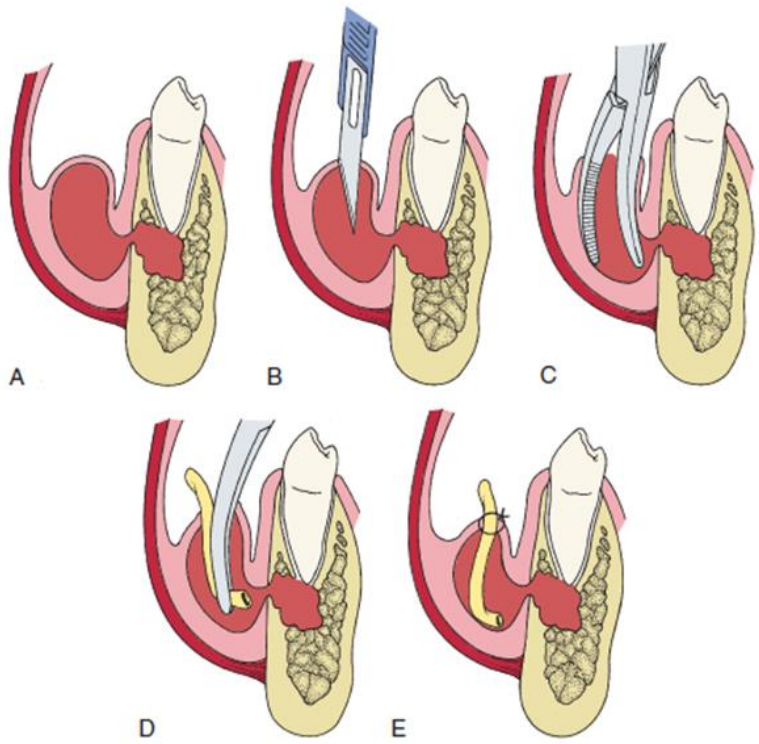

Fig. (5): A, vestibular abscess. B, stab incision. C, evacuation. D, drain insertion. E, drain stabilization.

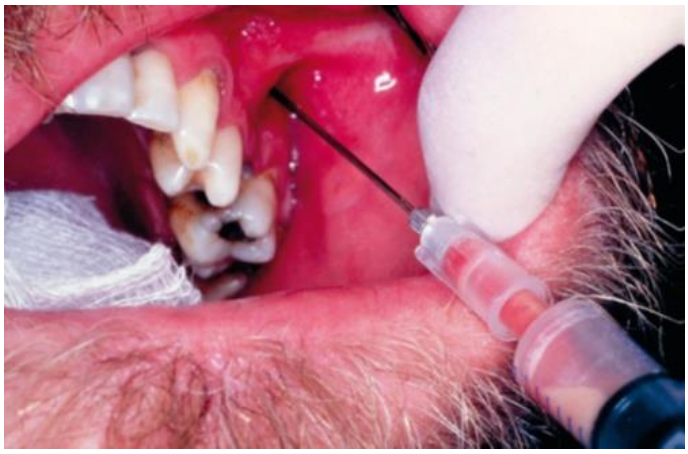

Fig. (6): Collecting pus specimen for bacteriologic studies.

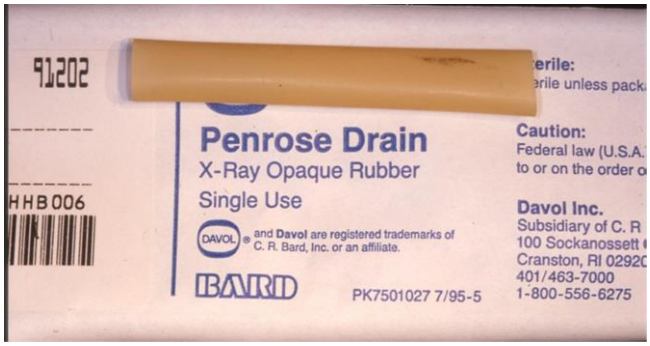

Fig. (7): Penrose drain.

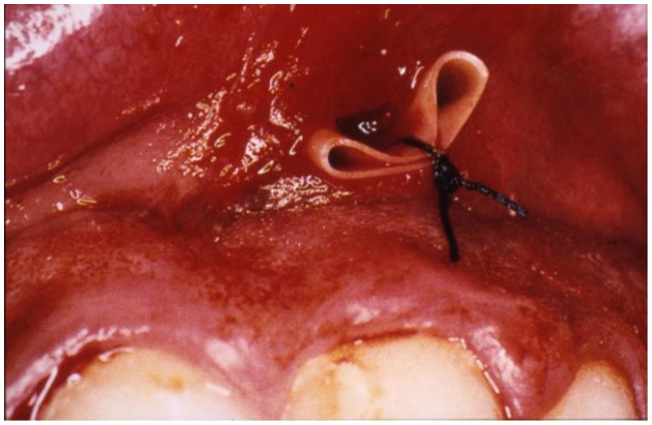

Fig. (8): Drain sutured to one edge of the incision line.

For severe odontogenic infections involving fascial plans, a debate exists as to whether immediate surgical drainage is indicated or if surgical drainage should be reserved only until a discrete abscess is formed (26,27). Some clinicians believe that incision and drainage of a cellulitis can disrupt the physiologic barriers and cause diffusion and extension of the infection. Deep infections that can be accurately identified in the cellulitis stage in a clinically stable patient can be successfully treated with intravenous antibiotics alone. The experience of others has shown that establishing drainage for a cellulitis serves to abort the spread of infection. Incision and drainage rid the body of toxic purulent material and decompress the tissues,

allowing better perfusion of blood containing antibiotics and defensive elements and increased oxygenation of the infected area. Ideally, abscesses should be drained when fluctuant before spontaneous rupture and drainage. Incision and drainage are best performed at the earliest sign of fluctuation, although surgical drainage also can be effective early before the development of classic fluctuance. In a prospective study of 37 patients hospitalized for severe odontogenic infection, approximately 25% of the cases had drainage in the cellulitis stage. In none of their cases did incision and drainage seem to hasten the spread of infection. (18).

The initial step in the treatment of odontogenic infections is to assure that a stable airway is established. A topical cleansing agent should then be applied, and aspiration of abscess should be completed using a syringe connected to a needle in a sterile fashion (fig.9). Aspirate should be sent for microbiologic culture examination. Prior to incision, local anesthetic infiltration can be administered. Depending on the involved fascial space, various skin incisions have been described (fig.10).

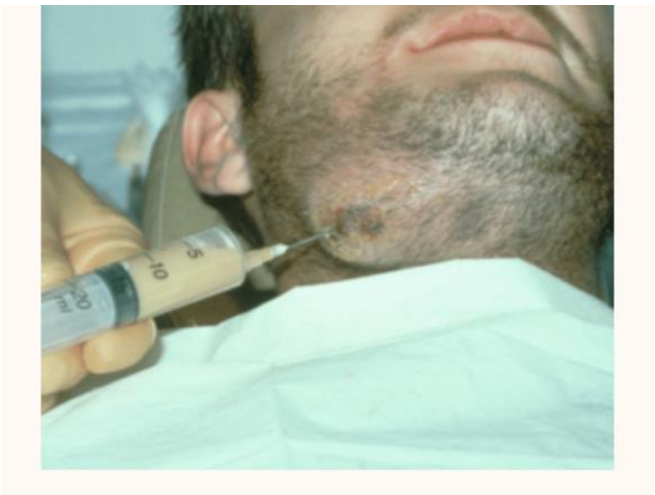

Fig. (9): Aspiration of pus from a submandibular abscess.

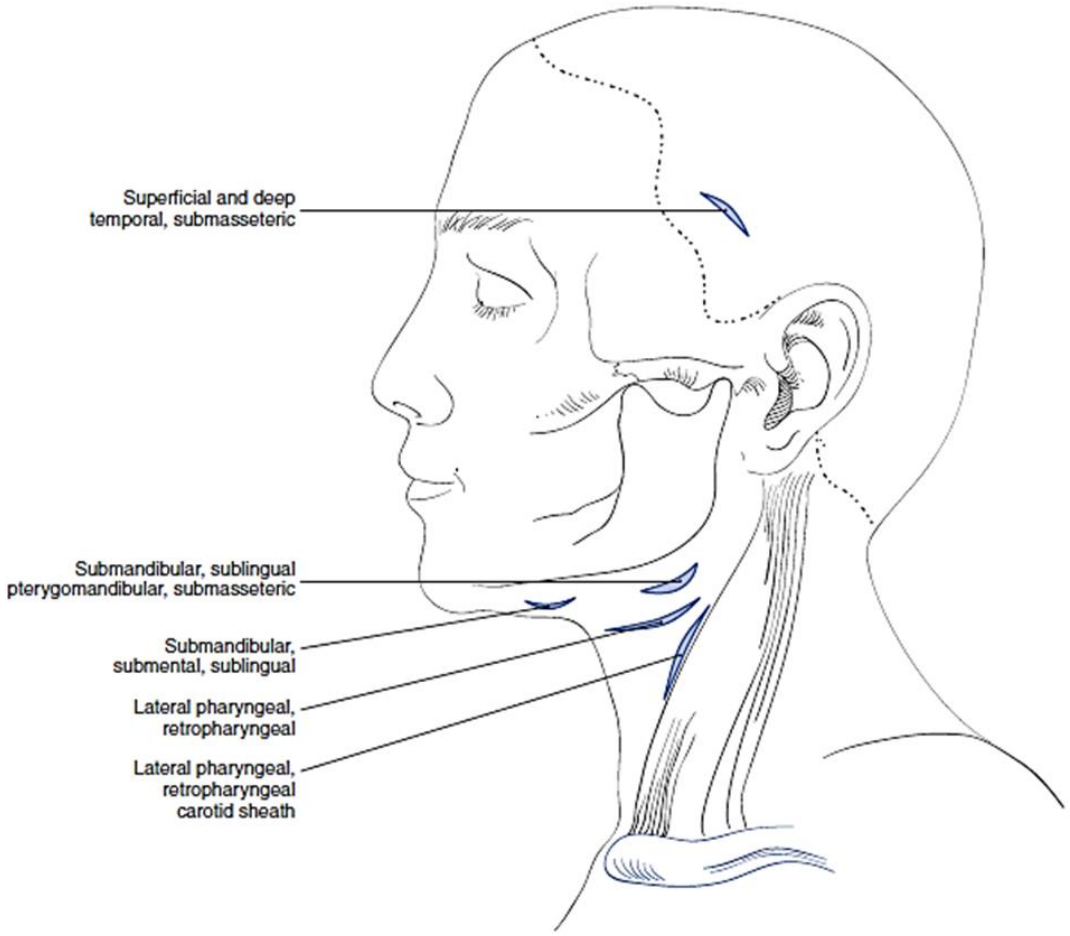

Fig. (10): Various skin incision lines for extraoral drainage of head and neck infections.

Blunt dissection is usually carried out utilizing a hemostat without direct exposure and visualization of the entire infected anatomic space. It is crucial to insert the instrument closed, then open it at the depth of penetration, and then withdraw the instrument in the open position. A hemostat should never be blindly closed while it is inside a surgical wound. Another important principle of surgical incision and drainage is the need to dissect a pathway for the drain that includes the locations where pus is most likely to be found. This can be guided by the preoperative CT examination and by knowledge of the pathways that odontogenic infection is most likely to take. For example, in drainage of the submandibular space, a skin incision

is made within 2 finger-width, and parallel to the inferior border of the mandible (fig. 11). The patients are usually intubated using a fiber-optic bronchoscope. Under general anaesthesia, blunt dissection is used to explore the involved space. The tip of the hemostat is advanced to hit bone at the inferior border of the mandible. It is then directed medially and somewhat anteriorly until the lingual plate of the mandible is contacted. The most likely pathway for odontogenic infections to enter the submandibular space is through the thin lingual plate of the mandible. Following drainage (fig.12), the cavity was irrigated with 0.9% saline, and suction catheters were placed in the cavity in a gravity-dependent position and fixed to the skin adjacent to the incision. Sometimes, where infection involves the submandibular, submental, and sublingual spaces, two incisions are placed over the anterior and posterior bellies of the digastric muscle (fig.10). Blunt dissection then passes superiorly and medially to evacuate the involved spaces. A large curved hemostat is directed from one incision upward to the medial side of the mandible and then down to the other incision. A Penrose drain can then be grasped in the tip of the hemostat and pulled through the dissected pathway from one incision to the other, in the so-called through-and-through drainage (fig.13). Drains should be discontinued when the drainage ceases.

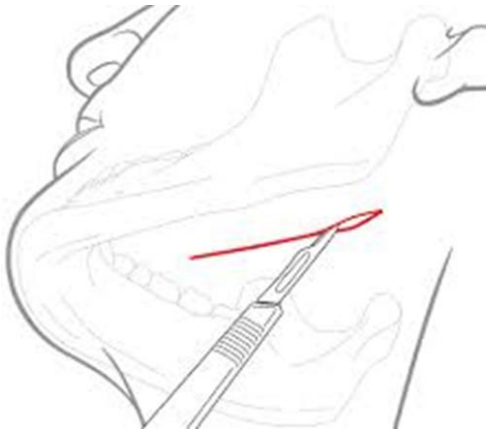

Fig. (11): Incision line for drainage of submandibular space.

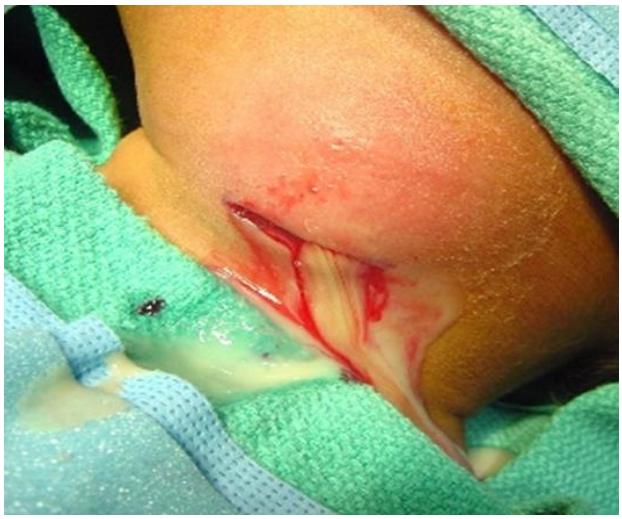

Fig. (12): Pus drained at the incision site.

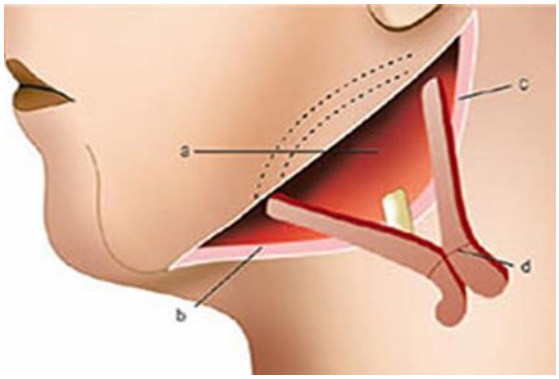

Fig. (13): Through-and-through drainage.

The following principles (28) should be used when possible with incision and drainage:

1. Incise in healthy skin and mucosa when possible. An incision placed at the site of maximum fluctuance where the tissues are necrotic or beginning to perforate can result in unaesthetic scar.

2. Place the incision in an esthetically acceptable area, such as under the shadow of the jaw or in a natural skin fold or crease.

3. When possible, place the incision in a dependent position to encourage drainage by gravity.

4. Dissect bluntly, with a closed surgical clamp or finger, through deeper tissues and explore all portions of the abscess cavity thoroughly so that compartmentalized areas of pus are disrupted and excavated.

5. Place a drain and stabilize it with sutures.

6. Consider the use of through-and-through drains in bilateral, submandibular space infections.

7. Do not leave drains in place for an overly extended period; remove them when drainage becomes minimal. The presence of the drain itself can produce some exudate and can be a portal for secondary bacterial invaders (29).

8. Clean wound margins daily under sterile conditions to remove clots and debris.

For better cosmetic outcome, intraoral approach was suggested. In a randomized clinical trial, 40 patients with submandibular abscess were subjected to surgical drainage under general anaesthesia. Subjects were randomly divided in 2 groups of the classic external approach with skin incision in the submandibular area and the intraoral approach for abscess drainage. This study reveals that submandibular abscess in selected cases can be successfully treated with an intraoral drainage approach, which is a better choice than the external technique in terms of better cosmetic outcome. Postoperative care in these patients is much easier because there is no need for daily irrigation and dressing of the wound (30).

To avoid the risk and costs of general anaesthesia, French, et al (31) presented a case series in which extra-oral drainage of the submandibular space was carried out under local anaesthetic. Despite trismus, mandibular nerve block was performed according to the closed mouth technique of Akinosi.

Another alternative is the minimally invasive technique (32). The main principle has been to drainage of well-localized abscesses with the use of a computed tomographic

(CT)-guided catheter. CT-guided catheterization allows precise location of the lesion without extensive dissection and subsequent scarring.

Important to note that:

1. Antibiotic availability in pus-filled spaces is limited by poor vascularity.
2. Treatment of a fascial space infection depends on open incision and dependent drainage. Large surgical incisions may be necessary to obtain adequate exposure of deep compartments.
3. Fascial spaces are contiguous, and infection can spread readily from one space to another. Multiple incisions may be necessary because frequently more than one space is involved in the infection. So, it is important to open all primary and secondary spaces; once opened, spaces need to have drains and possibly irrigation catheters placed.
4. Involved teeth should be extracted, ideally at the time of incision and drainage to ensure resolution of the infection; once a fascial space infection has occurred, it is prudent to extract the involved teeth rather than rely on endodontic treatment.

Medical therapy

For localized abscesses medical therapy consists mainly of supportive care: hydration, soft diet, analgesics, and good oral hygiene. Supportive therapy in the form of parenteral fluid, high-protein diet and multivitamin was given as indicated in the individual cases. Severe odontogenic infections that occur in patients with immune system compromise should be managed by a specialist. Often, hospitalization and medical consultation are required.

Pain control

Simple analgesics, such as paracetamol and non-steroidal anti-inflammatory drugs, should be used initially provided there are no contraindications for their use. The dose for paracetamol is 1 g every 4 h. Ibuprofen also has anti-inflammatory effects

and starting dose is 400 mg every 8 h (33). Patients, with previous history of peptic ulcers and/or upper gastrointestinal bleeding, concomitant anticoagulant therapy, asthma, or unstable cardiovascular disease should be given paracetamol instead. Opiates may be indicated for severe pain, but should be used cautiously, particularly where respiratory depression is suspected.

Corticosteroids

The rationale of employing exogenous corticosteroids is to augment the body's natural defense response to combat infection in conjunction with antibiotic administration. Corticosteroids such as methylprednisolone and dexamethasone are used routinely when airway compromise suspected (2).

Thromboprophylaxis

Deep vein thrombosis is a complication in patients undergoing surgery. All patients should be mobilized where appropriate and adequately hydrated as these are primary measures for prevention of venous thromboembolism. Mechanical prophylaxis with graduated compression stockings should be considered for all patients. Patients with additional risk factors such as immobility, thrombophilia, estrogen therapy, pregnancy, active inflammation, obesity, and strong family history of venous thromboembolism should also receive anticoagulant therapy with low molecular weight heparin such as enoxaparin at 40 mg daily.

Fluid and nutrition

A proportion of patients may have reduced oral intake over days because of pain, swelling and trismus. The presence of fever further increases fluid and caloric requirements. These patients are therefore vulnerable to malnourishment and dehydration. Maintenance fluids should be administrated intravenously.

Postoperatively, patients should be encouraged to eat, and drink as tolerated. The patients should have their vital sings checked hourly with their temperature recorded every 4 h. There should be improvement in swelling, drainage, malaise, and pain 48

h postoperatively. Patients should also be monitored for possible complications of surgery. If no clinical improvement is seen at 48 h post-surgery, reasons for treatment failure should be explored. The likely causes are inadequate surgical treatment, foreign body, impaired host defenses, poor choice of antibiotics and poor compliance.

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Chapter 4: Antibiotic therapy of odontogenic infections

Antibiotic therapy of odontogenic infections

Since their introduction in the 1930s and 1940s, antibiotics have saved countless lives and their availability has contributed to major advances in health. Antibiotics are antimicrobials used for the treatment and prevention of infections. They are classified as either bactericidal or bacteriostatic. Bactericidal antibiotics kill bacteria by inhibiting cell wall synthesis and bacteriostatic antibiotics inhibit bacterial growth and reproductions. Table (1) lists common antibiotics and their classification.

Table (1): Bactericidal and bacteriostatic antibiotics.

Bactericidal	Bacteriostatic
Beta-lactams Penicillins Cephalosporins Carbapenems Monobactams Aminoglycosides Vancomycin Metronidazole Fluoroquinolones	Macrolides Erythromycin Clarithromycin Azithromycin Clindamycin Tetracyclines Metronidazole Sulfa antibiotics

Antibiotics are used for therapeutic and prophylactic reasons. A common misconception is that all infections, by definition, require antibiotic administration. This is not necessarily the case. In some situations, antibiotics are not useful and may even be contraindicated. Therapeutic antibiotics are advised to treat infections in the oral cavity after local debridement has failed, whereas prophylactic antibiotics are given to prevent diseases caused by oral flora, introduced to distant sites, which puts the host at risk. Antibiotics are advised depending upon the severity of the infection, especially in cases of diffuse cellulites with moderate-to-severe pain and

are also advised in medically compromised individuals. The clinical indications for antibiotic therapy include fever, lymphadenopathy, and indurated or fluctuant swelling. A draining abscess or a fistula containing a chronic infection usually requires only root canal treatment or extraction. However, other disease processes, including periodontal abscesses, pericoronitis, acute periapical abscesses and deep fascial space infections may require antimicrobial therapy. Antimicrobials must never be used as a replacement for appropriate surgical drainage and/or debridement and should only be used as adjunctive therapy (1,2). In general, antibiotics should be used only for the management of active infection or to prevent the potential spread of infection. Further, not all odontogenic infections require antimicrobial treatment. In some cases, the best course of treatment is debridement, irrigation, and drainage. If antimicrobial therapy is advised soon after diagnosis and before surgery, it can shorten the period of infection and minimize associated risks (3).

Choice of Antibiotics

The ideal antibiotic would have a spectrum of coverage specific to the pathogens causing a given clinical manifestation, no toxicity to the host, no liability to bacterial resistance, and low cost. Clearly the currently available antibiotics fail to meet these goals.

The choice of antimicrobial therapy for patients with an odontogenic infection can be complex owing to numerous variables that must be considered. Factors involved in antibiotic selection include host-specific factors and pharmacologic factors. Host factors include the microbiology of odontogenic infections, history of allergic responses or intolerance, previous antibiotic therapy, age, pregnancy status, and immune system status (4). Traditional pathogens found to be in association with orofacial infections are mixed in origin and consist of facultative (can grow with or without oxygen) and obligate anaerobic bacteria. The duration of the infectious process aids in predicting which organisms predominate. Acute infections presented

as cellulitis may be characterized as predominantly aerobic streptococcal infections. As the infection progresses over time and gets deeper, the nature of the bacteria can change. Commonly, chronic abscesses may be characterized as anaerobic infections. Allergy to antibiotics is collected during acquisition of medical history as well as information regarding antibiotic intolerance. Previous antibiotic therapy, especially on a consistent basis, yields a propensity for resistant organisms to an antibiotic. Certain antibiotics should be avoided in children as well as pregnant patients. The immune competence of a patient may direct antibiotic therapy toward bactericidal, rather than bacteriostatic agents. Pharmacologic factors of interest include spectrum of antibiotics, pharmacokinetics, tissue distribution of antimicrobials, cost of antibiotics, adverse reactions, and potential drug interactions (4). The antibiotic spectrum is of important consideration, because it is best for the patient to receive therapy to be geared toward antibiotics that are effective against the involved microorganisms. Antibiotics that have narrow-spectrum activity against causative organisms are just as effective as antibiotics that have broad spectrum activity, but without upsetting normal host microflora populations and increasing the chances of bacterial resistance. The essence of the American Dental Association policy is that broad-spectrum antibiotics should be used for complex infections, and narrow spectrum antibiotics should be used for simple infections (5). Examples of commonly used narrow and broad-spectrum antibiotics are listed in table (2).

Table (2): Commonly used narrow and broad-spectrum antibiotics.

Narrow spectrum antibiotics	Broad spectrum antibiotics
Penicillin V Metronidazole Clindamycin	Amoxicillin Amoxicillin/clavulanate Cephalexin Azithromycin Doxycycline

The selection of antibiotics in clinical practice is either empirical or based on the results of microbial susceptibility testing. Ideally the choice of antibiotic therapy of odontogenic infection should be based on definitive laboratory results of culture and sensitivity testing. For diseases with known microbial causes for which the probable microbiota has been established, empirical therapy may be used. This is especially applicable to acute dental abscesses because culture-dependent antimicrobial tests of anaerobic bacteria can take too long to provide results about antibiotic susceptibility (around 7 to 14 days). Odontogenic infections are caused by a highly predictable group of bacteria. The bacteria that cause odontogenic infections are overwhelmingly facultative oral streptococci; anaerobic streptococci, including Peptostreptococci, Prevotella and Fusobacterium species. Other species of bacteria may also be cultured from these infections, but they appear to be opportunistic rather than causative. Fortunately, the antibiotic susceptibility of causative bacteria is predictable. So, the first choice of antibiotic is made empirically. However, if evolution is unfavorable, the antibiotic chosen can be substituted by another one or more than one after identifying the causal microorganisms by means of culture and antibiogram typing. Several antibiotics are indicated for odontogenic infections:

Penicillins

Penicillin remains the antibiotic of choice in the outpatient setting for the management of odontogenic infections when there is no history of allergy (6,7), especially in infections of less than 3 days' duration. Early infections appearing initially as a cellulitis may be characterized as predominantly aerobic streptococcal infections, and late, chronic abscesses may be characterized as anaerobic infections. Amoxicillin, semi synthetic penicillin is the drug of choice in treating dental infections and is the most common antibiotic used by dentists. The American Heart Association considers amoxicillin to be the first choice for prophylaxis against the

Endocarditis and prosthetic joint replacement therapy associated with dental procedures (8). Due to their effectiveness against facultative aerobic and anaerobic pathogens, they are the antibiotics of choice in the treatment of infections of mixed etiology in the oral cavity (9). However, there are more and more betalactamase producing bacteria, enzymes that are capable of hydrolyzing penicillins and, therefore, leading to treatment failure particularly when strains of the Prevotella, Porphyromonas and Fusobacterium genera are present (10). Bacterial resistance to penicillin is mostly because of the production of betalactamase by the bacteria. Whereas alteration of the target protein, enzymatic inactivation of the drug, preventing drug access to targets also can lead to resistance. In penicillin resistant cases betalactamase-stable antibiotics should be prescribed to the patient.

Amoxicillin and ampicillin increase penicillin/s spectrum to cover enteric gram-negative bacilli. Given the increased prevalence of betalactamase producing microorganisms, the association of a penicillin with a betalactamase inhibitor such as amoxicillin/ clavulanic acid has become the treatment of choice in many of these conditions. A new pharmacokinetically enhanced formulation of amoxicillin/ clavulanate has been developed (amoxicillin/ clavulanate, 1000/62.5 mg) that, in addition to lowering the number of daily doses to two, also eradicates strains considered to be resistant to conventional formulations (11). Moreover, this new formulation, when administered along with high doses of amoxicillin, can delay, or decrease the risk of increasing the prevalence rate of oral streptococci resistance. In long standing infections, gram negative anaerobic organisms may be suspected, therefore metronidazole may be added with amoxicillin. Metronidazole's excellent anaerobic gram-negative activity and its low degree of toxicity, make it an excellent drug in the treatment of odontogenic infections (12). Amoxicillin/ clavulanate, metronidazole and clindamycin are active against most of the microorganisms that are responsible for odontogenic infections. Other alternatives, such as

clarithromycin and azithromycin, complete the therapeutic arsenal. Ellison (13) has reviewed the rational use of penicillin, clindamycin, and metronidazole in dentistry. This study concludes that these 3 antibiotics could be effective, when combined with the appropriate surgical intervention, when signs of systemic involvement are present, such as fever, tachycardia, swelling, lymphadenopathy, or trismus. Ellison states that surgical treatment alone is effective when systemic signs are absent.

Cephalosporins

Cephalosporins are bactericidal drugs that are classified in generations, based on their antibacterial spectra, regardless of when they were synthesized. First generation of cephalosporins inhibit mainly Gram-positive bacteria, second and third generations have greater bactericidal activity against Gram-negative bacteria while fourth generation cephalosporins are broad spectrum antibiotics with bactericidal activity against both Gram-negative and Gram-positive bacteria (14). Individual cephalosporins differ in their: (a) Antibacterial spectrum and relative potency against specific organisms, and (b) Susceptibility to β-lactamases elaborated by different organisms. Though the incidence is low, resistance has been developed by some organisms, even against the third-generation compounds.

Tetracyclines

Tetracycline because of its side effects and widespread resistance is not commonly used to treat odontogenic infections. Newer drugs like doxycycline and minocycline possess better anaerobic activity than tetracycline, but they should not be considered first-line therapy for odontogenic infections. Because of their high affinity for bone and dental tissue, the use of tetracycline is not recommended during pregnancy, or in children less than eight years of age, since when deposited on teeth and bones during development they can produce alterations such as dental hypoplasia, bone deformities and abnormal tooth color (15).

Nitroimidazoles

Metronidazole, ornidazole and tinidazole are antibiotics with excellent activity against anaerobic gram-negative bacilli and spirochete, but hardly act, if they act at all, against anaerobic cocci and facultative, aerobic bacteria of the oral cavity. They should be administered in combination with other antibiotics in mixed infections of the oral cavity that involve oral aerobic or facultative streptococci. In one study the combination of metronidazole and penicillin have been highly effective against all strains of all species, consistent with oral infections (16).

Lincosamides

Clindamycin has excellent broad spectrum of action. Its efficacy in treating odontogenic infections is comparable to Penicillins. Clindamycin continues to be the treatment of choice in patients who are allergic to penicillin in most odontogenic infections. The American Heart Association recommends clindamycin, rather than erythromycin, to penicillin-allergic patients requiring endocarditis prophylaxis (12). It presents a good level of activity against anaerobic bacteria, although more and more resistant strains are emerging.

Macrolides

Commonly used macrolide antibiotics include erythromycin, clarithromycin, roxithromycin and azithromycin. They are mainly bacteriostatic but in high concentrations they can also be bactericidal. Macrolides are active against many Gram-positive bacteria but not Enterococcus spp. However, resistance to erythromycin and azithromycin has been reported to be high in odontogenic infections (12). The newer macrolides have improved pharmacokinetics compared to erythromycin, but they are not considered as first-line therapy in treating odontogenic infections.

In general, antibiotic efficacy is multifactorial and success depends on different parameters being met, such as dosing schedule, time, etc. The usual adult dose and time intervals of common oral antibiotics are presented in table (3), while that of intravenous antibiotics are given in table (4).

Table (3): Usual adult dose and intervals of common oral antibiotics.

Antibiotic	Usual dose (mg)	Usual interval (h)
Penicillins		
Amoxicillin	500	8
Penicillin V	500	6
Augmentin	875	12
Cephalosporins		
Cephalexin	500	6
Erythomycins		
Erythromycin	500	6
Azithromycin	250	12
Antiaerobic		
Clindamycin	150	6
Clindamycin	300	6
Metronidazole	500	6
Other		
Vancomycin	125	6
Ciprofloxacin	500	12
Moxifloxacin	400	24

Table (4): Usual adult dose and intervals of common intravenous antibiotics.

Antibiotics	Usual dose	Usual interval (h)
Penicillins		
Penicillin G	2 m.u.	4 hr.
Ampicillin	1 g.	6 hr.
Unasyn	3 g.	6 hr.
Oxacillin	2 g.	6 hr.
Cephalosporins(Generation)		
Cefazolin (1st)	1 g.	8 hr.
Cefotetan (2nd)	1 g.	12 hr.
Ceftriaxone (3rd)	1 g.	24 hr.
Cefepime (4th)	2 g.	12 hr.
Monobactam		
Aztreonam	1 g.	8 hr.
Penicillin-Allergy		
Erythromycin	1 g.	6 hr.
Azithromycin	0.5 g.	24 hr.
Vancomycin	0.5 g.	6 hr.
Antianaerobic		
Clindamycin	0.9 g.	8 hr.
Metronidazole	0.5 g.	6 hr.
Other		
Doxycycline	0.1 g.	12 hr.
Levofloxacin	750 mg.	24 hr.
Moxifloxacin	400 mg.	24 hr.

Treatment duration of antibiotics

Treatment duration with antibiotics depends on the type of infection, the extension of the condition and on the antibiotic chosen. A common antibiotic course for orofacial infection is 7 to 10 days. Flynn (17), compared duration of antibiotic therapy for odontogenic infections. He concluded that, within the limitations of the data available, there were no significant differences in clinical cure between shorter (3-4 day) and longer (7 day) courses of antibiotics when used in combination with appropriately administered surgical treatment. He hypothesized that antibiotic

therapy for 4 days or less combined with appropriate surgical treatment, results in equal or better clinical outcomes, as measured by time to resolution, morbidity, and expense. Chardin and colleagues (18) found no difference in clinical cure rate of antibiotic therapy after surgical intervention with amoxicillin 1 g for 3 days versus the same therapy for 7 days. Lewis and colleagues (19) found similar results when comparing surgical intervention followed by 3 g of amoxicillin for 2 doses 8 hours apart, with penicillin V 250 mg by mouth 4 times per day for 5 days. These studies support the emphasis on prompt and efficient surgical intervention in combination with antibiotic therapy. Moreover, regardless of the empirical antibiotic choice, surgical intervention that removes the source of the infection is considered the primary treatment modality.

Antibiotic resistance

A problem that has emerged regarding the effectiveness of selected antibiotic therapy for the management of odontogenic infections is antibiotic resistance. The increased prevalence of bacterial resistance means that antibiotics that have been useful in the past are currently no longer as effective as they once were, as is the case with certain dose levels. In this regard, in the last 10-15 years the number of resistant microorganisms in the oral cavity has doubled (20). Antibiotic resistance occurs by 4 mechanisms: alteration of a drug's target site, inability of a drug to reach its target, inactivation of an antimicrobial agent, or active elimination of an antibiotic from the cell (17). Antibiotics may be inactivated by bacterial enzymes or the enzymes can result in neutralization. Penicillinase and betalactamases are examples of this mechanism. Genes present in some bacteria produce proteins that prevent antibiotic uptake, leading to antibiotic resistance as well. Spontaneous mutation is considered the dominate source antibiotic resistance. Gene transfer occurs with transmissible DNA segments transfer and inserts genetic material after bacterial conjugation. Mosaic genomes are formed by bacteria incorporating fragmented DNA directly

from dead members of related species. Collectively these mechanisms allow the spread of genetic material from one bacterial species to another and can result in the resistant strain becoming the predominate strain for the species (17).

Complications of antibiotic therapy and drug interactions

Antibiotic drugs have the potential to alter the effectiveness, as well as to interfere with the metabolism of other drugs. The cytochrome p450 system is a complex set of drug-metabolizing enzymes in the liver and gastrointestinal system that breaks down many different drugs. When antibiotics that use this metabolic pathway inhibit cytochromes that are needed for metabolism of other drugs altering, the bioavailability of one of the involved drugs. Some of these interactions can lead to some severe adverse effects. Erythromycin and other macrolides, for example, have been found to have drug interactions with numerous drugs including statins, theophylline, warfarin, carbamazepine, triazolam/ midazolam, and antiarrhythmics. Side effects of these interactions range from bleeding issues, increased sedation, confusion, and seizures to cardiac dysrhythmias and death. Metronidazole has the potential for increased bleeding with co-administration of warfarin owing a decrease in the metabolism anticoagulants. Clindamycin may destroy gut flora and prevent absorption of vitamin K, which can cause an increase in anticoagulation. Metronidazole can also affect the renal clearance of lithium. Fluoroquinolones have been found to interfere with theophylline metabolism and to cause seizures. These drugs have also been found to cause spontaneous tendon rupture. Fluoroquinolones should be avoided in children owing to chondrotoxicity in growing cartilage (21).

Antibiotic allergy information should be obtained while recording a patient's medical history. It is important to inquire about the nature of an allergy to access whether a true anaphylactoid allergy exist. Penicillin is a common antibiotic for which patient's report an allergy. 1% to 10% of patients develop an allergic response to penicillin during an initial course and a less than 1% chance of development of an

allergic reaction exists with additional courses (22). There is a possibility for cross-allergy to cephalosporins. Recent literature shows that cross reactivity between penicillins and most second- and all third- and fourth generation cephalosporins is negligible. The cross reactivity between penicillins and cephalosporins in individuals who report a penicillin allergy is approximately 1% and, in those with a confirmed penicillin allergy 2.55%, therefore if a patient is having an allergic response to penicillin, it is safe to administer a cephalosporin with a side chain that is structurally dissimilar to that of the penicillin or to administer a third- or fourth-generation cephalosporin (23).

Antibiotic-associated colitis is another possible adverse effect of antimicrobial therapy. Antibiotic-associated colitis has been found to occur with clindamycin, beta-lactam/beta-lactamase inhibitor combinations, cephalosporins and other antibiotic therapy. Except for potentially fatal allergic reactions, the penicillins are not toxic drugs; whereas the new fourth generation fluoroquinolones, such as Moxifloxacin, while providing an excellent spectrum of coverage for head and neck infections, have the liability of many drug interactions involving the cytochrome P450 liver microsomal enzyme system, which can result in fatal cardiac dysrhythmias (21).

A patient who is taking oral contraceptive pills should be informed of the necessity to use other forms of birth control. Antibiotic therapy may kill enough the gut flora that inhibits recirculation of estrogen, which reduces the serum levels of estrogen and may allow for the patient to become pregnant. This has been found to only involve oral contraceptives, not the implantable nor injectable forms (24).

Cost of antibiotics: Considering the cost of antibiotics, amoxicillin is one of the least expensive oral formulations of antibiotics.

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Chapter 5: Life-threatening complications

Ludwig's angina

Ludwig's angina is described as a potentially lethal, rapidly spreading cellulitis, involving the sublingual, submandibular spaces, manifested by a brawny suprahyoid induration, tender swelling in the floor of the mouth and elevation and posterior displacement of the tongue (1). The infection does not usually result in abscess formation but is phlegmonous and spreads diffusely over both sides of the floor of the mouth. Male patients, in the fourth decade of life, and from a lower socioeconomic background are commonly affected. Odontogenic infections account for most cases (2). Other potential causes include peritonsillar abscess, mandibular fracture, penetrating injury to the floor of the mouth, mandibular osteomyelitis, otitis media, tongue piercing, and sialolithiasis of the submandibular glands (3). Most infections are polymicrobial and include anaerobic and aerobic bacteria. The most cultured organisms include Streptococcus viridans and anaerobes like Fusobacterium nucleatum, Peptostreptococcus species, and Actinomyces species (4). Comorbidities that are associated with the development of Ludwig's angina are diabetes mellitus, hypertension, and immunocompromised status (5). Patients usually present with fever, pain, and swelling of the floor of the mouth. Other commonly presenting symptoms include dysphagia and odynophagia, sore throat, otalgia, respiratory distress, and change of voice (6). On inspection, the patient may have neck swelling, trismus, halitosis, sialorrhea, gingival swelling, or muffled voice (6). Another physical examination finding described in the literature is a "double tongue sign" that involves an elevation of the floor of the mouth caused by edema of the submandibular space (7). On palpation, there may be cervical adenopathy and a characteristic "woody" induration of the floor of the mouth (8). Imaging may be performed to assess for airway patency and the presence of an underlying dental

abscess. Most commonly, CT shows significant airway deviation or narrowing. Generally, there is diffuse edema within and between the affected submandibular, sublingual, or submental spaces (fig.1). The presence of an abscess involving any of these spaces may raise concern. Accompanying swelling and elevation of the tongue may also be present. Airway compromise is always synonymous with the term Ludwig's angina, and it is the leading cause of death. The reported mortality rates range from 0.3% to 11.8% (5,9). Mortality occurs most often due to hypoxia or asphyxia rather than overwhelming sepsis. Larawin et al (10), documented that the early stage of Ludwig's angina is when the airway is not compromised, while the late stage is when features of airway obstruction are present. The airways were assessed on presentation based on clinical examination and pulse oximetry. Patient was said to have respiratory compromise in the presence of anxiety, cyanosis, stridor, greater than 25 respiratory rate, less than 95% O2 saturation, inability to lie in the supine position, alar flaring, supraclavicular and intercostal indrawing during inspiration (10). Although no specific guidelines are present for managing acute Ludwig's angina, decisions regarding airway protection are largely dependent on the "Practice Guidelines for Management of the Difficult Airway" that were adopted by the American Society of Anesthesiologists in 1992 and updated in 2003 (11). In these guidelines, a difficult airway is defined as "the clinical situation in which a conventionally trained anesthesiologist experiences difficulty with face mask ventilation of the upper airway, difficulty with tracheal intubation, or both." When that is the case, patients are intubated via awake assisted fiberoptic bronchoscope. When this fails a surgical tracheostomy is performed under local anaesthesia. The guidelines specify that these recommendations may be adopted, modified, or rejected according to the clinical needs and their purpose is to assist the practitioner in decisions about health care (11).

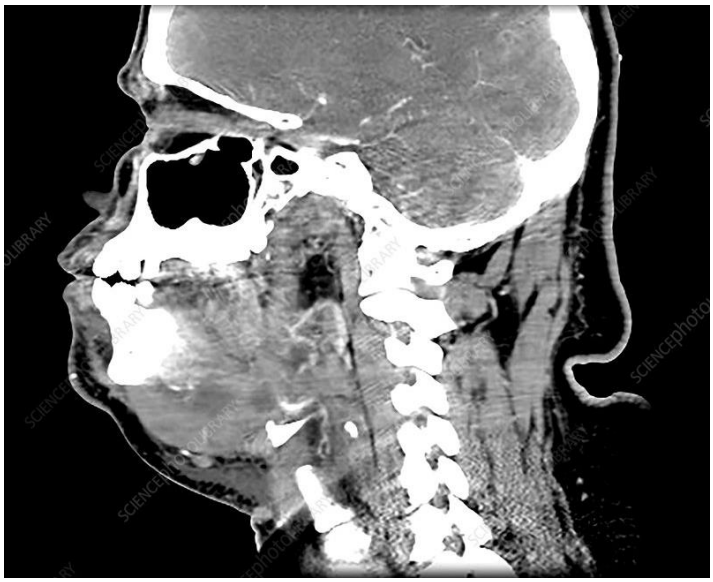

Fig. (1): Contrast-enhanced sagittal CT shows extensive inflammatory changes in the floor of mouth that extends to the epiglottis with mild narrowing of the airway. Small fluid pockets are seen. This represents Ludwig's angina which is a severe form of cellulitis/inflammation in the floor of the mouth.

Timely recognition and initiation of treatment are paramount because the infection can progress rapidly. Treatment includes secure and protect the airway, antibiotics, corticosteroids, and surgical debridement and drainage. Airway management is the most important aspect of immediate care and should not be delayed for a CT or for any other reason that may compromise the patient's health. Early antibiotic therapy is of critical importance for successful treatment. Commonly recommended initial regimens include penicillin G, metronidazole, and clindamycin. Because of the severity of this infection, most providers will often opt for broader coverage. However, in a retrospective review of 42 patients admitted for Ludwig's angina, the most common organisms were found to be susceptible to penicillin, and only 3 patients required a change of antibiotics (12). The addition of steroids has been suggested to allow for easier intubation and possibly avoiding a surgical airway. Steroids may also allow better penetration of antibiotics into the fascial space by

reducing edema. A course of dexamethasone 10 mg every eight hours for 48 hours has been suggested. A narrative review of 17 articles investigating the utility and safety of steroids concluded that even though the role of steroids in Ludwig's angina remains uncertain, there is no suggestion of adverse effects in the described cases, and steroids may be beneficial (13). Surgical drainage and debridement are reserved for the severe cases of Ludwig's angina or in cases in which there is no improvement with antibiotics and steroids. Surgical intervention involves decompressing the submental, sublingual, and submandibular spaces bilaterally, by external incision and drainage (14). Tube drains are placed and secured to the skin with silk sutures (fig.2). Surgical drainage facilitates decompression of the spaces involved in the cellulitis and relieve or prevent airway compromise. Early surgical drainage also serves other purposes such as enhancing antibiotic penetration, allowing prompt drainage should suppuration develop, providing samples for gram staining, culture and sensitivity and allowing the placement of a drain to drain pus collection. Culture and sensitivity tests should be sent for analysis as often and as soon as possible for any major infection. Subsequent antibiotic therapy will be based on the results.

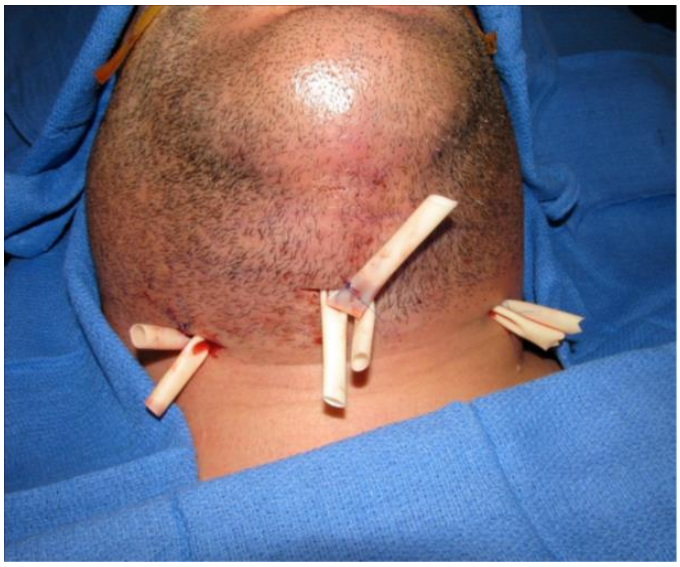

Fig. (2): Ludwig's angina; through-and-through drainage.

Cavernous Sinus thrombosis

The cavernous sinus (CS) is an important sinus for drainage of the brain. It is dual, symmetrical, and located laterally to the Sella Turcica of the Sphenoid bone in the middle cranial fossa. The CS is related to the internal carotid artery, trigeminal ganglion as well as the oculomotor, trochlear, ophthalmic, maxillary and abducens nerves. It communicates with the facial vein via the angular and ophthalmic veins as well as with the pterygoid plexus. Cavernous sinus thrombosis (CST) is a rare condition in which blood clots form within the cavernous sinus. It can be classified as aseptic or septic, depending on its etiology. The aseptic form is associated with trauma, thromboembolic events, dehydration, and anemia. The most common cause of septic cavernous sinus thrombosis is infection of the sphenoid and ethmoid sinuses; otitis media is the second most common cause, with maxillary odontogenic infection accounting for only 10% of the dural infections (15). Most commonly, cavernous sinus thrombosis occurs secondary to the spread of infection by veins and by direct extension. Vascular flow can occur in either direction from the emissary veins into the dural sinuses because these structures lack valves. Spread can occur in anterograde fashion through the ophthalmic veins connected to the angular veins, which results in the classic clinical presentation of periorbital edema. Spread can also occur in retrograde fashion by the emissary veins connected to the pterygoid plexus (fig.3), which tends to be a slower, more insidious progression (16). The origin of the infection can also be from infections of the ‘‘dangerous facial triangle.’’ The danger triangle of the face consists of the area from the corners of the mouth to the bridge of the nose, including the nose and maxilla (fig.4). Infection of one side can easily spread to the contralateral side and cause bilateral multiple cranial nerve paralysis.

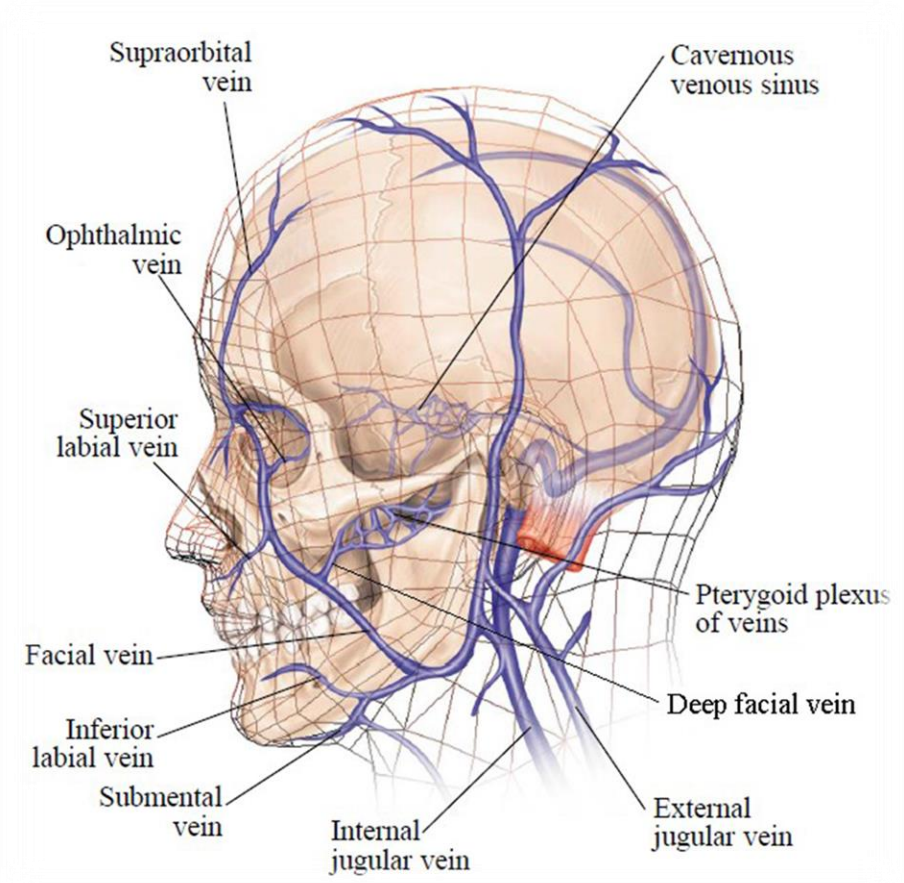

Fig. (3): Route of spared: Anterior pathway; ophthalmic vein, infraorbital vein, and deep facial vein. Posterior pathway; pterygoid plexus through foramen oval or foramen spinosum.

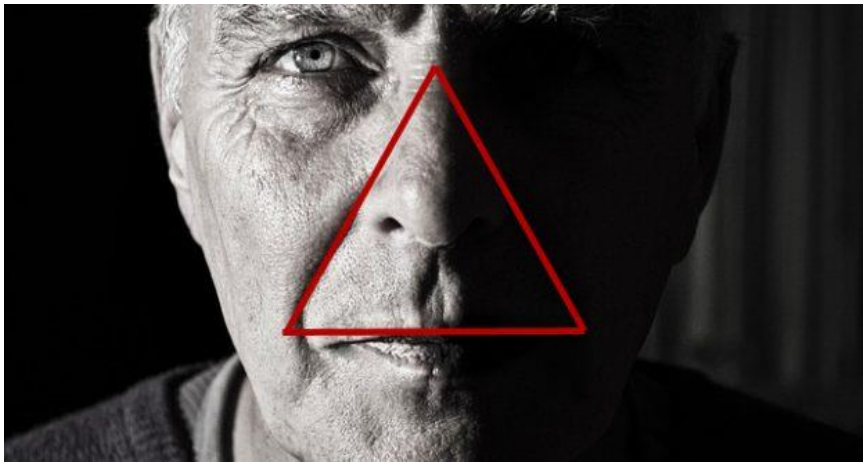

Fig. (4): Danger triangle of the face. Be careful with the “death triangle” of the face.

Staphylococcus accounts for approximately 70% of CST, and streptococcal species account for 20%. Other potential pathogens include pneumococcus, bacteroides, fusobacterium, proteus, haemophilus, pseudomonas, and corynebacterium (16). The clinical characteristics of septic CST are the same as those observed in any infectious process, i.e., fever, headache, nausea, vomiting, dehydration, and prostration. In addition, there are other characteristics related to the anatomical structures associated with the cavernous sinus, such as ophthalmoplegia, proptosis, conjunctival chemosis, diplopia, photophobia, palpebral edema, retro-orbital headache, loss of visual acuity, reduction in pupillary reflexes, anesthesia of the innervation territories of the ophthalmic and maxillary nerves, facial paralysis and meningitis (17). The diagnosis of CST depends on a strong initial suspicion, and MRA is the gold standard method to identify the filling defect of the cavernous sinus (18). Optimal therapy for CST includes the concomitant administration of Nafcillin, Metronidazole, and Ceftriaxone/Cefotaxime. Corticosteroid therapy must be considered if adrenal insufficiency occurs due to cranial nerve dysfunction or pituitary necrosis. Some studies have reported that anticoagulating with heparin, for example, within seven days after CST reduces the mortality rate (19). Treatment must include proper management of the primary infection site. The pre-antibiotic days had mortality rates for thrombosis of the cavernous sinus in the range of 100% (20). Morbidity and mortality remain elevated today, with 20% to 34% of patients still dying with treatment. More than 50% of those who recover do so with permanent deficits, including blindness, nerve palsy, coma, or neurologic abnormalities.

Necrotizing fasciitis

Necrotizing fasciitis is a progressive, life-threatening, bacterial infection of the skin, the subcutaneous tissue, and the underlying fascia. The condition begins with rapidly progressive vascular compromise, thrombosis, or rupture, along with necrosis of adipose, integumentary, muscular, and subcutaneous and cutaneous tissues. The most common cause of necrotizing fasciitis in the head and neck area is odontogenic infection, but the condition can also occur secondary to pharyngitis, tonsillitis, acute otitis media and dermatological infections (21).The disease is caused by a polymicrobial or mixed aerobic-anaerobic infection (22). The pathogens most found include Group A b-hemolytic streptococci, staphylococci, and gram-negative rods. Preexisting immunosuppressive conditions such as diabetes mellitus may predispose patients to odontogenic necrotizing fasciitis and may increase the mortality risk. The mortality rate was reported to be 20-75% (23). Patients tend to present critically ill and often the overlying skin is discolored or gangrenous (fig.5). Superficial nerves are damaged, producing the characteristic localized anesthesia.

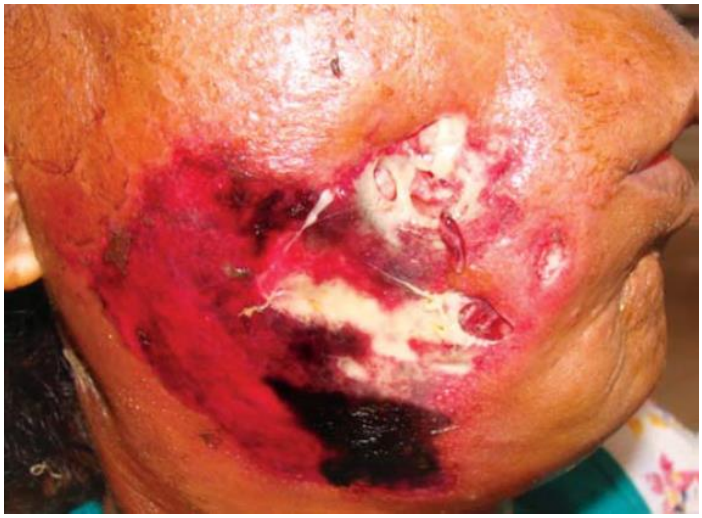

Fig. (5): Necrotizing fasciitis of the cheek; the color of the skin changed to dark purple and black.

Palpation may demonstrate subcutaneous crepitation. Systemic symptoms include fever, toxicity, malaise, confusion, weakness, hypotension, and tachycardia. Contrast CT is necessary to determine the location and extent of the infection. Moreover, it shows asymmetric fascial thickening, gas bubbles along the fascial planes, oedema of muscle and soft tissues, and possibly fluid accumulation in fascial spaces indicating an abscess (24).

Patients with odontogenic necrotizing fasciitis should be treated aggressively with surgical debridement of necrotic tissue and close monitoring with serial debridement and/or frequent dressing changes as indicated. Broad-spectrum IV antibiotics targeting the most common organisms are also vital. The most common antibiotics are metronidazole, clindamycin, penicillin, and ceftriaxone but antimicrobial treatment may need to be adjusted once culture results are available in each case. Debridement of necrotic tissue until viable tissue that bleeds is reached is typically recommended. Hyperbaric oxygen, if available, may be a useful adjunct in refractory cases. Critical care team involvement is often necessary, and airway management and management of hypotension, hypovolemia, and malnutrition may be necessary in patients with odontogenic necrotizing fasciitis. Survivors of odontogenic necrotizing fasciitis may also have extensive skin and soft tissue loss that may necessitate weeks to months of dressing changes or secondary reconstructive procedures such as skin grafts.

Descending mediastinitis

Descending mediastinitis is a life-threatening infection involving the mediastinal connective tissue that fills the interpleural space and surrounds the adjacent thoracic organs. The most frequent cause (25) of descending necrotizing mediastinitis used to be odontogenic infection (36% to 47%) then pharyngeal (33% to 45%), cervical (15%), and other head and neck infections (5%). Inflammatory process usually

descends from the parapharyngeal spaces to mediastinum and pleural cavities, rarely to the pericardium and abdomen causing cellulitis and abscess in mediastinum. Estrera, et al (26) defined three criteria for the diagnosis of mediastinitis of odontogenic origin:

1. Clinical evidence of severe oropharyngeal infection.
2. Characteristic radiological features of mediastinitis (radiographs of the chest will generally show gas in the tissues, air fluid levels, and mediastinal widening).
3. Establishment of the relationship between mediastinitis and the oropharyngeal process.

Despite the presently available broad-spectrum antibiotic therapy, DNM remains a very serious disease with a reported 30-40% mortality rate (26). Several factors contribute to this high mortality, including the rapid spread of the infection, delay in making the diagnosis, poor general health, generalized sepsis, and major respiratory and cardiac complications. Proper mediastinal drainage, aggressive long-term combination antibiotics and adequate nutritional support constitute the cornerstones of management.

Lemierre's syndrome

Lemierre's syndrome refers to infectious thrombophlebitis of the internal jugular vein and bacteremia classically following oropharyngeal infection. The causative agent is usually Fusobacterium species or rarely other Gram-negative bacteria. Septic embolization occurs in most cases, most commonly in the lungs and large joints, but septic emboli in the brain, skin, liver and pericardium have also been reported (28). In addition to signs and symptoms resulting from any emboli, patients often have unilateral neck pain, fever, trismus, a palpable mass corresponding to the internal jugular vein, and positive blood cultures. Since the advent of antibiotics, Lemierre's syndrome has become relatively rare however there is evidence to show

that it is having a resurgence in recent times. Successful management is dependent on a general awareness of the condition, early treatment, and a multidisciplinary team approach. Treatment consists of long-term antibiotic therapy, which has improved the prognosis from a mortality rate of 90 % in the pre-antibiotic era to less than 18 % in modern times (27). The use of anticoagulation is controversial.

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Chapter 6: Osteomyelitis of the jaws

Osteomyelitis of the jaws

Osteomyelitis is an inflammatory condition of bone and bone marrow, which tends to involve the adjacent cortex, periosteum, and soft tissue. The term "osteomyelitis" is mostly used in the medical literature to describe a true infection of the bone induced by pyogenic microorganisms (1). Most frequent sources are odontogenic foci, periodontal diseases and pulpal infections, extraction wounds, and infected fractures. Some other reasons such as traumatic injuries, radiation, and certain chemical substances, among others, may also produce inflammation of the medullar space. The disease begins in the medullar cavity and havarian systems and extended to involve the periosteum of the affected area. The infection becomes established in calcified portion of the bone when pus and edema in the medullary cavity and beneath the periosteum compromises or obstructs the local blood supply. Following ischemia, the infected bone becomes necrotic and leads to sequester formation, which is considered a classical sign of osteomyelitis (2). Osteoclastic activity is then responsible for separating the dead bone from vital bone. The elevated periosteum involved in the inflammatory process still contains vital cells. These cells, once the acute phase has passed, form a new bony shell (involucrum) covering the sequester. The involucrum may be penetrated by sinuses called cloacae, through which pus discharges, elevating the periosteum or forming mucosal or cutaneous fistula. Osteomyelitis is more common in the mandible than the maxilla because of the mandibular bone thickness, the low vascularization of the cortical plate, the blood supply that only comes from the inferior alveolar neurovascular bundle. In the mandible, the most common sites are the body, followed by the symphysis, angle, ascending ramus and condyle (3). Contrary to the mandible, the maxilla is only very rarely affected (4).

Classifications

An overview of the literature on osteomyelitis reveals a wide variety of proposed classifications based on different aspects such as clinical course, pathological-anatomical and/or radiological features, etiology, and pathogenesis. Unfortunately, there is a lack of international consensus about their respective definitions, which makes it difficult to analyze and evaluate the reported data. Likewise, there are counter reports of differing treatment plans and find great variation in diagnostic approaches and follow-up regimens.

Two main types of osteomyelitis are described. The presence of pus and/or fistulas and/or sequestrations are characteristics of the suppurative variants, thereby distinguishing them from the non-suppurative variants, which are chronic inflammatory processes of unknown etiology (5). Suppuration is the clinical sign of bacterial infection. Infectious pathogens can be identified, appearing at different stages in pus, abscess/fistula, and sequestration (6). In many of these cases, there is an apparent odontogenic, infectious etiology. Blood-borne pathogens are also capable of initiating osteomyelitis of the jaw, which is mostly seen in pediatric patients and in immune-compromised patients (7). Acute, subacute, and chronic are frequently used to diagnose and classify suppurative osteomyelitis lesions. The clinical course of acute stage usually shows impressive signs of inflammation. The clinical presentation in cases of a subacute course is less severe. If the symptoms continue, the diagnosis is changed to chronic suppurative osteomyelitis. Several reports have identified lesions as chronic if symptoms continued 1 to 4 months after onset of the disease (1,8). The term secondary suppurative osteomyelitis is used to identify a chronic osteomyelitis that develops secondary to acute symptoms. Thus, acute, and secondary chronic osteomyelitis are basically the same disease. They usually represent a true bacterial infection of the jawbone. Suppuration, fistula formation, and sequestration are characteristic features of this disease entity. Acute

means severe and chronic indicates long duration. Furthermore, symptoms of acute exacerbation in chronic osteomyelitis are identical to those of acute osteomyelitis. The typical pathogenic organisms are Staphylococcus species, Peptostreptococcus species, and Pseudomonas aeruginosa, among others. Less common causes, including mycobacterial infections, syphilis, actinomycosis, and fungal infections must also be considered (9-12). The condition may be subclassified, based on the causative organisms.

Lesions without suppuration are frequently diagnosed as chronic non-suppurative osteomyelitis or primary chronic osteomyelitis (13). This is defined as a chronic inflammatory disorder of the cortical and cancellous bone of unknown etiology, occasionally without culturable/detectable pathogens (4). It is characterized as a strictly nonsuppurative chronic inflammation of the jawbone with the absence of pus formation, extra- or intraoral fistula, or sequestration. The absence of these symptoms clearly differentiates primary from acute and secondary chronic osteomyelitis in most cases. The term "primary chronic osteomyelitis" also implies that the patient has never undergone an appreciable acute phase and lacks a definitive initiating event. The disease tends to arise without preceding actual acute phase and follows an insidious course. In most cases of primary chronic osteomyelitis, periodic episodes of onset with varying intensity last from a few days to several weeks and are intersected by periods of silence where the patient may experience little to no clinical symptoms. Primary chronic osteomyelitis of the jaws almost always targets the mandible. On rare occasion, other sites may be affected. Flygare et al (14) reported a case of primary chronic osteomyelitis with involvement of both jaws, which is a unique case. Different terminologies and classification systems are used identify the chronic nature of nonsuppurative osteomyelitis. This definition applies to Primary Chronic osteomyelitis (13), Diffuse Sclerosing osteomyelitis (15), Juvenile Mandibular Chronic osteomyelitis (16), Chronic Recurrent Multifocal osteomyelitis

(17), and chronic nonbacterial osteomyelitis (18). Although primary chronic osteomyelitis has been described in all age groups, most reported cases afflict adults. Few reports exist of in childhood or adolescent onset, usually termed Garre's osteomyelitis. Garre's osteomyelitis is a distinctive type of chronic osteomyelitis associated with gross thickening of the periosteum of the bones and peripheral reactive bone formation resulting from mild irritation or infections (19).

The association between primary chronic osteomyelitis and dermato-skeletal disorders, such as the SAPHO-syndrome (synovitis, acne, pustulosis, hyperostosis and osteitis) and chronic recurrent multifocal osteomyelitis, has been described. The diagnostic criteria for SAPHO syndrome are 1- chronic recurrent multifocal osteomyelitis, 2- acute, subacute, or chronic arthritis with palmoplantar pustulosis, pustular psoriasis, or severe acne or 3- severe osteitis with palmoplantar pustulosis, pustular psoriasis, or severe acne (20).

Osteoradionecrosis (21) is a chronic non-healing wound of the affected jaw (most commonly mandible), typically with exposure of bone, in a patient with a history of radiation therapy to the head and neck region. According to the most recent literature, osteoradionecrosis of the jaws is defined as exposed irradiated bone that fails to heal over a period of 3 months without any evidence of persisting or recurrent tumour. The mechanism of pathogenesis is still under investigation. However, the most frequently reported reason is radiation arteritis. Radiation arteritis leads to the development of a hypocellular, hypovascular and hypoxic environment, which results in a pathological outcome. Necrosis might involve the bone superficially or deeply. It might be a process that progresses slowly or an active progressive state that can lead to a pathological fracture.

Some other reasons such as steroids, chemotherapeutic agents, and biphosphonates are also linked to osteomyelitis of the jaw. Bisphosphonate-related osteonecrosis of the jaw was first reported by Marx in 2003 (22). The disease represents a serious

adverse effects of bisphosphonates treatment, which are used to manage oncologic patients and to prevent fractures in osteoporosis. Osteoclasts are thought to be qualitatively impaired, particularly with intravenous forms of bisphosphonate medication leading to inadequate remodeling of bone and necrosis. Current knowledge on bisphosphonate use states that the incidence of bone necrosis is dependent on the potency of the drug, the dosage, the frequency of administration, and the duration of the therapy. Without other risk factors present, the disease is unlikely to develop.

Clinical features

Generally, one may distinguish three clinical stages; acute, subacute, and chronic, although there may be some overlap between these stages. The clinical course of acute suppurative osteomyelitis usually show intense signs of inflammation. Pain can be severe and is mostly described by a deep sensation within the bone. Local swelling and edema due to abscess formation can also be substantial causing trismus and limitation of jaw function. The patients experience a general malaise caused by high intermittent fever with temperatures reaching up to 39–40°C, often accompanied by regional lymphadenopathy. In some instances, paresthesia or anesthesia of the lower lip is described, indicating involvement of the inferior alveolar nerve. Pus may exude around the gingival sulcus and through mucosal and, possibly cutaneous, fistulas. A fetid oral odor caused by anaerobic pyogenic bacteria often is present. Teeth in the affected region may demonstrate increased mobility even leading to malocclusion and show decreased or loss of sensitivity. Sequester formation and appositional neoosteogenesis are limited, if not absent, due to the short period since establishment of deep bone infection, which is the definition of acute osteomyelitis (23).

Chronicity is associated with mild or moderate symptoms. However, acute exacerbations may occur intermittently in the chronic stage. The degree and duration

of the symptoms depend on various factors such as the virulence of the causative organisms, the presence of underlying disease, and the immune status of the host. Most symptoms, such as pain and swelling, are usually less extensive in the chronic than in the acute stage. The deep and intense pain frequently observed in the acute stage is replaced by a duller pain. Painful swelling caused by local edema and abscess formation in the acute stage is subsided by a harder palpable tenderness caused by periosteal reaction. The noted fetid odor often noted in cases of acute abscess formation is less frequent in patients with secondary chronic osteomyelitis. A disturbed occlusion can sometimes be noted when teeth of an affected region become more mobile. Other symptoms are somewhat more predominant in advanced stages, such as sequester, fig. (1) and fistula formation, fig. (2), and are regarded as classical signs of secondary chronic osteomyelitis. The condition may be complicated by pathologic fractures, fig. (3). Secondary chronic osteomyelitis may, however, begin as a hideous disease with little and somewhat unspecific clinical symptoms. In such instances the cause of the infection is a low-grade infection, which, however, cannot be fully eradicated by host defenses. These cases of secondary chronic osteomyelitis demonstrate less pus, fistula, and sequester formation, or may even lack these symptoms at a certain (progressive) stage of the disease (23).

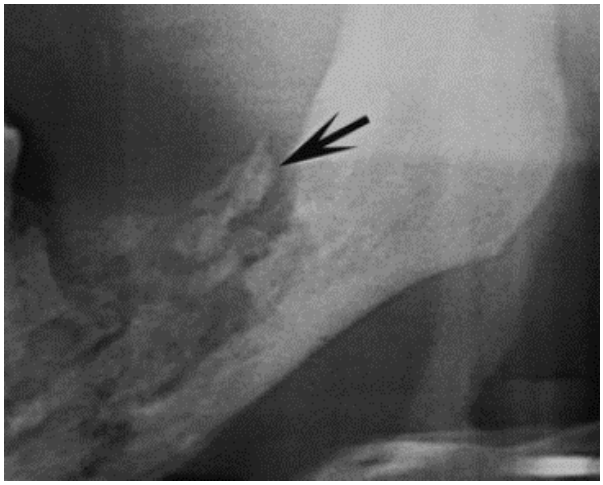

Fig. (1): Panoramic image reveals a large sequestrum.

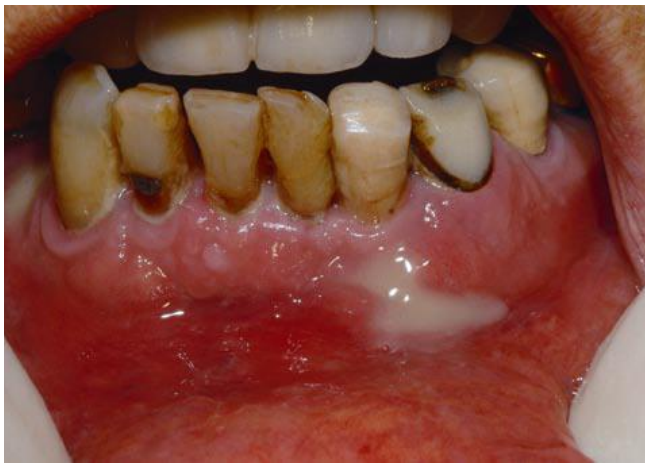

Fig. (2): secondary chronic osteomyelitis with multiple fistulae.

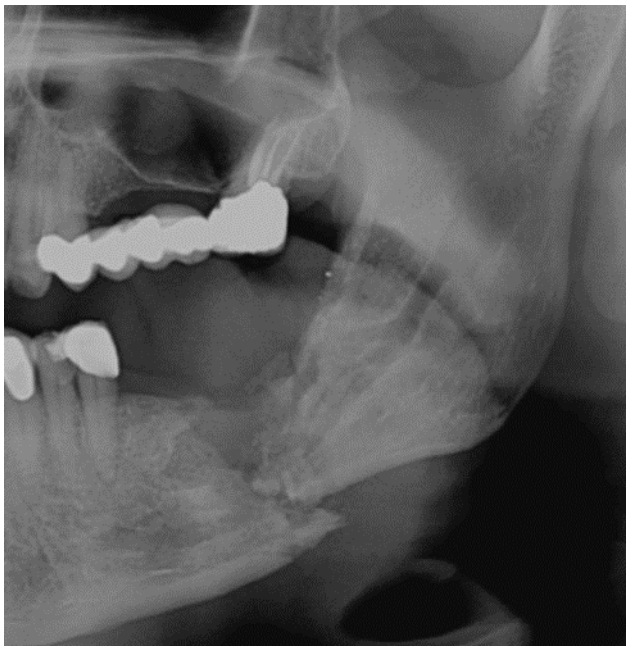

Fig. (3): Panoramic image reveals a pathologic fracture of the mandible.

Primary chronic osteomyelitis is characterized as a strictly nonsuppurative chronic inflammation of the jawbone with the absence of pus formation, extra- or intraoral fistula, or sequestration. The absence of these symptoms clearly differentiates primary from acute and secondary chronic osteomyelitis in most cases. The term

“primary chronic osteomyelitis” also implies that the patient has never undergone a preceding acute phase and lacks a definitive initiating event. In most cases of primary chronic osteomyelitis, periodic episodes of onset with varying intensity last from a few days to several weeks and are intersected by periods of silence where the patient may experience little to no clinical symptoms. In active periods dull to severe pain, limitation of jaw opening and/or myofacial pain, as well as variable swelling, may be observed. Regional lymphadenopathy and reduced sensation of the inferior alveolar nerve are also accompanying symptoms (23).

Radiographic features

Radiographs are used to detect pathological changes in the bone. The significance of radiological evaluation is twofold: to differentiate osteomyelitis from other conditions that show similar signs and symptoms, and to check the progress of the disease and its response to treatment. Panoramic view is the first examination in a patient clinically suspected of having developed osteomyelitis of the jaw. It depicts the status of the dentition, displays the osseous confines and internal osseous structure of the jaws, and is the adequate basis for a follow-up examination. Early in the acute stage, radiographs may fail to reveal any bony change for 4−8 days. Bone resorption due to osteoclastic activity requires 30−50% focal reduction of bone mineral content in order to be recognized by radiographs (24) therefore, it is not uncommon for plain films to be interpreted as normal up to 2 weeks or occasionally 3 weeks after the onset of symptoms. Within the third- and fourth-weeks radiographs tend to become mostly pathological. The first sign of osteomyelitis is loss of the trabecular structure of the bone, commonly related to an empty tooth socket (fig.4). Destruction of bone initially proceeds within cancellous bone. Bone resorption is

prominent, and radiography shows an osteolytic pattern. Sclerotic areas may be seen around the osteolytic area in long-standing lesions (fig.5).

The cortical plate is secondarily involved by progressive bone resorption. Cortical perforation may be seen (fig.6). The periosteal reaction is usually lamellated, and appears as a thin, faint, radiopaque line adjacent to, and almost parallel or slightly convex to, the surface of the bone. A radiolucent band separates the new periosteal bone from the bone surface. If the process occurs repeatedly, an "onionskin" appearance is observed, caused by the presence of multiple lamellae, (fig.7). The occurrence of sequester is considered rare within the first 4 weeks and more typically is referred to the chronic stage (25).

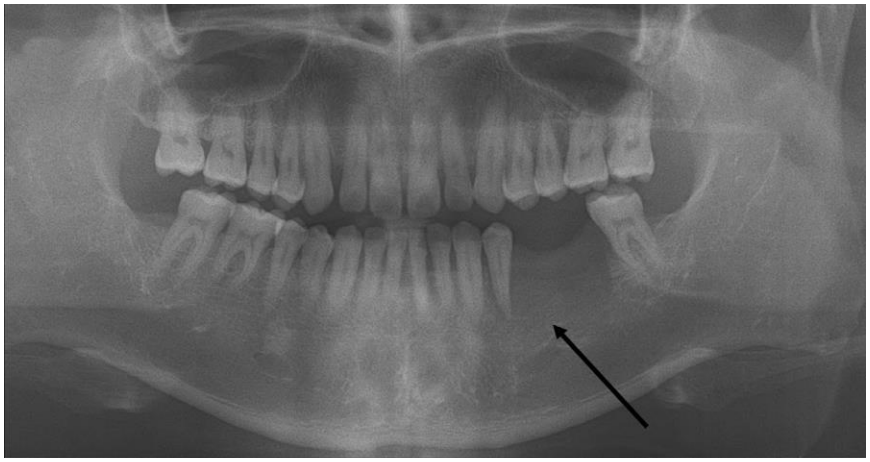

Fig. (4): Osteolytic bone change. An ill-defined area of radiolucency in the left premolar and molar region.

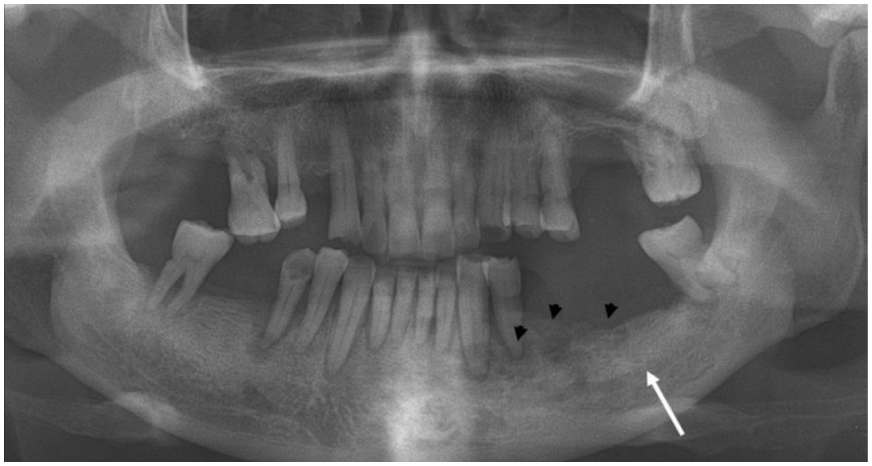

Fig. (5): Mixed lesion exhibiting osteolytic (black arrowheads) and sclerotic (white arrow) bone change.

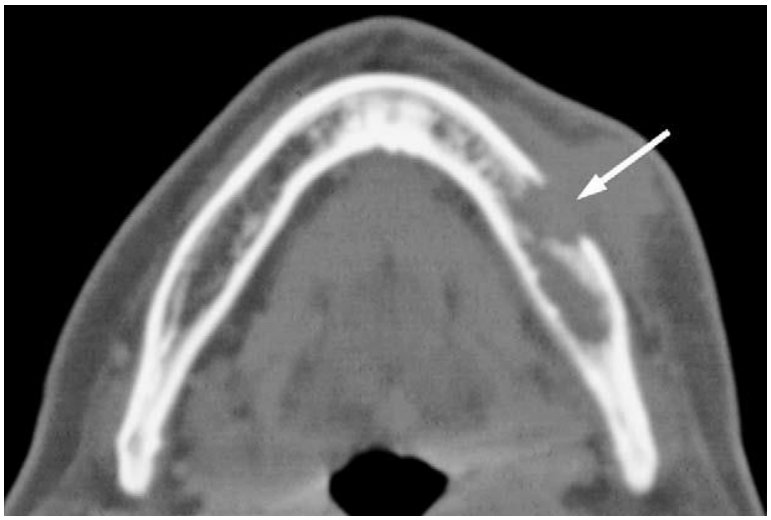

Fig. (6): Axial CT image of a suppurative osteomyelitis with cortical bone perforation (arrow).

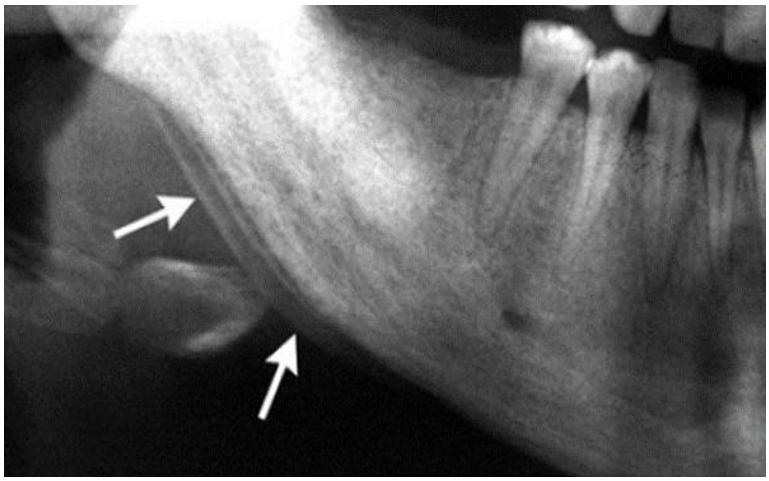

Fig. (7): Panoramic image of osteomyelitis revealing at least two layers of new bone (arrows) produced by the periosteum at the inferior aspect of the mandible.

Currently, computerized tomography (CT) scans are mostly used (26). CT revealed the exact location and extent of infection as well as the relationship between soft tissue and bony lesions. Findings consist of usually ill-defined areas of radiolucency, sequestra, calcified periosteal reactions and occasionally fistulae. Sequestra (fig.8) and periosteal bone formation (fig.9) serve as radiological “indicators” in the advanced stage of acute osteomyelitis and thus play a significant role in arriving at the diagnosis. The differential diagnosis of osteomyelitis includes pathologies like fibrous dysplasia, metastases from prostate gland, Paget’s disease, and osteosarcoma.

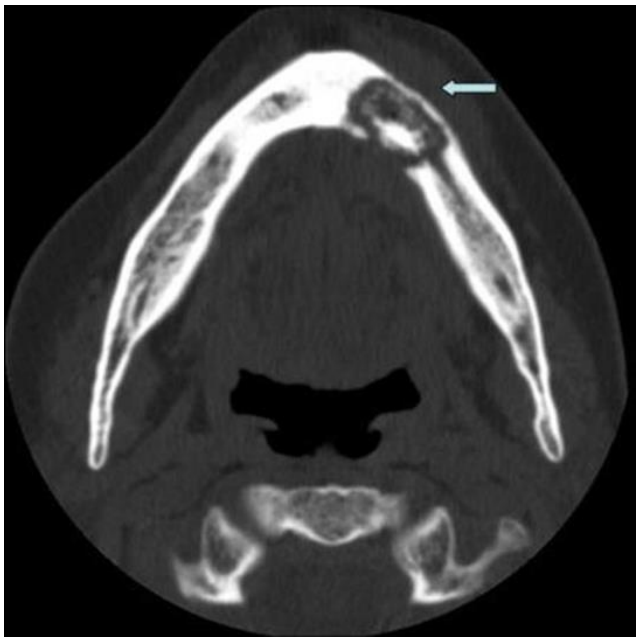

Fig. (8): Axil CT image reveals sequestra (arrow).

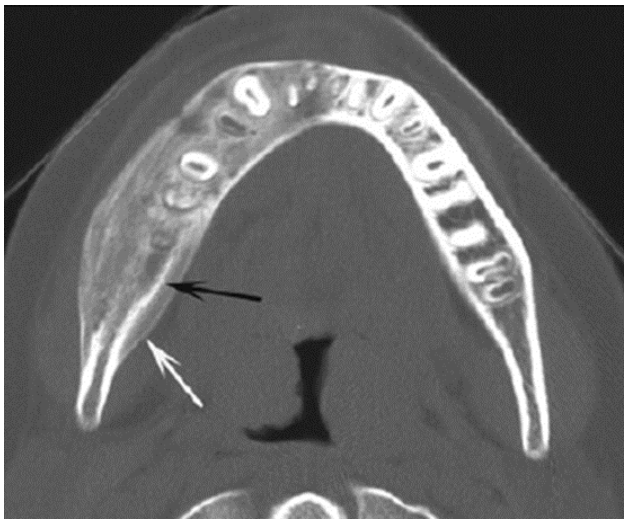

Fig. (9): Axial CT image reveals periosteal new bone (white arrow) and evidence of the original cortex (black arrow). Note the increased width of the mandible.

Magnetic Resonance Imaging (MRI) can detect osteomyelitis in the early stage when the bone marrow changes take place (27). Additionally, scintigraphy seems to be important in the diagnosis and assessment of disease activity in osteomyelitis (28).

Management

Initial correct diagnosis of osteomyelitis must be established prior to any successful treatment. Adequate diagnosis can usually be achieved based on history, clinical evaluation, and imaging studies. Diagnostic imaging, CT scans are considered the gold standard in determining the extent of the lesion prior to surgery. In special situations when an underlying malignancy is suspected, a biopsy procedure prior to the actual surgical intervention is advisable. If an underlying host defense deficiency exists, this requires immediate attention and correction if possible, preferably prior to surgical intervention. Consultation with the appropriate medical specialist will be helpful in resolving many of these underlying problems. Whenever possible, specimens should be obtained for Gram staining, aerobic and anaerobic culture, and sensitivity testing. Extremely loose teeth and sequestra that are readily accessible should be removed early in the course of the disease. A suitable course of parental antibiotics should be given along with supportive measures to control the acute infection. Antibiotic therapy is usually started empirically with a broad-spectrum antibiotic and adapted to a more specific culture-guided therapy, if necessary, as soon as possible. If the infection does not respond adequately, the regime must be questioned and adjustments must be made, including repeated cultures to ensure correct antibiotic therapy. Preoperative definitive antibiotic coverage is given at least for one week for every patient before final surgical intervention. Other supportive treatments include: a) Non-narcotic analgesics for pain control in different doses and through different routes, b) Intravenous fluid and electrolysis therapy for hydration; 2 units in 24 hrs. c) Nutritious diet; high protein and vitamins for malnutrition d) Povidine iodine antiseptic mouthwash to maintain good oral hygiene.

Treatment depends on the type of osteomyelitis, acute suppurative osteomyelitis usually responds to antibiotic therapy. In the case of chronic osteomyelitis, management entailed a course of antibiotic in combination with surgical

debridement (sequestrectomy). The minimum duration of antibiotic therapy to treat chronic suppurative osteomyelitis should be at least two weeks. The local tissue perfusion can be further accomplished by surgical decortication which includes the removal of non-viable buccal and inferior cortical bone thus creating a direct contact between the vascularized periosteum and the medullary portion of the bone. Surgical treatment in conjunction with antibiotics and non-steroid anti-inflammatory drugs proved to be beneficial and improve considerably the patients' quality of life (13). Nevertheless, exacerbation of the disease may occur, and regular follow-up of the patients is necessary. Hyperbaric oxygen and platelet-rich plasma have been recommended for the treatment of both primary and secondary chronic osteomyelitis. However, the benefits of these therapies are inconsistent in the literature (29,30).

Surgical intervention

Patients with osteomyelitis usually require treatment as in-patients. Only in few instances was treatment conducted on solely an out-patient basis. Surgery is a traditional way of treating osteomyelitis and with the aim to remove the infected bone, to improve healing and increase the blood supply to the area (31).

Sequestrectomy

Sequester formation is a classical sign of secondary chronic and advanced acute osteomyelitis cases. Usually a time frame of at least 2 weeks after onset of infection is necessary until presentation. In general, sequestra are confined to the cortical bone but may also be cancellous or cortical-cancellous. Once a sequester is fully formed, it may persist for several months in untreated cases before being resorbed or spontaneously expelled through the oral mucosa or the facial skin. Completely separated sequester may be removed with minimal surgical trauma. While this approach may be applicable in cases of localized osteomyelitis with superficial sequester formation, it is contraindicated in advanced cases with protracted

spreading of the infection and sequester formation in more profound regions of the bone. Here a more aggressive surgical debridement is necessary which clearly must exceed the sole removal of sequester. In these advanced cases sequestrectomy is often the first part of the surgical debridement followed by decortication (32).

Saucerization

The next more extensive step in the surgical debridement of infected jawbone is saucerization. This surgical procedure describes the “de-roofing” of the oral-faced jawbone to expose the medullary cavity for subsequent thorough debridement. The margins of necrotic bone overlying the focus of osteomyelitis are excised creating direct visualization of the infected medullary cavity. The saucerization procedure is usually performed by an oral approach with the advantage of direct access to the jawbone and avoidance of facial scarring. Since the removal of bone by this procedure is limited, the strength of the mandible is not critically jeopardized and healing by secondary intention is sufficient (32).

Decortication

In advanced acute and secondary chronic osteomyelitis, use of decortication promotes resolution based on the premise that the affected cortical bone is avascular and harbors microorganisms (2). The major purpose of the decortication procedure is to remove the chronically infected cortex of the jawbone and gain access to affected medullary cavity to allow a sufficient decompression of intramedullary pressure and meticulous surgical debridement under direct visualization. Furthermore, this procedure allows bringing well-perfused tissue (e.g., masseter muscle) into contact with bone, promoting further healing. While the decortication procedure was originally described as a procedure with an extraoral approach, the standard approach is intraoral to prevent facial scarring. If extensive debridement is required and the remaining bone is suspected to be prone to fracture, appropriate stabilization and reconstruction should be achieved by osteosynthesis with a thick

reconstruction plate. Maxillary-mandibular fixation may be performed if additional stabilization and immobilization is required. Following surgical debridement, drainage may be beneficial for 24−48 h to prevent hematoma formation (32).

Resection and reconstruction

Although decortication may be appropriate in select patients, more definitive options should be considered in patients who have rapidly progressive disease, pathologic fracture, recurrent cases, involvement of the mandibular condyle, and circumferential involvement (fig.10) on CT scans (33), as well as those who have not responded to decortication. More aggressive surgery, that is, segmental resection, appears to have more favorable outcomes (34). One must still consider the drawbacks with segmental resection, which include creation of a mandibular continuity defect; the need for reconstruction, which often includes another surgical procedure; and sacrifice of the inferior alveolar nerve. Many surgeons may elect for secondary reconstruction because of the presence of infection and possible oral contamination. Marx (1) advocates a two-stage procedure to reconstruct continuity defects as early as 3 months after surgery, provided that skin and mucosa are intact, and the tissue is free of contamination and infection. However, primary reconstruction could be successful even in the clinically infected mandible (35).

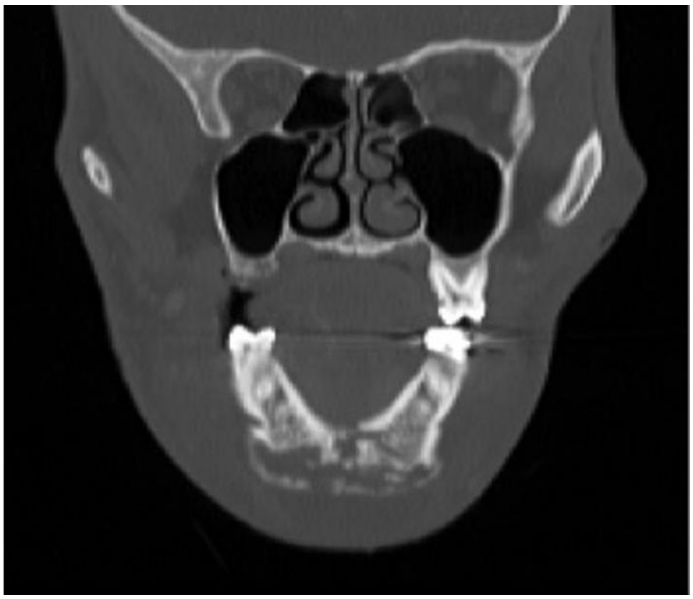

Fig. (10): Coronal CT scan showing circumferential destruction of the anterior mandible bilaterally.

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