Osteomyelitis of the Jaws

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Osteomyelitis of the Jaws: Definition and Classification

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Contents

2.1 Summary

Osteomyelitis of the jaws is still a fairly common disease in maxillofacial clinics and offices, despite the introduction of antibiotics and the improvement of dental and medical care. The literature on this disease is extensive. Different terminologies and classification systems are used based on a variety of features such as clinical course, pathological–anatomical or radiological features, etiology, and pathogenesis. A mixture of these classification systems has occurred throughout the literature, leading to confusion and thereby hindering comparative studies. An overview of the most commonly used terms and classification systems in osteomyelitis of the jaws is given at the beginning of this chapter.

The Zurich classification system, as advocated in this textbook, is primarily based on the clinical course and appearance of the disease as well as on imaging studies. Subclassification is based on etiology and pathogenesis of the disease. Mainly three different types of osteomyelitis are distinguished: acute and secondary chronic osteomyelitis and primary chronic osteomyelitis. Acute and secondary chronic osteomyelitis are basically the same disease separated by the arbitrary time limit of 1 month after onset of the disease. They usually represent a true bacterial infection of the jawbone. Suppuration, fistula formation, and sequestration are characteristic features of this disease entity. Depending on the intensity of the infection and the host bone response, the clinical presentation and course may vary significantly. Acute and secondary chronic osteomyelitis of the jaws is caused mostly by a bacterial focus (odontogenic disease, pulpal and periodontal infection, extraction wounds, foreign bodies, and infected fractures).

Primary chronic osteomyelitis of the jaw is a rare, nonsuppurative, chronic inflammation of an unknown cause. Based on differences in age at presentation,

clinical appearance and course, as well as radiology and histology, the disease may be subclassified into early- and adult-onset primary chronic osteomyelitis. Cases with purely mandibular involvement are further distinguished from cases associated with extragnathic dermatoskeletal involvement such as in SAPHO syndrome or chronic recurrent multifocal osteomyelitis (CRMO).

2.2 Definition

The word "osteomyelitis" originates from the ancient Greek words osteon (bone) and muelinos (marrow) and means infection of medullary portion of the bone. Common medical literature extends the definition to an inflammation process of the entire bone including the cortex and the periosteum, recognizing that the pathological process is rarely confined to the endosteum. It usually encompasses the cortical bone and periosteum as well. It can therefore be considered as an inflammatory condition of the bone, beginning in the medullar cavity and havarian systems and extending 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 (Topazian 1994, 2002).

Although other etiological factors, such as traumatic injuries, radiation, and certain chemical substances, among others, may also produce inflammation of the medullar space, the term "osteomyelitis" is mostly used in the medical literature to describe a true infection of the bone induced by pyogenic microorganisms (Marx 1991).

2.3 History

The prevalence, clinical course, and management of osteomyelitis of the jawbones have changed profoundly over the past 50 years. This is due to mainly one factor: the introduction of antibiotic therapy, specifically penicillin. The integration of antibiotics into the therapeutic armamentarium has led to a complete renaissance in the treatment of most infectious diseases, including osteomyelitis (Hudson 1993). Further factors, such as sophistication in medical and dental science as well as the widespread availability for adequate treatment, have additionally led to improvement in the management of this disease. Modern diagnostic imaging allows much earlier treatment of bone infections at a more localized stage.

In the preantibiotic era, the classical presentation of jawbone osteomyelitis was an acute onset, usually followed by a later transition to a secondary chronic process (Wassmund 1935; Axhausen 1934). Massive clinical symptoms with widespread bone necroses, neoosteogenesis, large sequester formation, and intra- and extraoral fistula formation were common presentations, sometimes leading to significant facial disfigurement (Fig. 2.1).

After the introduction of antibiotics, acute phases were often concealed by these antimicrobial drugs without fully eliminating the infection. Subacute or chronic

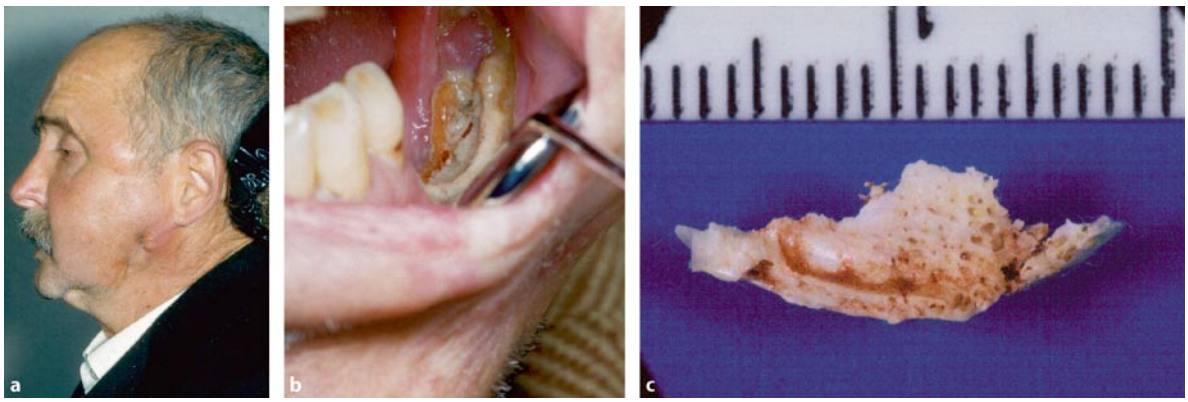


Fig. 2.1a–c Elder case of advanced secondary chronic osteomyelitis of the left mandible. The massive affection of the left mandible demonstrates extraoral fistula and scar formation (**a**). Intraoral view of the same patient with large exposure of infected bone and sequestra (**b**). Large sequester collected from surgery (**c**) (Courtesy of N. Hardt)

forms of osteomyelitis have therefore become more prominent, lacking an actual acute phase (Becker 1973; Bünger 1984).

2.4 Overview of Currently Used Classification Systems and Terminology

One of the first widely accepted staging systems for osteomyelitis in long bones was first described by Waldvogel and Medoff (1970) and Waldvogel et al. (1970a,b). The authors distinguished three categories of osteomyelitis: osteomyelitis from hematogenous spread; from a contagious focus; and due to vascular insufficiency. The classification is primarily based on etiology and pathogeneses of infection and does not readily lend itself to guiding therapeutic strategies such as surgery and antibiotic therapy. A more comprehensive classification proposed by Cieny et al. (1985) and Mader and Calhoun (2000) is based upon the anatomy of the bone infection and the physiology of the host. It divides the disease into four stages combining four anatomical disease types and three physiological host categories resulting in the description of 12 discrete clinical stages of osteomyelitis. Such a classification system, although it may be important in dealing with numerous sites of the skeletal system and allowing stratification of infection and the development of comprehensive treatment guidelines for each stage, is unnecessarily complex and impractical when dealing with infections of the jawbones.

Because of its unique feature bearing teeth and hence connecting to the oral cavity with the periodontal membrane, osteomyelitis of the jaws differs in several

Table 2.1 Classification systems described in the literature for osteomyelitis of the jaws

Reference	Classification	Classification criteria
Hudson JW Osteomyelitis of the jaws: a 50-year perspective. *J Oral Maxillofac Surg 1993 Dec; 51(12):1294-301*	I. Acute forms of osteomyelitis (suppurative or nonsuppurative) A. Contagious focus 1. Trauma 2. Surgery 3. Odontogenic Infection B. Progressive 1. Burns 2. Sinusitis 3. Vascular insufficiency C. Hematogenous(metastatic) 1. Developing skeleton (children) II. Chronic forms of osteomyelitis A. Recurrent multifocal 1. Developing skeleton (children) 2. Escalated osteogenic (activity < age 25 years) B. Garrè's 1. Unique proliferative subperiosteal reaction 2. Developing skeleton (children and young adults) C. Suppurative or nonsuppurative 1. Inadequately treated forms 2. Systemically compromised forms 3. Refractory forms (chronic recurrent multifocal osteomyelitis CROM) D. Diffuse sclerosing 1. Fastidious microorganisms 2. Compromised host/pathogen interface	Classification based on clinical picture and radiology. The two major groups (acute and chronic osteomyelitis) are differentiated by the clinical course of the disease after onset, relative to surgical and antimicrobial therapy. The arbitrary time limit of 1 month is used to differentiate acute from chronic osteomyelitis (Marx 1991; Mercuri1991; Koorbusch1992).

Table 2.2 Classification systems described in the literature for osteomyelitis of the jaws

Reference	Classification	Classification criteria
Hudson JW Osteomyelitis of the jaws: a 50-year perspective. *J Oral Maxillofac Surg 1993 Dec;51(12):1294-301*	I. Hematogenous osteomyelitis II. Osteomyelitis secondary to a contiguous focus of infection III. Osteomyelitis associated with or without peripheral vascular disease	Classification based on pathogenesis. From Vibhagool 1993
Hudson JW Osteomyelitis of the jaws: a 50-year perspective. *J Oral Maxillofac Surg 1993 Dec;51(12):1294-301*	I. Anatomic Types Stage I: medullar osteomyelitis – involved medullar bone without cortical involvement; usually hematogenous Stage II: superficial osteomyelitis – less than 2 cm bony defect without cancellous bone Stage III: localized osteomyelitis – less than 2 cm bony defect on radiograph, defect does not appear to involve both cortices Stage IV: diffuse osteomyelitis – defect greater than 2 cm. Pathologic fracture, infection, nonunion II. Physiological class A host: normal host B host: systemic compromised host, local compromised host C host: treatment worse than disease	Dual classification based on pathological anatomy and pathophysiology From Vibhagool 1993 and Cierny 1985
Mittermayer CH Oralpathologie. *Schattauer, Stuttgart-New York 1976*	I. Acute suppurative osteomyelitis (rarefactional osteomyelitis) II. Chronic suppurative osteomyelitis (sclerosing osteomyelitis) III. Chronic focal sclerosing osteomyelitis (pseudo-paget, condensing osteomyelitis) IV. Chronic diffuse sclerosing osteomyelitis V. Chronic osteomyelitis with proliferative periostitis (Garrè's chronic nonsuppurative sclerosing osteitis, ossifying periostitis) VI. Specific osteomyelitis 1. Tuberculous osteomyelitis 2. Syphilitic osteomyelitis 3. Actinomycotic osteomyelitis	Classification based on clinical picture, radiology, pathology, and etiology

important aspects from osteomyelitis of long bones. The specific local immunological and microbiological aspects determine a major factor in the etiology and pathogenesis of this disease, and hence also have a direct impact on its treatment; therefore, to extrapolate from long bone infections to disease of the jaws is only possible with limitations. This is reflected by the long-standing recognition of osteomyelitis of jawbones as a clinical entity, which differs in many important aspects from the one found in long bones; hence, a wide variety of classifications, specifically for the jawbones, have been established by several authors in the medical literature. Classifications proposed are based on different aspects such as clinical course, pathological–anatomical

Table 2.3 Classification systems described in the literature for osteomyelitis of the jaws

Reference	Classification	Classification criteria
Hjorting-Hansen E Decortication in treatment of osteomyelitis of the mandible. *Oral Surg Oral Med Oral Pathol 1970 May;29(5):641-55*	I. Acute/subacute osteomyelitis II. Secondary chronic osteomyelitis III. Primary chronic osteomyelitis	Classification based on clinical picture and radiology
Marx RE Chronic Osteomyelitis of the Jaws *Oral and Maxillofacial Surgery Clinics of North America, Vol 3, No 2, May 91, 367-81* Mercuri LG Acute Osteomyelitis of the Jaws *Oral and Maxillofacial Surgery Clinics of North America, Vol 3, No 2, May 91, 355-65*	I. Acute osteomyelitis 1. Associated with Hematogenous spread* 2. Associated with intrinsic bone pathology or peripheral vascular disease* 3. Associated with odontogenic and nonodontogenic local processes* II. Chronic osteomyelitis 1. Chronic recurrent multifocal osteomyelitis of children 2. Garrè's osteomyelitis 3. Chronic suppurative osteomyelitis – Foreign body related – Systemic disease related – Related to persistent or resistant organisms 4. True chronic diffuse sclerosing osteomyelitis	Classification based on clinical picture and radiology, etiology, and pathophysiology Classification of acute osteomyelitis by Mercuri, classification of chronic osteomyelitis by Marx. The arbitrary time limit of one month is used to differ acute from chronic osteomyelitis * From Waldvogel and Medoff 1970
Panders AK, Hadders HN Chronic sclerosing inflammations of the jaw. Osteomyelitis sicca (Garre), chronic sclerosing osteomyelitis with fine-meshed trabecular structure, and very dense sclerosing osteomyelitis. *Oral Surg Oral Med Oral Pathol 1970 Sep;30(3):396-412*	I. Primarily chronic jaw inflammation 1. Osteomyelitis sicca (synonymous osteomyelitis of Garrè, chronic sclerosing nonsuppurative osteomyelitis of Garrè, periostitis ossificans) 2. Chronic sclerosing osteomyelitis with fine-meshed trabecular structure 3. Local and more extensive very dense sclerosing osteomyelitis II. Secondary chronic jaw inflammation III. Chronic specific jaw inflammations – Tuberculosis – Syphilis – Lepra – Actinomycosis	Classification based on clinical picture and radiology Classification of chronic osteomyelitis forms only

and/or radiological features, etiology, and pathogenesis. A mixture of these classification systems has been used in many instances, leading to confusion and thereby hindering comparative studies and obscuring classification criteria. An overview of the most commonly cited classifications of jawbone osteomyelitis are listed in Tables 2.1–2.4.

Table 2.4 Classification systems described in the literature for osteomyelitis of the jaws

Reference	Classification	Classification criteria
Schelhorn P, Zenk W [*Clinics and therapy of the osteomyelitis of the lower jaw*]. *Stomatol DDR 1989 Oct;39(10):672-6*	I. Acute osteomyelitis II. Secondary chronic osteomyelitis III. Primary chronic osteomyelitis IV. Special forms – Osteomyelitis sicca (pseudo-paget Axhausen) – Chronic sclerosing osteomyelitis Garrè	Classification based on clinical picture
Topazian RG *Osteomyelitis of the Jaws. In Topizan RG, Goldberg MH (eds): Oral and Maxillofacial Infections.* *Philadelphia, WB Saunders 1994, Chapter 7, pp 251-88*	I. Suppurative osteomyelitis 1. Acute suppurative osteomyelitis 2. Chronic suppurative osteomyelitis – Primary chronic suppurative osteomyelitis – Secondary chronic suppurative osteomyelitis 3. Infantile osteomyelitis II. Nonsuppurative osteomyelitis 1. Chronic sclerosing osteomyelitis – Focal sclerosing osteomyelitis – Diffuse sclerosing osteomyelitis 2. Garrè's sclerosing osteomyelitis 3. Actinomycotic osteomyelitis 4. Radiation osteomyelitis and necrosis	Classification based on clinical picture, radiology, and etiology (specific forms such as syphilitic, tuberculous, brucellar, viral, chemical, *Escherichia coli* and *Salmonella* osteomyelitis not integrated in classification)
Bernier S, Clermont S, Maranda G, Turcotte JY *Osteomyelitis of the jaws.* *J Can Dent Assoc 1995 May;61(5):441-2, 445-8*	I. Suppurative osteomyelitis 1. Acute suppurative osteomyelitis 2. Chronic suppurative osteomyelitis II. Nonsuppurative osteomyelitis 1. Chronic focal sclerosing osteomyelitis 2. Chronic diffuse sclerosing osteomyelitis 3. Garrè's chronic sclerosing osteomyelitis (proliferative osteomyelitis) III. Osteoradionecrosis	Classification based on clinical picture and radiology
Wassmund M Lehrbuch der praktischen Chirurgie des Mundes und der Kiefer. *Meusser, Leipzig 1935*	I. Exudative osteitis II. Resorptive osteitis III. Productive osteitis IV. Acute necrotizing osteitis (osteomyelitis) V. Chronic osteomyelitis 1. Chronic course of an acute osteomyelitis 2. Occult osteomyelitis 3. Chronic necrotizing osteomyelitis with hypertrophy 4. Chronic exudative osteomyelitis 5. Productive osteomyelitis	Classification based on clinical picture and radiology (note that classification was developed before introduction of antibiotic therapy)

2.5 Currently Used Terms in Classification of Osteomyelitis of the Jaws

2.5.1 Acute/Subacute Osteomyelitis

Although acute forms of osteomyelitis are seen only rarely these days, most authors in common medical literature still describe this form as an entity of its own. Mercuri (1991) and Marx (1991) arbitrarily defined the time element as being 1 month after onset of symptoms. Endurance past this arbitrary set time limit is then considered as chronic osteomyelitis reflecting the inability of host defense mechanisms to eradicate the responsible pathogen. Many authors have agreed on this classification and have used the term likewise in their publications (Koorbusch et al. 1992; Hudson 1993; Schuknecht et al. 1997; Schuknecht and Valavanis 2003; Eyrich et al. 1999; Baltensperger et al. 2004).

The term "subacute osteomyelitis" is not clearly defined in the literature. Many authors use the term interchangeably with acute osteomyelitis, and some use it to describe cases of chronic osteomyelitis with more prominent (subacute) symptoms. In some instances, subacute osteomyelitis is referred to as a transitional stage within the time frame of acute osteomyelitis and corresponds to the third and fourth week after onset of symptoms (Schuknecht et al. 1997; Schuknecht and Valavanis 2003).

2.5.2 Chronic Osteomyelitis

The classification of chronic osteomyelitis is incoherent and confusing. Different disease processes have been described by this one term in some instances, whereas several terms have been designated for lesions that represent the same entity in other instances (Groot et al. 1996; Eyrich et al. 1999).

Many authors agree that chronic osteomyelitis involving the jawbone may be divided in two major categories: suppurative and nonsuppurative forms (Mittermayer 1976; Hudson 1993; Topazian 1994, 2002; Bernier et al. 1995).

2.5.3 Chronic Suppurative Osteomyelitis: Secondary Chronic Osteomyelitis

Chronic suppurative osteomyelitis is an often preferred term in Anglo-American texts (Marx 1991; Bernier et al. 1995; Topazian 1994, 2002) and can mostly be used interchangeably with the term "secondary chronic osteomyelitis," which is predominantly used in literature from continental Europe (Hjorting-Hansen 1970; Panders and Hadders 1970; Schelhorn and Zenk 1989). It is by far the most common osteomyelitis type, which is usually caused by bacterial invasion from a contagious focus. Most frequent sources are odontogenic foci, periodontal diseases and pulpal infections, extraction wounds, and infected fractures. Pus, fistula, and sequestration are typical clinical findings of this disease. Clinically and radiographically, a broad spectrum ranging from an aggressive osteolytic putrefactive phase to a dry osteosclerotic phase may be observed (Eyrich et al. 1999).

2.5.4 Chronic Non-suppurative Osteomyelitis

The term "nonsuppurative osteomyelitis" describes a more heterogenic group of chronic osteomyelitis forms, which lacks the formation of pus and fistula. Topazian (1994, 2002) includes chronic sclerosing types of osteomyelitis, proliferative periostitis, as well as actinomycotic and radiation-induced forms to this group, whereas Bernier et al. (1995) advocate a more restrictive use of this term. Hudson (1993) uses the term to describe a condition of prolonged refractory osteomyelitis due to inadequate treatment, a compromised host, or increased virulence and antibiotic resistance of the involved microorganisms. This classification therefore also incorporates those cases in which a suppurative form of osteomyelitis can present as a nonsuppurative form in an advanced stage.

2.5.5 Diffuse Sclerosing Osteomyelitis, Primary Chronic Osteomyelitis, Florid Osseous Dysplasia, Juvenile Chronic Osteomyelitis

One of the most confusing terms among the currently used osteomyelitis nomenclature is "diffuse sclerosing osteomyelitis" (DSO). This term has apparently led to great confusion in the medical literature. A variety of denominations were used to describe this disease. One of the first descriptions was by Thoma in 1944, who used the term "ossifying osteomyelitis" and considered that a disease which was caused by a subpyogenic infection that could be found in tertiary syphilis. Sclerosing osteomyelitis was later described and divided into a focal

and diffuse types (Shafer 1957; Shafer et al. 1974; Pindborg and Hjorting-Hansen 1974; Mittermayer 1976; Topazian 1994, 2002). The focal type, also known as periapical osteitis/osteomyelitis or condensing osteitis, is a rather common condition with a pathognomonic, well-circumscribed radioopaque mass of sclerotic bone surrounding the apex of the root. Since the infection in these cases is limited to the apex of the root with the absence of deep bone invasion, sufficient endodontic treatment with or without apex surgery or extraction of the affected tooth usually leads to regression of these lesions or residual sclerosis may remain as a bone scar.

True diffuse sclerosing osteomyelitis, however, is a rare disease of unknown etiology that can cause major diagnostic and therapeutic problems (Jacobson 1984). The absence of pus, fistula, and sequestration are characteristic. The disease shows an insidious onset, lacking an acute state. It is therefore considered to be primary chronic and has been named primary chronic osteomyelitis by several authors, predominantly in the German and continental European medical and dental literature (Hjorting-Hansen 1970; Panders and Hadders 1970; Schelhorn and Zenk 1989; Eyrich at al 1999). Periods of onset usually last from a few days up to several weeks and may demonstrate a cyclic course with symptom-free intervals. Pain, swelling, and limitation of mouth opening, as well as occasional lymphadenopathy, dominate the clinical picture.

The term DSO is primarily descriptive of the radiological appearance of the pathological bone reaction; however, although the term is usually used synonymously with primary chronic osteomyelitis, it represents a description of a strictly radiological appearance that can be caused by several similar processes. These processes include primary and secondary chronic osteomyelitis, chronic tendoperiostitis, and ossifying periostitis or Garrè's osteomyelitis (Hjorting-Hansen 1970; Ellis et al. 1977; Eisenbund et al. 1981; Bünger 1984; Van Merkestyn et al. 1990; Groot et al. 1992b, 1996; Eyrich et al. 1999). This fact has most likely contributed to this diversity in nomenclature, as the terms are often used interchangeably.

A further pathological disease entity has been confused with diffuse sclerosing osteomyelitis, since it may mimic DSO radiographically by presenting sclerosing opaque and dense masses: florid osseous dysplasia (FOD). These masses are, however, confined to the alveolar process of either or both jaws in cases of FOD. Florid osseous dysplasia is mostly observed in black women and in many cases lacks clinical symptoms. Patients suffering from this disease, similar to true DSO, may in some instances also experience cyclic episodes of unilateral pain and mild swelling. This is usually the case when superinfection occurs (Schneider et al. 1990; Groot et al. 1996)

As with all pathologies of the bone which compromise local blood flow and host resistance, FOD makes the jaw more susceptible to secondary infection. In these instances pus and fistula formation may occur as well as sequestration (Carlson 1994). Many cases like these in the literature have, in retrospect, been incorrectly labeled as diffuse sclerosing osteomyelitis where these symptoms are by definition always absent. The FOD should therefore be considered more a bone pathology facilitating osteomyelitis once infection of the bone has been established and not equated with the infection itself.

As mentioned above, the exact etiology of true DSO remains unknown. A common theory is a low-grade infection of some kind; however, most biopsy specimens taken from the enoral and extraoral approach have failed to be conclusive, showing either no growth in cultures or growth only from suspected contaminants (Jacobson et al. 1982; Jacobson 1984; Van Merkesteyn et al. 1988). A study by Marx et al. (1994) demonstrated a high frequency of *Actinomyces*, *E. corrodens* species, *Arachnia* and *Bacteroides* spp. in cortical and medullar samples from patients with DSO. This study, like many others, still demonstrated insufficiencies regarding the protocol for collecting bone specimens and therefore was inconclusive. Moreover, a variety of antibiotics used over a long period consistently failed to fully eradicate the disease or arrest the symptoms (Jacobson 1984; Van Merkesteyn et al. 1988, 1990). Van Merkesteyn et al. (1990) and Groot et al. (1992a) have advocated other etiologies such as aberrant jaw positioning and parafunction; however, their theory lacks an explanation for those cases of true DSO in edentulous patients.

In our recent publications (Eyrich et al. 1999, 2003; Baltesperger et al. 2004) we used the term "juvenile chronic osteomyelitis," which resembles the clinical and radiological picture of Garrè's osteomyelitis as used by various authors. Heggie et al. (2000, 2003) made a similar observation when analyzing his young osteomyelitis patients and used the term "juvenile mandibular chronic osteomyelitis." This disease usually peaks at puberty and is characterized mostly by voluminous expansion of the mandibular body, periosteal apposition of bone ("periostitis ossificans"), and a mixed sclerotic-lytic appearance of the cancellous bone. The clinical

picture resembles primary chronic osteomyelitis, sharing the lack of pus formation, fistulae, or sequestration. Juvenile chronic osteomyelitis is therefore considered to be an early-onset form of primary chronic osteomyelitis. A further and more detailed description of this disease entity is described later in this chapter.

2.5.6 SAPHO Syndrome, Chronic Recurrent Multifocal Osteomyelitis (CRMO)

In 1986 Chamot et al. described a syndrome associated with synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO syndrome). Soon, several case reports and studies were published, concluding a possible relationship between SAPHO syndrome and DSO of the mandible (Brandt et al. 1995; Kahn et al. 1994; Garcia-Mann et al. 1996; Suei et al. 1996; Schilling et al. 1999; Eyrich et al. 1999; Roldan et al. 2001; Fleuridas et al. 2002). Kahn et al. (1994) presented a small series of seven patients with DSO of the mandible out of 85 cases of SAPHO syndrome. Eyrich et al. (1999) presented a series of nine patients with DSO, eight of which also represented a SAPHO syndrome, supporting the hypothesis of a possible association of the two.

Chronic recurrent multifocal osteomyelitis (CRMO) is characterized by periods of exacerbations and remissions over many years. This rare disease is noted in adults as in children, although it is predominant in the latter group. In several articles published in the past few years, a possible nosological relationship between diffuse sclerosing osteomyelitis and chronic recurrent multifocal osteomyelitis has been described (Reuland et al. 1992; Stewart et al. 1994; Suei et al. 1994, 1995; Flygare et al. 1997; Zebedin et al. 1998; Schilling 1998; Schilling et al. 1999). In correlation with advanced age, there seems to be an increased association with palmoplantar pustulosis, a part of the SAPHO syndrome (Shilling et al. 2000). Because of its possible relationship with other dermatoskeletal associated diseases, CRMO has been integrated in the nosological heterogeneous SAPHO syndrome by several authors (Chamot et al. 1994; Schilling and Kessler 1998; Schilling et al. 2000).

2.5.7 Periostitis Ossificans, Garrès Osteomyelitis

Strictly periostitis ossificans or ossifying periostitis is, like diffuse sclerosing osteomyelitis, a descriptive term for a condition that may be caused by several similar entities. It is merely a periosteal inflammatory reaction to many nonspecific stimuli, leading to the formation of an immature type of new bone outside the normal cortical layer.

Probably the most confusing and misinterpreted term regarding osteomyelitis is "Garrè's osteomyelitis." While most medical pathologists discard the term, it has still enjoyed great acceptance in the medical and dental literature, where occurrence in the jaws has been termed unequivocally (Eversole et al. 1979). Many terms have been used synonymously in the literature and attributed to Garrè, such as periostitis ossificans, chronic nonsuppurative osteomyelitis of Garrè, Garrè's proliferative periostitis, chronic sclerosing inflammation of the jaw, chronic osteomyelitis with proliferative periostitis, and many more. Table 2.5 gives an overview of the use of the term "Garrè's osteomyelitis" in the medical and dental literature; however, in his historical article in 1893, Carl Garrè did not actually describe a singular, specific type of osteomyelitis. Moreover he described special forms and complications of a single disease: acute infective osteomyelitis. He used 72 illustrative cases (98 sites) to discuss ten specific manifestations and complications of acute osteomyelitis. This is a direct contradiction to those authors who assume that he described a new form of chronic osteomyelitis (Wood et al. 1988).

2.5.8 Other Commonly Used Terms

2.5.8.1 Alveolar Osteitis (Dry Socket)

The clinical term "dry socket" or alveolar osteitis may also be regarded as a localized form of infection. Various authors have used this term differently. Hjorting-Hansen (1960) describes three principle forms of dry socket: alveolitis simplex; alveolitis granulomatosa; and an alveolitis sicca. Amler (1973) differentiates among alveolar osteitis, suppurative osteitis, and fibrous osteitis. The author concludes that the three types of osteitis correspond to disturbances during the natural healing process of an extraction alveolus. Meyer (1971) took great effort in demonstrating the histopathological changes in alveolar osteitis. He classifies this condition according to the degree of local invasion of the surrounding bone and uses the terms "osteitis circumscripta superficialis", "media" and "profunda". The term latter may be seen as a localized form of osteomyelitis; however, the

Table 2.5 Use of the term Garrè's osteomyelitis in medical and dental literature

Reference	Term used	Type of Publication
Batcheldor GD, Giansanti JS, Hibbard ED, Waldron CA (1) Garrè's osteomyelitis of the jaws: a review and report of two cases *J Am Dent Assoc 1973;87:892-7* Ellis DJ, Winslow JR, Indovina AA (2) Garrè's osteomyelitis of the mandible. Report of a case. *Oral Surg Oral Med Oral Pathol. 1977 Aug;44(2):183-9* Marx RE (3) Chronic Osteomyelitis of the Jaws Oral and Maxillofacial Surgery Clinics of North America, Vol 3, No 2, May 91, 367-81	Garrè's osteomyelitis	Case report (1 & 2) Review article (3)
Perriman A, Uthman A Periostitis ossificans. Br J Oral Surg 1972; 10:211-6	Periostitis ossificans	Review article
Smith SN, Farman AG. Osteomyelitis with proliferative periostitis (Garrè's osteomyelitis). Report of a case affecting the mandible. *Oral Surg Oral Med Oral Pathol. 1977 Feb;43(2):315-8*	Osteomyelitis with proliferative periostitis	Case report
Eisenbud L, Miller J, Roberts IL Garrè's proliferative periostitis occurring simultaneously in four quadrants of the jaws. *Oral SurgOral Med Oral Pathol. 1981 Feb;51(2):172-8*	Garrè's proliferativ e periostitis	Case report
Panders AK, Hadders HN Chronic sclerosing inflammations of the jaw. Osteomyelitis sicca (Garrè), chronic sclerosing osteomyelitis with finemeshed trabecular structure, and very dense sclerosing osteomyelitis. *Oral Surg Oral Med Oral Pathol 1970 Sep;30(3):396-412*	Osteomyelitis sicca (synonymous osteomyelitis of Garrè, chronic sclerosing nonsuppurative osteomyelitis of Garrè, periostitis ossificans)	Review article
Mittermayer CH Oralpathologie. *Schattauer, Stuttgart-New York 1976*	Chronic osteomyelitis with proliferative periostitis (Garrè's chronic nonsuppurative sclerosing osteitis, ossifying periostitis)	Textbook
Schelhorn P, Zenk W [Clinics and therapy of the osteomyelitis of the lower jaw]. *Stomatol DDR 1989 Oct;39(10):672-6* Bernier S, Clermont S, Maranda G, Turcotte JY Osteomyelitis of the jaws J Can Dent Assoc 1995 May;61(5):441-2, 445-8	Chronic sclerosing osteomyelitis Garrè, Garrè's chronic sclerosing osteomyelitis (proliferative osteomyelitis)	Review article
Topazian RG Osteomyelitis of the Jaws. In Topizan RG, Goldberg MH (eds): Oral and Maxillofacial Infections. *Philadelphia, WB Saunders 1994, Chapter 7, pp 251-88*	Garrè's sclerosing osteomyelitis	Textbook

term "alveolar osteitis" (dry socket) is generally used in the medical and dental literature to describe an absence of invasion into the bone. It should therefore not be regarded as a form of osteomyelitis (Marx 1991). In alveolar osteitis the commonly advocated theory suggests a clot breakdown due to the release of fibrinolysins either from microorganisms or trauma. In both situations the bacteria remain on the surface of the exposed bone, and an actual invasion does not occur. Although not considered a true infection, alveolar osteitis may lead to acute or secondary chronic osteomyelitis once the bacterial invasion into the medullar and cortical bone has occurred and a deep bone infection has been established.

2.5.8.2 Osteoradionecrosis and Radioosteomyelitis

Radiotherapy is considered a major column in the treatment of head and neck malignancies. Despite recent advances in radiotherapy, such as using modern three-dimensional techniques, as well as hyperfractionation or moderately accelerated fractionation and consequent prophylactic dental treatment, osteoradionecrosis is still an observed condition in maxillofacial units.

Aside from its effect on the tumor cells, radiation also has serious side effects on the soft and hard tissues adjacent to the neoplasm. Mucositis, atrophic mucosa, xerostomia, and radiation caries are well-known side effects of head and neck radiotherapy. Because of its mineral composition, bone tissue absorbs more energy than soft tissues and is therefore more susceptible to secondary radiation. In cases where the bone is irradiated exceeding a certain local dose, osteoradionecrosis may develop, leading to marked pain in the patient and possible loss of bone leading to functional and aesthetic impairment.

Osteoradionecrosis was once considered an infection initiated by bacteria, which invaded the radiation-damaged bone; hence, the term "radiation-induced osteomyelitis" or radioosteomyelitis was commonly used. Marx (1983) conclusively identified this condition as a radiation-induced avascular necrosis of bone. He was able to demonstrate that radiation caused a hypoxic, hypocellular, and hypovascular tissue, leading to a spontaneous or trauma-initiated tissue breakdown. The result is a chronic nonhealing wound, susceptible to superinfection. As in florid osseous dysplasia and other bone pathologies, microorganisms are responsible for contamination and, if invasion occurs, secondary infection of the bone, resulting in osteomyelitis.

2.5.8.3 Osteochemonecrosis

The medical literature describes several drugs and substances that facilitate or induce conditions known as osteonecrosis of the jaws, such as corticosteroids and other cancer and antineoplastic drugs. Exposure to white phosphorous among workers in the matchmaking industry in the nineteenth century has led to unusual necroses of the jaws, which became known in the literature as phossy jaw or phosphorous necrosis of the jaw.

In the recent years bisphosphonate therapy has become a widely accepted mainstay of therapy in various clinical settings such as multiple myeloma, metastatic cancer therapy, and treatment of advanced osteoporosis. With the increased prescription of these drugs, the incidence and prevalence of bisphosphonate-associated complications of the jaw continues to be elucidated. This trend seems to be even more the case in patients receiving injectable bisphosphonates, such as pamidronate and zoledronic acid, but cases involving osteochemonecrosis of the jaw associated with chronic peroral administered bisphosphonates have also been reported (Ruggiero et al. 2004, 2006).

The pathophysiological mechanisms leading to bisphosphonate-induced osteochemonecrosis of the jaws are yet far from being fully understood; however, it seems apparent that important differences to the pathogenesis of osteoradionecrosis do occur (Hellenstein and Marek 2005). In bisphosphonate-induced osteochemonecrosis of the jaws osteoclastic action is reduced, but osteoblastic production continues, leading to an osteopetrosis-like condition (Whyte et al. 2003). These alterations in bone physiology with eventual increase of the medullary bone as the disease progresses and the inability of osteoclasts to remove superinfected "diseased" bone are regarded as causative factors. In contrast to osteoradionecrosis, where a radiation-induced avascular necrosis is the major cause, avascularity does not appear to be a major cofactor to date; however, inhibition of angiogenesis is currently being actively investigated (Fournier et al. 2002; Wood et al. 2002), and further research will hopefully help fully understanding its role in pathogenesis of this disease.

Regarding the current data and knowledge, we favor the term "bisphosphonate-induced osteochemonecrosis of the jaw" because it is not restricted to a certain pathogenesis. The term "bisphosphonate osteomyelitis" should not be used for the same reasons as the term radioosteomyelitis should be abandoned. The jawbone

with bisphosphonate-induced osteochemonecrosis is far more susceptible to bacterial invasion due to its strongly altered physiology; however, infection of the bone is to be considered a secondary phenomenon and not the primary cause of this disease entity.

2.6 Osteomyelitis of the Jaws: The Zurich Classification System

2.6.1 General Aspects of the Zurich Classification System

Osteomyelitis of the jaw as a clinical entity has long been recognized in the medical literature. As mentioned previously, various classification systems and nomenclatures of the disease have evolved with time. The heterogeneity of the classification systems is borne by the fact that several modalities are used to describe and define maxillofacial osteomyelitis. These modalities include etiology and pathogenesis, clinical presentation and course, radiology, and histopathology. Furthermore, most classification forms represent a mixture of these criteria, causing confusion, thereby hindering comparative studies.

At the Department of Cranio-Maxillofacial Surgery at the University of Zurich, the classification system for osteomyelitis of the jaws uses a hierarchical order of classification criteria. It is primarily based on clinical appearance and course of the disease, as well as on radiological features. Based on these criteria, three major groups of osteomyelitis can be distinguished:

1. Acute Osteomyelitis (AO)
2. Secondary Chronic Osteomyelitis (SCO)
3. Primary Chronic Osteomyelitis (PCO)

Within these major groups, the clinical presentation is similar in the majority of cases; however, as will be described later, a certain variety of the clinical course is noted, especially in cases of primary and secondary chronic osteomyelitis.

Histopathology is considered a secondary classification criterion, taking into account that findings are mostly unspecific and nonconclusive when considered by themselves; however, tissue examinations of biopsies are irreplaceable for confirmation of the diagnosis in cases of unclear and atypical clinical and radiological appearance, and moreover in excluding possible differential diagnosis.

Furthermore, in some cases of osteomyelitis with an atypical appearance a synthesis of medical history, clinical presentation, imaging studies, histopathology, and other diagnostic tools may be necessary to achieve an appropriate diagnosis.

Analysis of the osteomyelitis patients treated in the Department of Cranio-Maxillofacial Surgery in Zurich using the abovementioned major classification groups showed a clear predominance of cases diagnosed as secondary chronic osteomyelitis at the time of presentation, whereas cases of acute osteomyelitis and primary chronic osteomyelitis were significantly less often diagnosed (Table 2.6). In a small group of nine patients, despite meticulous work-up of all data including clinical course and symptoms, diagnostic imaging, laboratory

Table 2.6 Distribution of osteomyelitis cases treated at the Department of Cranio-Maxillofacial Surgery in Zurich, 1970–2000 (Baltensperger 2003)

Major groups of osteomyelitis of the jaws	Cases	
	N	%
Acute osteomyelitis (AO)	48	16.6%
Secondary chronic osteomyelitis (SCO)	203	70.0%
Primary chronic osteomyelitis (PCO)	30	10.3%
Not clearly classifiable/questionable osteomyelitis	9	3.1%
Total	290	100.0%

findings, and histopathology, no clear diagnosis was possible. Most of these cases showed a chronic course resembling primary chronic osteomyelitis or a (diffuse) sclerosing form of secondary chronic osteomyelitis. In some of these cases the diagnosis of osteomyelitis was even questionable. The problems in diagnosis of these challenging cases and possible related differential diagnosis are outlined later in this chapter.

Further subclassification of these major osteomyelitis groups is based on presumed etiology and pathogenesis of disease. These criteria are therefore considered tertiary classification criteria. These tertiary criteria are helpful in determining the necessary therapeutic strategies which may differ somewhat among the subgroups. The nature of these subgroups are outlined in more detail later in this chapter.

An overview of the Zurich classification of osteomyelitis of the jaws and the classification criteria are given in Fig. 2.2 and Table 2.7.

2.6.2 Acute Osteomyelitis and Secondary Chronic Osteomyelitis

2.6.2.1 Definitions

The basic terminology used in the Zurich classification of osteomyelitis of the jaws was promoted by Hugo Obwegeser, among others. The general principles of this classification system were described and published by E. Hjorting-Hanson, a former staff member at the Department of Cranio-Maxillofacial Surgery Zurich, in 1970. Hjorting-Hanson, as many other authors before and after him, gave an excellent description of the clinical and radiological picture of acute and secondary chronic osteomyelitis; however, he fell short of clearly defining at what stage an acute/subacute osteomyelitis should be considered chronic. To our knowledge, Marx (1991) and Mercuri (1991) were the first and only authors to define the duration for an acute osteomyelitis

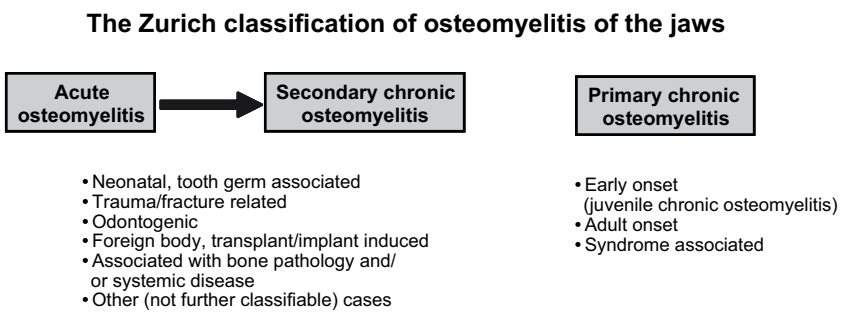


Fig. 2.2 The Zurich classification of osteomyelitis of the jaws: since secondary chronic osteomyelitis is a sequel of the prolonged and chronified acute form, both basically have the same subclassification groups

Table 2.7 Classification criteria upon which the Zurich classification of osteomyelitis is based

Hierarchic order of classification criteria	Classification criteria	Classification groups
First	Clinical appearance and course of disease Radiology	Major Groups Acute osteomyelitis (AO) Secondary chronic osteomyelitis (SCO) Primary chronic osteomyelitis (PCO)
Second	Pathology (gross pathology and histology)	Differentiation of cases that cannot clearly be distinguished solely on clinical appearance and course of disease; important for exclusion of differential diagnosis in borderline cases.
Third	Etiology Pathogenesis	Subgroups of AO, SCO, and PCO

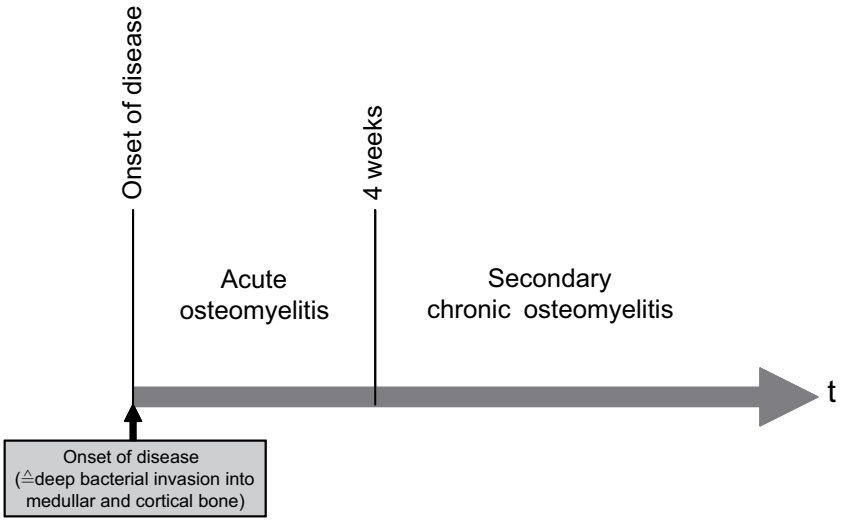


Fig. 2.3 Definition of acute and secondary chronic osteomyelitis of the jawbone (Adapted from Marx and Mercuri 1991)

until it should be considered as chronic. They set an arbitrary time limit of 4 weeks after onset of disease. Pathological–anatomical onset of osteomyelitis corresponds to deep bacterial invasion into the medullar and cortical bone. After the period of 4 weeks, a persisting bone infection should be considered as secondary chronic osteomyelitis (Fig. 2.3). Although the onset of the disease is a debatable point in time, it is still a simple and clear classification criterion and therefore of practical use for the clinician. This same definition was later used by several other authors (Eyrich et al. 1999; Schuknecht et al. 1997; Koorbusch et al. 1992). Because of its simplicity and clarity, this criterion is also used in the Zurich classification to differentiate acute osteomyelitis from secondary chronic osteomyelitis cases.

The term "subacute osteomyelitis" is not clearly defined in the literature. Most clinicians would probably agree that this term describes a condition somewhat in between acute and chronic osteomyelitis with relatively moderate symptoms. To avoid confusion and keep the classification as simple as possible, this term has been abandoned in the Zurich classification.

According to this definition, acute and secondary chronic osteomyelitis are to be considered the same disease at different stages of their course; hence, both groups are presented and discussed together in this chapter.

2.6.2.2 Predisposing Factors, Etiology, and Pathogenesis

2.6.2.2.1 General Considerations

As mentioned previously, there are several etiological factors, such as traumatic injuries, radiation, and certain chemical substances, among others, which may cause inflammation in the medullar space of the bone; however, acute and secondary chronic osteomyelitis, as these terms are generally used in the medical and dental literature and in this textbook, represent a true infection of the bone induced by pyogenic microorganisms.

The oral cavity harbors a large number of bacteria, among which many may be identified as possible pathogens to cause infection of the jawbone. Regarding the high frequency and sometimes severity of odontogenic infections in the daily dental and oral surgery practice, and the intimate relationship of dental roots apices with the medullar cavity of the jawbone, it is remarkable that osteomyelitis cases are not more frequently observed. Explanation for the low incidence of osteomyelitis of the jawbones can be explained by four primary factors which are responsible for deep bacterial invasion into the medullar cavity and cortical bone and hence establishment of the infection:

1. Number of pathogens
2. Virulence of pathogens
3. Local and systemic host immunity
4. Local tissue perfusion

Close interaction of these factors, as shown in Fig. 2.5, determine the pathological pathway of disease formation. In the healthy individual with sufficient host immunity mechanisms these factors form a carefully balanced equilibrium. If this equilibrium is disturbed by altering one or more of these factors, deep bone infection will be established (Figs. 2.4, 2.5).

2.6.2.2.2 Local and Systemic Host Immunity

The oral cavity, like no other part of the human body, is constantly exposed to various potential aggressors. Many of these bacteria, given the chance, may cause severe infection and damage to the tissue if they are not kept at distance. Due to its unique environment, many potent strategies have been developed to prevent deep tissue invasion of bacteria. Specific local immunological mechanisms, potent barrier systems, such as the periodontal membrane and a rich local vascular supply, are the most important. A more detailed description of these and other defense systems is provided extensively in specific literature and is beyond the scope of this book.

Every systemic disease with concomitant alterations in host defenses may influence profoundly the onset and course of acute and secondary chronic osteomyelitis. An alteration of some extent is probably the reason why osteomyelitis of the jaws develops in most cases, regardless of whether or not such deficiencies can be detected. Although the data is limited and lacks evidence-based criteria in most instances, osteomyelitis has been associated with a variety of systemic diseases and pathological conditions. A list of such diseases and conditions, as well their mechanisms, are given in Tables 2.8 and 2.9. In our retrospective study of 244 cases of acute and secondary chronic osteomyelitis of the jaws, alcohol and tobacco consumption were observed in 33.2 and 47.5% of the cases, respectively, while other conditions, as shown in Table 2.8, were only observed in a scarce number of patients (Baltensperger 2003); however, more important in this study than the mentioned systemic factors seemed to be the high prevalence of local infection in the examined patients with acute and secondary chronic osteomyelitis. Especially periodontal disease, which leads to a breakdown of the periodontal barrier membrane, facilitating deep invasion pathogens, seems to be an important condition leading to osteomyelitis. Significant periodontal disease was found in 51% of the patients of the same study.

It is important for the treating physician to consider host compromise and treat any compromising condition, when feasible, concomitantly with the infection.

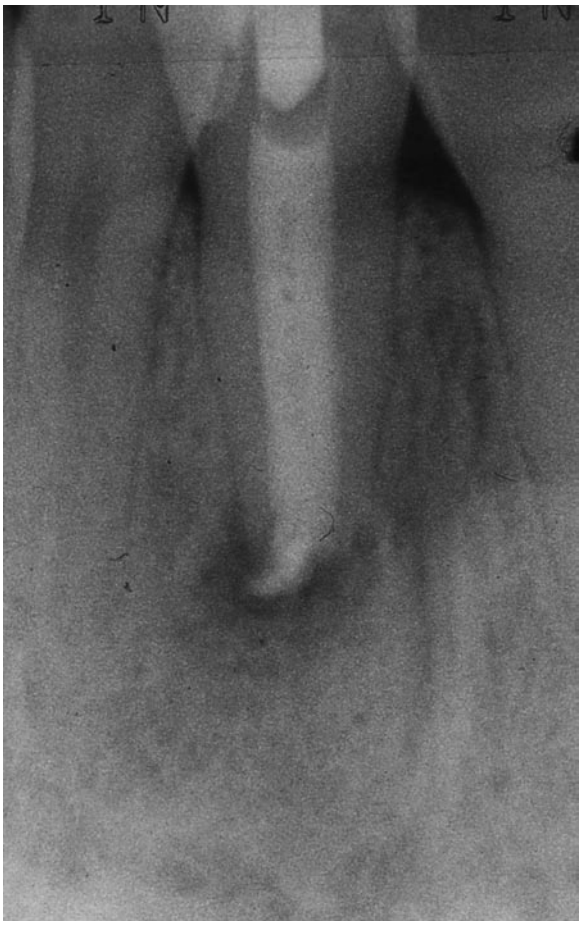


Fig. 2.4 Chronic infection of the periapical bone as a sequel of endodontic disease. This frequently observed condition represents a classical equilibrium between microbiological aggressors and host factors hindering further spread of the bacteria. If this balance is disturbed and shifts toward the side of the microorganisms, deep invasion into the medullar and cortical bone may occur and osteomyelitis is established

2.6.2.2.3 Local and Systemic Alterations in Bone Vascularity

Compromise of local blood supply must be considered a critical factor in the establishment of osteomyelitis. Systemic and local conditions that alter the vascularity of bone predispose the development of osteomyelitis. In these conditions immune cells and oxygen cannot reach the target area in an adequate manner. This facilitates the growth and spread of microorganisms, especially anaerobes, leading to establishment and progression of osteomyelitis. An overview of conditions compromising

blood supply of the jawbone is given in Table 2.10. In many cases of acute and secondary chronic osteomyelitis none of these factors may be apparent or detected; however, they must always be considered, looked for, and ultimately treated (Baltensperger 2003).

2.6.2.2.4 Microbiology

Acute and secondary chronic osteomyelitis are considered true infections of the bone induced by pyogenic microorganisms. As shown in Fig. 2.5, the number and virulence of these pathogens are important factors in the establishment of a bone infection.

Although until recently involvement of *S. aureus*, *S. epidermidis*, and *Actinomyces* were still discussed as the major pathogens in cases of osteomyelitis of the jaws, more recent studies favor the concept of a polymicrobic infection with several responsible pathogens. This shift in doctrine is explained mainly by modern, sophisticated culture methods, especially involving anaerobic media, which enable identification of possible pathogens more accurately. Consequently, many pathogens, which are mostly found in the healthy oral flora, have been associated with cases of jawbone osteomyelitis; however, prolonged antibiotic therapy prior to harvesting of the specimen and possible oral contamination complicate the interpretation of each result.

A more detailed overview and in-depth information on this topic is provided in Chap. 7.

2.6.2.2.5 Etiology and Pathogenesis, Subclassification Groups

According to the classification criteria stated previously, subclassification of acute and secondary chronic osteomyelitis is based on presumed etiology and pathogenesis of disease (Tables 2.7 and 2.11). Acute and secondary chronic osteomyelitis are initiated by a contagious focus of infection or by hematogenous spread. In osteomyelitis of long bones, hematogenous spread is the leading cause, especially in infants and children, because of the distinct anatomy of the metaphyseal region. In most of these cases a single responsible pathogen can be isolated (Mader and Calhoun 2000). *Staphylococcus* spp. are the most common organisms isolated in adults and are also prominent in children and infants.

Osteomyelitis of the jaws induced by hematogenous spread has become a rarity since the introduction of antibiotics; however, in regions of limited medical access these forms may still be noted. Especially one form of osteomyelitis of hematogenous spread merits special mention: neonatal or tooth-germ-induced acute osteomyelitis of the jaws. Because of its risks of involvement of the eye, spreading to the dural sinuses and creating loss of teeth and facial bone deformities if treated inadequately, this type of osteomyelitis should be remembered. Neonatal or tooth-germ-induced acute osteomyelitis occurs most often within the first few weeks after birth, affecting the upper jaw in most instances. This infection showed a mortality rate of up to 30% before the advent of an-

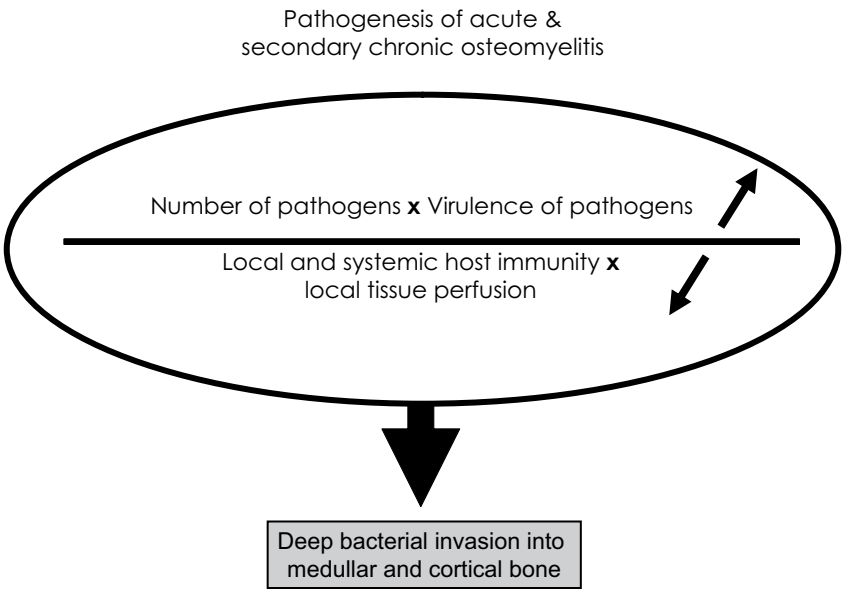


Fig. 2.5 Schematic illustration showing the interaction of host and pathogens. If the balance is shifted to the advantage of the aggressor, deep bone infection will be established (Modified after Marx 1999 and Mercuri 1999)

Table 2.8 Systemic host factors facilitating development of acute and secondary chronic osteomyelitis of the jawbone due to impairment of immune response mechanisms (Modified from Marx 1991; Mercuri 1991; Sanders 1978; Barbaglio et al. 1998; Battaglia et al. 1991; Bishop et al. 1995; Cheung et al. 1999; Exner et al. 1995; Groot et al. 1995; Hovi et al. 1996; Lawoyin et al. 1988; Melrose et al. 1976; Podlesh et al. 1996; Shroyer et al. 1991; Topazian 1994, 2002; Diktaban 1992; Koorbush et al. 1992; Eversole et al 1979; Meer et al. 2006)

Systemic factors altering host immunity	
• Diabetes mellitus • Autoimmune disorders • AIDS • Agranulocytosis • Anemia (especially sickle cell) • Leukemia • Syphilis	• Malnutrition • Chemotherapy • Corticosteroid and other immunosuppressive therapy • Alcohol and tobacco • Drug abuse • Prior major surgery • Herpes simplex virus (Zoster) and cytomegalovirus infection

Table 2.9 Mechanisms of systemic diseases/conditions predisposing to osteomyelitis (Adapted from Marx 1991)

Disease	Mechanism facilitating bone infection
Diabetes	Diminished leukocyte chemotaxis, phagocytosis, and lifespan; diminished vascularity of tissue due to vasculopathy, thus reducing perfusion and the ability for an effective inflammatory response; slower healing rate due to reduced tissue perfusion and defective glucose utilization
Leukemia	Deficient leukocyte function and associated anemia
Malnutrition	Reduced wound healing and reduction of immunological response
Cancer	Reduced wound healing and reduction of immunological response
Osteopetrosis (Albers–Schonberg disease)	Reduction of bone vascularization due to enhanced mineralization, replacement of hematopoietic marrow causing anemia and leukopenia
Severe anemia (particularly sickle-cell anemia)	Systemic debilitation, reduced tissue oxygenation, bone infarction (sickle cell anemia), especially in patients with a homozygous anemia trait
IV drug abuse	Repeated septic injections, spreading of septic emboli (especially with harboring septic vegetation on heart valves, in skin or within veins)
AIDS	Impaired immune response
Immunosuppression (steroids, cytostatic drugs)	Impaired immune response

Table 2.10 Host factors facilitating development of acute and secondary chronic osteomyelitis of the jawbone due to compromise of local blood supply (Modified from Marx 1991; Mercuri 1991; Sanders 1978; Barbaglio et al. 1998; Battaglia et al. 1991; Bishop et al. 1995; Cheung et al. 1999; Exner et al. 1995; Groot et al. 1995; Hovi et al. 1996; Lawoyin et al. 1988; Melrose et al. 1976; Podlesh et al. 1996; Shroyer et al. 1991; Topazian 1994, 2002; Diktaban 1992; Koorbush et al. 1992; Eversole et al 1979)

Local and systemic factors altering bone vascularity	
• Smoking • Diabetes mellitus • Florid osseous dysplasia • Fibrous dysplasia • Paget's disease • Osteopetrosis (Albers–Schonberg Disease)	• Osteoporosis • Bisphosphonate induced osteochemonecrosis • Other forms of osteonecrosis (mercury, bismuth, arsenic) • Tobacco • Radiation therapy and osteoradionecrosis • Bone malignancy (primary or metastatic)

tibiotics. The route of infection is considered by most clinicians to be hematogenous (Bass 1928; Lacey and Engel 1939; Heslop and Rowe 1956; Nade 1983), although a local infection caused by perinatal trauma of the oral mucosa and local trauma to the overlying mucosa of the alveolar ridge (Hitchin and Naylor 1957; Nade 1983; Topazian 1994, 2002), as well as extension of infection from adjacent teeth or soft tissues, are also discussed (Loh and Ling 1993). *Staphylococcus aureus* has been implicated as the organism responsible for this type of acute osteomyelitis (Asherson 1939; Haworth 1947; McCasch and Rowe 1953; Niego 1970; Nade 1983; Loh and Ling 1993).

The vast majority of cases of acute and secondary chronic osteomyelitis involving the jaws are usually caused by infection primarily spreading by a contagious focus. The most common foci are odontogenic, originating from infected pulp or periodontal tissue or infected pericoronal tissue from retained teeth, especially third molars.

Trauma, especially compound fractures, is also a major condition, which if not treated or treated inadequately, facilitates the development of osteomyelitis. But also every type of jawbone surgery, including surgical removal of impacted third molars, inevitably leads to a certain degree of local trauma to the bone, which causes local ischemia and may facilitate deep invasion of bacteria into the medullar cavity; hence, osteomyelitis can be established. Especially additional trauma to a preexisting chronic local infection carries a great risk of causing deep bone infection. Foreign bodies as well as the various transplants and implants used in maxillofacial and dental surgery also may harbor microorganisms and hence facilitate further spreading to the surrounding bone.

Several types of bone pathologies and systemic conditions, as mentioned previously, influence local tissue perfusion and immunity and therefore are important cofactors in establishing bone infection. In rare cases, infections derived from periostitis after gingival ulceration, furuncles, and facial and oral lacerations may also be considered causative.

In some instances the etiology and pathogenesis remains unclear or can only be speculated. These cases are subclassified as "other" in the classification system proposed in this book.

A distribution of acute and secondary chronic osteomyelitis cases, according to their etiology and pathogenesis, and their subclassification, respectively, is given in Table 2.12.

The distribution of acute and secondary chronic osteomyelitis shows a clear predominance of the mandible. In our patient data from 251 cases of acute and secondary chronic osteomyelitis only 16 patients (6.4%) demonstrated involvement of the upper jaw, whereas in the vast majority of cases (n=235; 93.6%) the mandible was the infected bone (Baltensperger 2003). The different anatomy of maxilla and mandible is probably the most important factor explaining the distribution of osteomyelitis involving the jawbones. The maxillary blood supply is more extensive than in the mandible. Additional thin cortical plates and the paucity of medullary tissues in the maxilla preclude confinement of infections within the bone and permit dissipation of edema and pus into the soft tissues of the midface and the paranasal sinuses (Topazian 1994, 2002). Maxillary osteomyelitis with tooth exfoliation after herpes zoster reactivation and concomitant cytomegalovirus infection has recently gained attention based on a review of the literature and 27 previous reports of herpes zoster-induced jaw infections (Meer et al. 2006).

The mandible is like a squashed long bone which has been shaped in a U-form. Like all long bones there is a clear distinction of a medullary cavity, dense cortical plates, and a well-defined periosteum on the outer border of the cortical bone. The medullary cavity is lined by

Table 2.11 Subclassification of acute and secondary chronic osteomyelitis of the jaws

Subclassification of acute and secondary chronic osteomyelitis of the jaws
Induced by hematogenous spread:
Neonatal, tooth germ associated
Extension from a local infection:
Trauma/fracture related
Odontogenic
Foreign body, transplant/implant induced
Associated with bone pathology and/or systemic disease
Other

the endosteum, which, like the periosteum, is a membrane of cells containing large numbers of osteoblasts. Within the medullary cavity a large variety of cells, such as reticuloendothelial cells, erythrocytes, granulocytes, platelets, and osteoblastic precursors, are harbored, as well as cancellous bone, fat, and blood vessels. Bone spicules radiate centrally from cortical bone to produce a scaffold of interconnecting trabeculae (Copehaver et al. 1978). The architecture of mandibular cortical bone resembles that of other long bones. Longitudinally orientated haversian systems (osteons), each with a central canal and blood vessel that provide nutrients by means of canaliculi to osteocytes contained within lacunae. These canals communicate with adjunct haversian systems as well with the periosteum and the marrow space by Volkmann's canals, thus forming a complex interconnecting vascular and neural network that nourishes bone and enables bone metabolism, necessary for repair, regeneration, and functional adaptation.

Acute and secondary chronic osteomyelitis of the mandible affects most commonly the body of the mandible, followed by the symphysis, angle, ascending ramus, and condyle (Calhoun et al. 1988; Baltensperger 2003).

The compromise of local blood supply is the critical factor and final common pathway in the establishment of acute and secondary chronic osteomyelitis (Fig. 2.7). Wannfors and Gazelius (1991) demonstrated by means of laser Doppler flowmetry (LDF) that long-standing local inflammation of the mandible was associated with a persistent reduction in blood flow.

Except for the coronoid process, which is supplied primarily from the temporalis muscle and the mandibular condyle, which is supplied in part by vessels from the lateral pterygoid muscle and the temporomandibular joint (TMJ) capsule, the major blood supply of the rest of the mandible consists of the inferior alveolar artery (Fig. 2.6). A secondary source is provided by the vessels of the periosteum. These vessels are organized in a reticular manner and run alongside of the cortical surface, giving off small nutrient vessels that penetrate the cortical bone and anastomose with branches of the inferior alveolar artery (Fig. 2.6; Castelli 1963; Cohen 1959); however, the value of the periosteal circulation probably cannot be seen as full replacement of the vascular supply of the marrow space. Hence, despite this adjunctive vascularization of the mandible through the periosteum, the main blood supply is derived from the inferior alveolar artery which, especially in elderly patients, is a vessel of small caliber and most susceptible to damage. This context can be transferred to the clinical appearance of osteomyelitis of the mandible, where occlusion of the inferior alveolar artery inevitably boosts the progress of the infection even if an intact periosteum is still present.

In most incidences periapical and periodontal infections are localized by a protective pyogenic membrane or soft tissue abscess wall which serves as a certain barrier (Schroeder 1991). As mentioned above, this condition represents a carefully balanced equilibrium between microorganisms and host resistance preventing further spreading of the infection. If the causative bacteria are sufficient in number and virulence, this barrier can be destroyed. Furthermore, permanent or temporary reduction of host resistance factors for various reasons mentioned previously facilitate deep bone invasion

Table 2.12 Etiology and pathogenesis of acute and secondary osteomyelitis cases treated at the Department of Cranio-Maxillofacial Surgery in Zurich, 1970-2000, according to Baltensperger (2003)

Subclassification groups of acute and secondary chronic osteomyelitis	Cases	
	N°	%
Induced by hematogenous spread	2	0.80
Neonatal, tooth germ associated		
Extension from a local infection		
Trauma/fracture related	42	16.73
Odontogenic	173	68.92
Foreign body, transplant/implant induced	13	5.18
Associated with bone pathology and/or systemic disease	5	1.99
Other	16	6.37
Total	251	100.00

of the microorganisms. This invasion induces a cascade of inflammatory host responses causing hyperemia, increased capillary permeability, and local inflammation of granulocytes. Proteolytic enzymes are released during this immunological reaction creating tissue necrosis, which further progresses as destruction of bacteria and vascular thrombosis ensue. Accumulation of pus inside the medullary cavity, consisting of necrotic tissue and dead bacteria within white blood cells, increases intramedullary pressure. This leads to vascular collapse, venous stasis, thrombosis, and hence local ischemia (A in Fig. 2.7; Topazian 1994, 2002). Pus travels through the haversian and nutrient canals and accumulates beneath the periosteum, elevating it from the cortical bone and thereby further reducing the vascular supply (B in Fig. 2.7; Topazian 1994, 2002). Elevation of the periosteum is usually observed more extensively in children, presumably because the periosteum is less firmly attached to the cortical bone than in adults. When pus accumulates continually underneath the periosteum, perforation may occur, leading to mucosal and cutaneous abscesses, and fistulas may develop.

In mandibular osteomyelitis, the increased intramedullary pressure also leads to direct compression of the neurovascular bundle, accelerating thrombosis and ischemia resulting in dysfunction of the inferior alveolar nerve, known as Vincent's symptom. The mandibular canal is also an anatomical pathway with no barrier function, alongside which pus can spread quickly (Fig. 2.8).

2.6.2.2.6 Chronification of Bone Infection

The chronification of the disease reflects the inability of the host to eradicate the pathogen due to lack of treat-

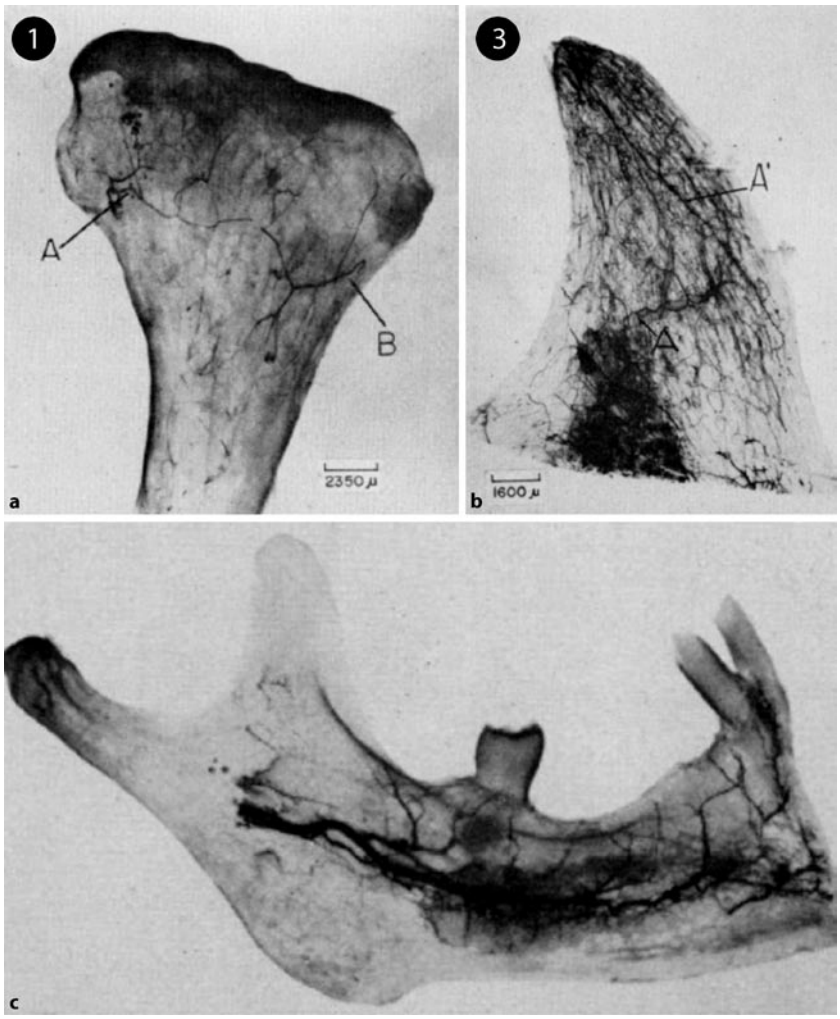


Fig. 2.6 **a** Condylar process arteries of an injected human head. Mandible soft parts were discarded after injection was performed through the common carotid artery. *A* artery coming from the lateral pterygoid muscle, *B* artery coming from vessels of the temporomandibular joint capsule (Teichmann's paste injection; decalcified and cleared). **b** Coronoid process arterial vessels. Two arterioles (*A* and *A'*) are present, both coming from the temporalis muscle (China-ink solution injection; decalcified and cleared). **c** Overall view of injected inferior alveolar artery (Teichmann's paste injection; decalcified and cleared). (From Castelli 1963)

ment or inadequate treatment, resulting in failure to reestablish the carefully balanced equilibrium between host factors and pathogens found in a healthy oral environment.

After the acute inflammatory process occurs and local blood supply is compromised, necrosis of the endosteal bone takes place. The bone fragments die and become sequestra (Fig. 2.9). Osteoclastic activity is then responsible for separating the dead bone from vital bone. Devital bone tissue clinically appears dirty, whitish-gray with an opaque appearance. Its fatty tissue has been destroyed and it does not bleed if scraped (Marx 1991). In some instances the bone sequester can demonstrate considerable dimensions (Fig. 2.10).

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 fistula. As chronification progresses this scenario may be repeated (Figs. 2.11, 2.12). The involucrum tends to hinder sequester from extruding, which perpetuates the process because the whole area is bathed in increasing amounts of pus unless treated promptly and adequately (Killey and Kay 1970).

In secondary chronic osteomyelitis of the jaws, eventually a new equilibrium is established between the host and the aggressor causing the infection. The nature of this newly formed equilibrium is dependent on host immunity supported by medical therapy and the causative bacteria. It dictates the further course of the infection:

- If adequate therapy is administered on time, balance is shifted in favor of the host, resulting in complete healing of the infection.
- If no or inadequate therapy is provided, the disease may progress slowly or faster depending on the number and virulence of the bacteria and the remaining host defenses.
- If the number and virulence of the bacteria are small, host mechanisms may overwhelm, but still fail to fully eradicate the pathogen. In these instances a strong and diffuse sclerosis of the bone with or without a significant periosteal reaction can be noted. The clinical and radiological picture may then resemble primary chronic osteomyelitis.

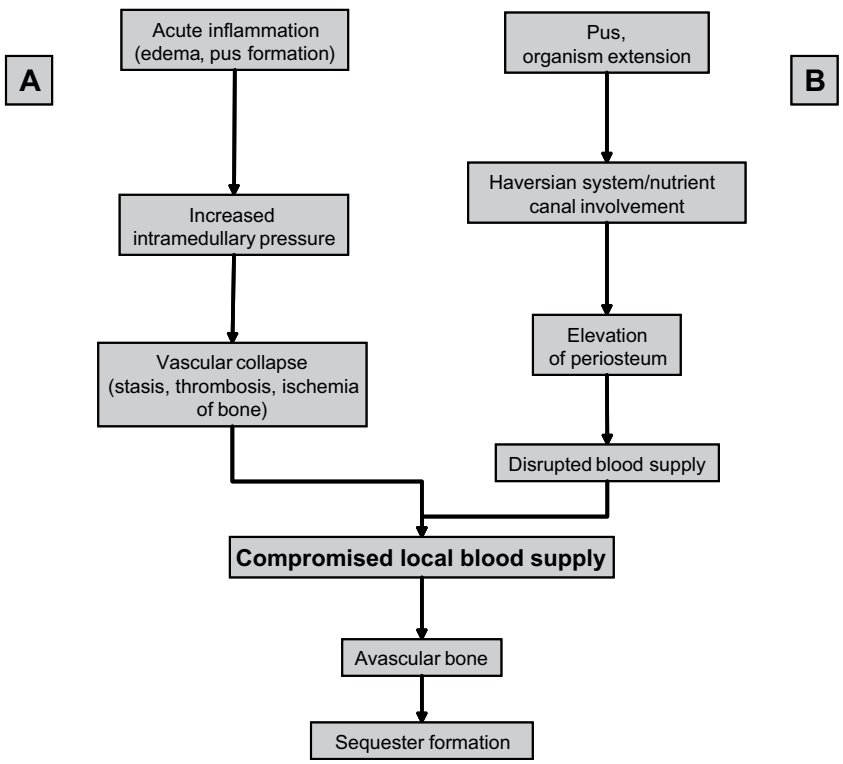
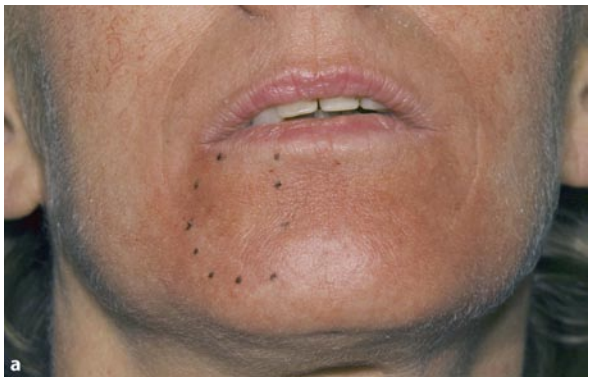


Fig. 2.7 Pathogenesis of acute and secondary chronic osteomyelitis of the jaws. Pathway *A* shows the role of inflammation and pathway *B* the role of pus formation in compromising blood supply of the infected bone, which can be considered as the final common pathway in the formation of sequestra (Modified from Topazian 1994, 2002)



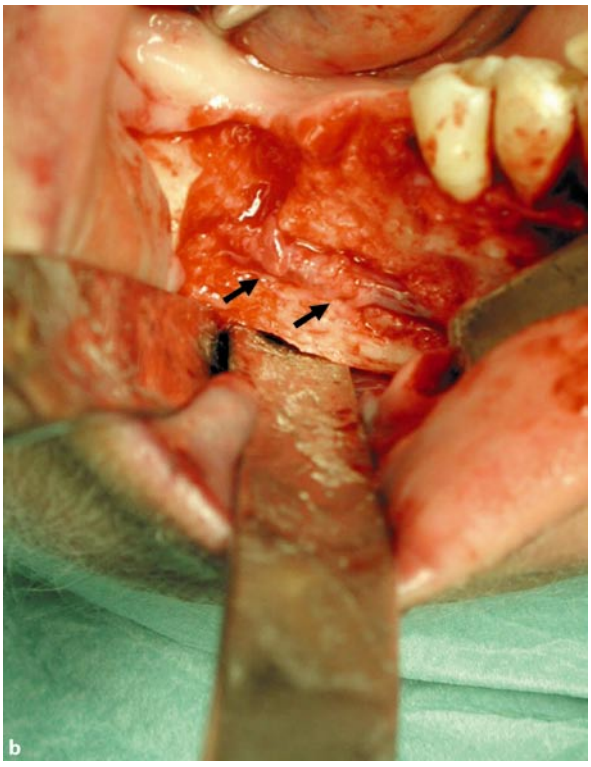
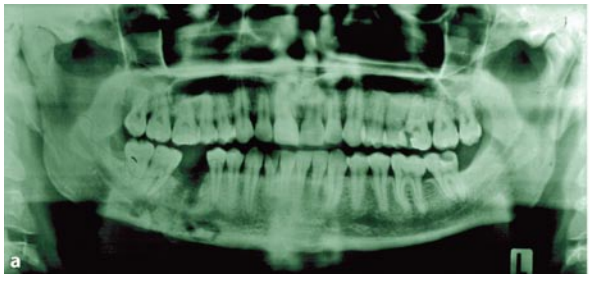


Fig. 2.8a,b Patient with acute osteomyelitis, beginning secondary chronic osteomyelitis of the right mandible following extraction of the lower right second molar. Her chief complaint was a marked hypoesthesia of the right inferior alveolar nerve (Vincent's symptom), which was documented preoperatively in **a**. **b** The intraoperative view after removal of the buccal cortical plate by decortication: note the granulation tissue alongside the inferior alveolar nerve (*arrows*) as a primary pathway for spread of the infection. (This case is described in detail in Chap. 12, case report 4)



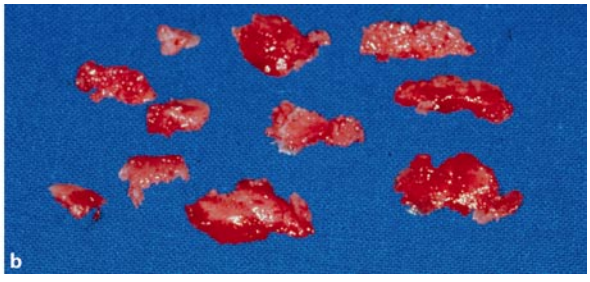


Fig. 2.9 **a** An OPG of a secondary chronic osteomyelitis case demonstrates osteolysis in the mandibular corpus around the alveolar region of the right first molar. A sequester is noted at the base of the right mandibular corpus with adjacent periosteal reaction. **b** Surgical specimen of the case shown in **a**: multiple sequesters and necrotic bone collected during debridement surgery

2.6.3 Clinical Presentation

2.6.3.1 Demographics

Acute and secondary chronic osteomyelitis may affect all ages and both sexes. In our retrospective analysis of 251 cases of acute and secondary chronic osteomyelitis there was a male predominance with a 2:1 ratio (Baltensperger 2003). Koorbush et al. (1992) described a male to female ratio of 3:1 in a survey of 35 patients. An equal gender distribution was noted by Daramola et al. (1982) in a larger African patient population.

The mean age of onset of disease in our studied cases was almost the same in cases of acute and secondary chronic osteomyelitis: 42.9 years (range 1–81 years) and 44.1 years (range 6–89 years; Baltensperger 2003), respectively. These figures are comparable with those described by previous investigators (Adekeye 1985; Calhoun 1988; Koorbush 1992; Daramola 1982).

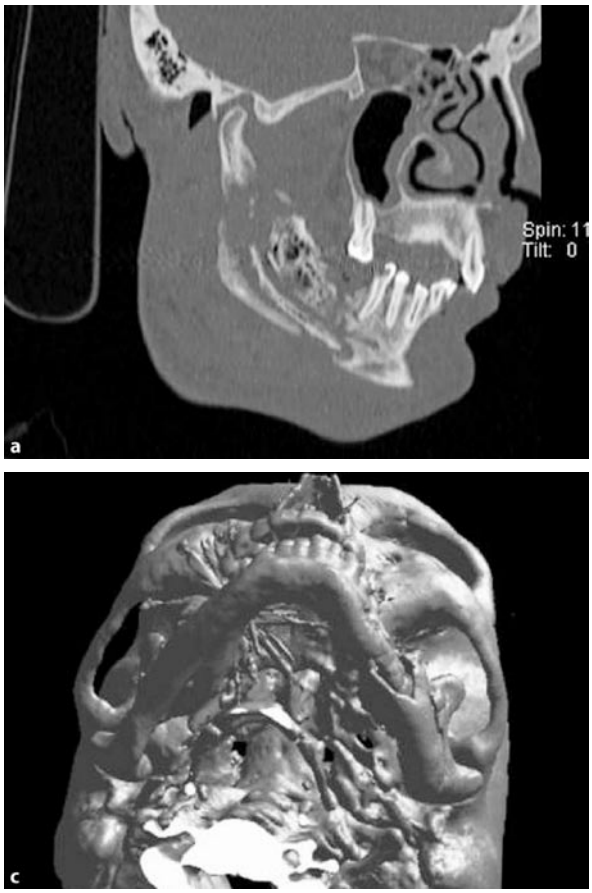


Fig. 2.10a–c The CT scans of a patient with secondary chronic osteomyelitis of the left mandible developing a giant sequester on the bases of the mandibular corpus. The progressive infection has weakened the bone and hence a pathological fracture has resulted. Sagittal CT scan (**a**) and 3D reconstructions (**b,c**). (Courtesy of N. Hardt)

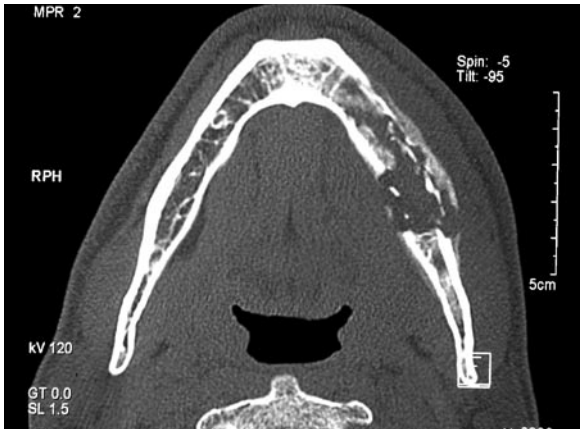


Fig. 2.11 Axial CT scan of an extended secondary chronic osteomyelitis of the left mandible. A strong periosteal reaction with neoosteogenesis has formed an involucrum over several sequestra. (This case is described in detail in Chap. 12, case report 6)

2.6.3.2 Acute Osteomyelitis

The clinical appearance of acute osteomyelitis of the jaws may show a great variety, depending on the intensity of the disease and the magnitude of imbalance between the host and the microbiological aggressors. Three principal types of clinical courses of acute osteomyelitis can be distinguished:

- Acute suppurative
- Subacute suppurative
- Clinically silent with or without suppuration

Cases of acute osteomyelitis of the jawbone with an acute suppurative clinical course usually show impressive signs of inflammation. Pain can be intense and is mostly described by a deep sensation within the bone by the patient, which may be a valuable clue in the patient's history. Local swelling and edema due to abscess formation can also be substantial causing trismus and limitation of jaw function. The patients experiences a general malaise caused by high intermittent fever with temperatures reaching up to 39–40°C, often accompa-

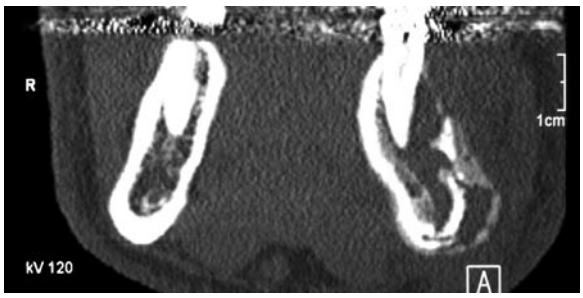


Fig. 2.12 Coronal view corresponding to axial CT scan shown in Fig. 2.11. (This case is described in detail in Chap. 12, case report 6)

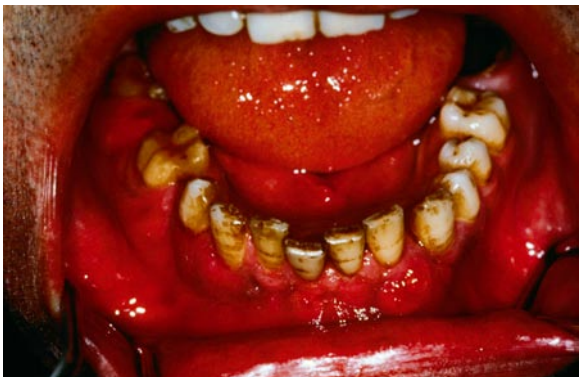


Fig. 2.13 Acute odontogenic osteomyelitis with massive suppuration. Oral examination at initial presentation revealed pus in the sulci of the anterior incisors and canines on both sides, extending distally to the molars in the right lower jaw with multiple fistula formation

nied by regional lymphadenopathy. In some instances paresthesia or anesthesia of the lower lip is described (Vincent's symptom), indicating involvement of the inferior alveolar nerve. In most cases the cause of infection is odontogenic (Table 2.12) and can easily be identified. Pus may exude around the gingival sulcus and through mucosal and, possibly cutaneous, fistulas (Figs. 2.13–2.15). 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 (Fig. 2.16).

Neonatal or tooth-germ-induced acute osteomyelitis of the jaws, as described previously, is a classical representative of this group, although this form of osteomyelitis has become a rarity in modern maxillofacial practice. But also in elderly patients this form of acute osteomyelitis has been seen much less frequently since the introduction of antibiotics and sophistication of medical and dental practice.

In cases of a subacute or silent course, with or without suppuration, the clinical presentation is by definition less impressive. This can make an early diagnosis increasingly difficult, and in many instances these cases are not detected until they have become secondary chronic.

An overview of symptoms at initial presentation of our patient data is given in Table 2.13.

2.6.3.2.1 Laboratory Findings

Depending on the intensity of the infection, laboratory results in acute osteomyelitis may demonstrate a wide range. While in cases with little inflammation the laboratory will only reveal moderate evidence of acute infection, cases which are accompanied by abscess formation will show more pronounced findings. Examination of our own patient data is demonstrated in Table 2.14.

2.6.3.3 Secondary Chronic Osteomyelitis

As a sequel of acute osteomyelitis, the clinical presentation of secondary chronic osteomyelitis of the jaws may also show a great variety, depending on the intensity of the disease and the magnitude of imbalance between the host and the microbiological aggressors and the time (Fig. 2.16). Following an acute or subacute clinical phase with suppuration, the chronification of the disease is reflected by the clinical course and findings. 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 more dull 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 (see Figs. 2.11, 2.12). Other symptoms are somewhat more predominant in advanced stages, such as sequester and fistula formation, and are regarded as classical signs of secondary

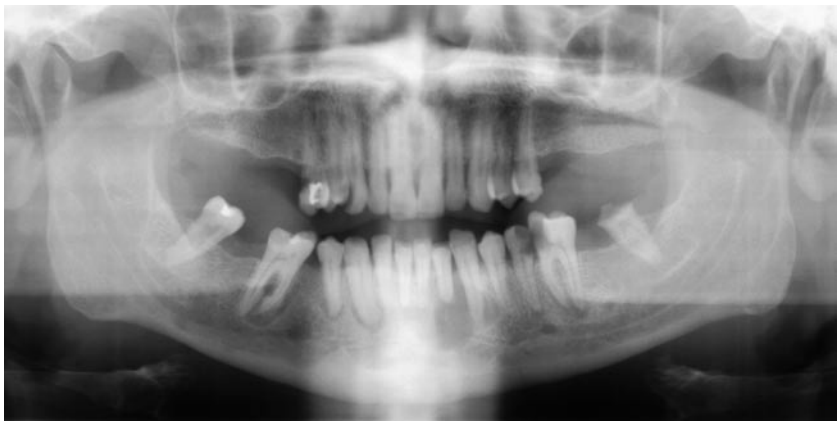


Fig. 2.14 OPG at initial presentation (same patient as shown in Fig. 2.13). Osteolysis of the neighboring bone, derived from apical pathology, is noted in the incisor and canine region on both sides as well as in the molar region on the right side

chronic osteomyelitis (see Figs 2.10, 2.11, 2.12). 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 and elongate due to rise of intraosseous pressure or a fracture present as a result or initiator of the osteomyelitic process.

An overview of symptoms at initial presentation of our patient data is given in Table 2.15.

In cases where the acute phase was clinically silent, secondary chronic osteomyelitis may begin as a hideous disease with little and somewhat unspecific clinical symptoms. In such instances the cause of the infection is considered to be 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. Furthermore, their radiological appearance may predominantly show a diffuse sclerosis with little to no osteolysis. Probably a large portion of the cases described in the literature as diffuse sclerosing osteomyelitis (DSO) falls into this category. A differentiation from primary chronic osteomyelitis may be difficult, if not impossible, in such cases (Figs. 2.17, 2.18); hence, it is most important to review the whole course of the disease and possibly obtain repeated imaging over time in such cases to establish the correct diagnosis.

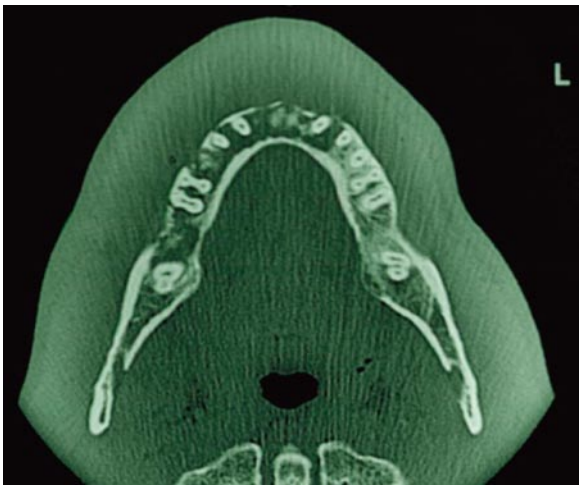


Fig. 2.15 Corresponding axial CT scan to OPG shown in Fig. 2.14 with a more detailed view of the osteolysis in the anterior and right sided alveolar bone

2.6.3.3.1 Actinomycotic and Other Rare Secondary Chronic Osteomyelitis of the Jaws

Specific clinical findings can be found in acute and especially in secondary chronic osteomyelitis caused by *Actinomyces*, *Nocardia*, and *Mycobacteria*. While *Actinomyces* is infrequently observed, the other pathogens are rarely associated with osteomyelitis of the jaws; however, if they are the causative pathogen, the clinical picture is somewhat atypical and hence deserves special recognition. In our studied cases we identified 5 patients with actinomycotic secondary chronic osteomyelitis, while osteomyelitis cases associated with *Nocardia* and *Mycobacteria* were not observed (Baltensperger 2003).

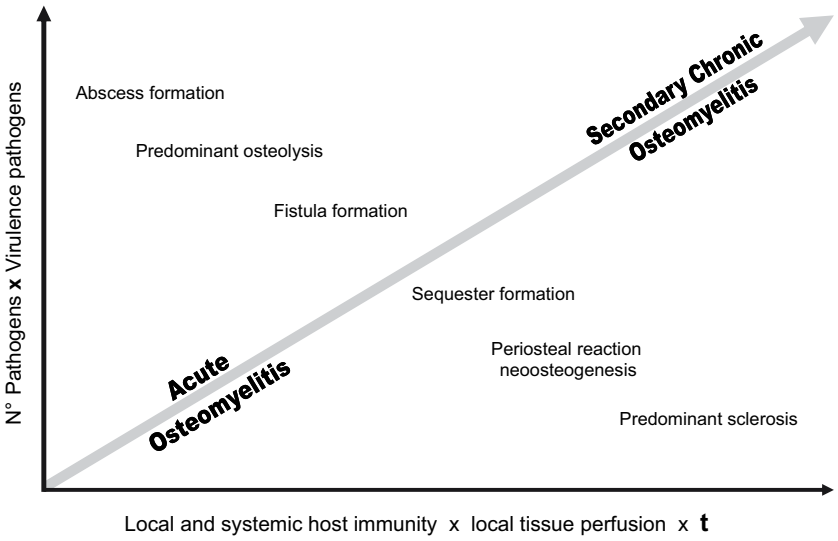


Fig. 2.16 Clinical and radiological features of acute and secondary chronic osteomyelitis of the jaws: the formation of certain clinical and radiological findings is dependent on the intensity of the disease and the magnitude of imbalance between the host and the microbiological aggressors, as well as the time frame

Table 2.13 Acute osteomyelitis: clinical symptoms at initial presentation at the Department of Cranio-Maxillofacial Surgery in Zurich (Baltensperger 2003)

Clinical Symptoms	Cases	
	N°	%
Pain	48	100.0
Swelling	43	89.6
Hypoesthesia[a]	25	52.1
Clinical abscess/pus formation	30	62.5
Extraoral fistula formation	0	0.0
Intraoral fistula formation	7	14.6
Sequester formation[b]	3	6.3
Exposed bone	3	6.3
Limited mouth opening	24	50.0
Lymphadenopathy	5	10.4
Fracture evident[c]	12	25.0
Myofacial, temporomandibular joint pain	1	2.1

[a]Hypoesthesia of the inferior alveolar nerve (Vincent's symptom)

[b]Only clinically diagnosed sequester formation without use of imaging

[c]Cases of trauma/fracture-related acute osteomyelitis

Table 2.14 Acute osteomyelitis: laboratory findings at initial presentation at the Department of Cranio-Maxillofacial Surgery in Zurich (From Baltensperger 2003)

	Cases	
	N°	%
Erythrocyte sedimentation rate		
Data available	23	100.0
Normal (♂ ≤15; ♀ ≤20)	4	17.4
Elevated (♂>15; ♀ >20)	19	82.6
C-reactive protein		
Data available	15	100.0
Normal (<5)	5	33.3
Markedly elevated (>50)	5	33.3
Moderately elevated (3–50)	5	33.3
Leukocyte count		
Data available	38	100.0
Normal (age 2–3 years: 6000–17000; age 4–12 years: 5000–13000; adults: 3800–10500)	23	60.5
Moderately elevated (age 2–3 years: 17000–20000; age 4–12 years: 13000–15000; adults: 10500-13000)	4	10.5
Markedly elevated (age 2–3 years: >20000; age 4–12 years: >15000; adults: >13000)	11	28.9
Body temperature		
Data available	43	100.0
Normal temperature (≤37°C)	20	46.5
Subfebrile temperature (37°–38°C)	17	39.5
Febrile temperature (≥38°C)	6	14.0

Table 2.15 Secondary chronic osteomyelitis: clinical symptoms at initial presentation at the Department of Cranio-Maxillofacial Surgery in Zurich (Baltensperger 2003)

Clinical symptoms	Cases	
	N°	%
Pain	178	87.7
Swelling	162	79.8
Hypoesthesia[a]	78	38.4
Clinical abscess/pus formation	117	57.6
Extraoral fistula formation	15	7.4
Intraoral fistula formation	27	13.3
Sequester formation[b]	30	14.8
Exposed bone	38	18.7
Limited mouth opening	42	20.7
Pathological fracture due to secondary chronic osteomyelitis	4	2.0
Lymphadenopathy	29	14.3
Pseudarthroses[c]	3	1.5
Fracture evident[c]	29	14.3
Myofacial, temporomandibular joint pain	6	3.0

[a]Hypoesthesia of the inferior alveolar nerve (Vincent's symptom)

[b]Only clinically diagnosed sequester formation without use of imaging

[c]Cases of trauma/fracture-related acute osteomyelitis

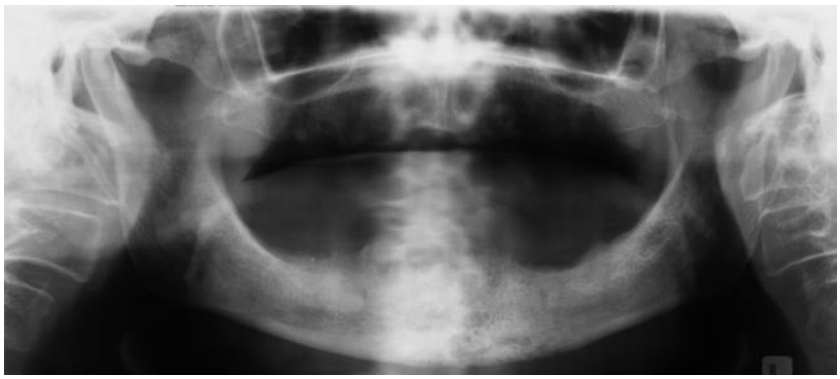


Fig. 2.17 Patient with secondary chronic osteomyelitis. After an initial phase of pus and fistula formation with local surgical drainage and prolonged antibiotic therapy, the process advanced with little clinical symptoms and demonstrated a diffuse sclerosing pattern of the left and right mandibular corpus and symphyseal region in the further course mimicking primary chronic osteomyelitis

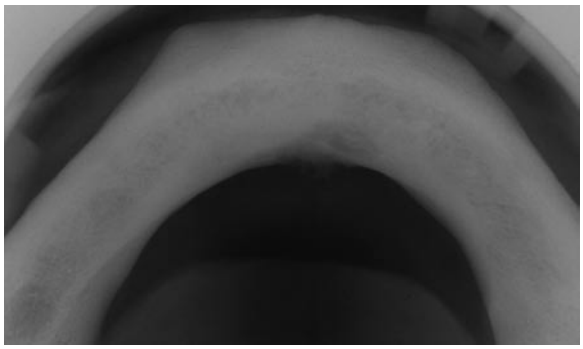


Fig. 2.18 Same as Fig. 2.17

Cervicofacial actinomycosis is a slowly progressive infection with both granulomatous and suppurative features. The disease predominantly affects the soft tissue of the head and neck with primary involvement of nearly every structure (Lerner 1988); however, in some instances the underlying bone, predominantly the mandible, can be infected by direct extension to the underlying bone or hematogenous spread (Topazian 1994, 2002).

As in most cases of secondary chronic osteomyelitis, infection with *Actinomyces* is mostly of endogenous origin, since the pathogen is known to be an oral saprophyte, present in periodontal pockets, carious teeth, tonsillar crypts, and other structures. Local infection, as well as surgical or nonsurgical trauma, facilitates penetration of the mucosal and periodontal barrier structures and allows penetration of deep tissue and bone (Bowden 1984). Advanced cervicofacial *Actinomycosis* spreads without regard for fascial planes and typically appears on cutaneous, rather than mucosal, surfaces.

Firm soft tissue masses are present on the skin with purplish to dark-red oily areas and occasionally small zones of fluctuance (see Fig. 9.1, 9.2, Chap. 9). Spontaneous drainage of serous fluid containing granular material may occur. When placed on a piece of gauze, these granular, yellowish substances, also called sulfur granules, can be seen clearly and represent colonies of bacteria (Topazian 1994, 2002). The underlying affected bone demonstrates the clinical and radiological picture of secondary chronic osteomyelitis with zones of osteolysis, delayed healing of extraction sites, and sclerosis on radiographs. Occasionally sequester formation is also noted.

Nocardiosis is also a chronic disease that may resemble actinomycotic infection. Although the primary target is usually the lungs, from where hematogenous spread leads the pathogen to other organs, the cervicofacial region, including bone, is occasionally involved (Schwartz and Tio 1987).

Tuberculosis is still a widespread infectious disease worldwide with also an increasing incidence again in countries with poor socio-economic conditions, concomitant with the AIDS pandemic. The etiology, pathogenesis, diagnosis, and treatment of tuberculosis are well described in other textbooks and are beyond the scope of this book.

Osteomyelitis of the jaws caused by infection with *Mycobacterium tuberculosis* is uncommon and, in most described instances, the tuberculosis infection is rarely confined to the bone. Adults are predominantly affected, although cases of affected children are also described (Bhatt and Jayakrishnan 2001; Hock-Liew et al. 1996; Kothari et al. 1998; Dimitrakopoulos et al. 1991; Fukuda et al. 1992). Oral tuberculous lesions are generally quite rare, despite the fact of high incidence of systemic involvement. A possible reason for this observation may be the inhibition of *Mycobacterium tuberculosis* by saliva and intact oral mucosa (Hock-Liew et al. 1996; McCarthy and Shklar 1980). The mechanisms of spread of infection are, in analogy to other osteomyelitis cases, caused by other bacteria, by direct inoculation, through tooth-extraction sockets, through any breach in the mucosa during tooth eruption, spread from adjacent soft tissue sites, or by hematogenous spread (Mishra and Bhoyar 1986). The clinical and radiological picture may resemble that of regular secondary chronic osteomyelitis with features similar to a dento-alveolar abscess; however, cervical lymphadenopathy, producing discrete or matted masses which are usually nontender, may be a distinctive presenting feature in some patients (Lee and Schecter 1995). This resemblance to conventional osteomyelitis cases underlines the importance of considering tuberculous osteomyelitis in the differential diagnosis of jaw lesions, especially if the patient's medical history is suspicious for possible infection (Bhatt and Jayakrishnan 2001).

Candida albicans has also been described as a potential microorganism to cause osteomyelitis in various bones of the skeleton, especially in conjunction with prosthesis. In the facial skeleton, however, documented cases of osteomyelitis caused by *Candida albicans* are extremely rare, despite the fact that *Candida* is known commensal of the oral cavity. Arranz-Caso

et al. (1996) report of a case of *Candida albicans* osteomyelitis of the zygomatic bone probably caused by self-inoculation of spores from muguet plaques on the oral mucosa to the exposed bone tissue by hand contact. The authors conclude that such a mechanism should be considered especially in patients who frequently have oral candiasis (e.g., diabetic, cancer, and HIV patients).

Cases of acute and secondary chronic osteomyelitis of the jaws have also been reported by bacteria which are rarely or not considered to be oral commensals. These cases, however, are extremely scarce, and hence the literature on these infections consists mainly of case reports.

2.6.3.3.2 Secondary Chronic Osteomyelitis Masquerading Malignancy

The clinical and radiological signs of secondary chronic osteomyelitis may share many similarities with malignancy complicated by secondary bone infection (Figs. 2.19, 2.20). This may lead to delay definite diagnosis and appropriate treatment in certain instances (Vezeau et al. 1990).

Lesions believed to be osteomyelitis that do not respond to treatment as expected within a short time should be viewed with concern. The patient's medical history, determining possible risk factors for developing oral carcinoma such as smoking, alcohol abuse, and poor oral hygiene, may be indicative, but imaging studies and representative biopsies should be performed to establish the diagnosis (Topazian 1994, 2002).

As much as the presence of a malignancy with invasion into the underlying jawbone may facilitate secondary infection, the opposite pathway may also be the case in rare instances. Ongoing bone infection may also lead to malignancy by neoplastic conversion of infectious tissue (Lemière et al. 2000; Niederdellmann et al. 1982).

2.6.3.3.3 Secondary Chronic Osteomyelitis Associated with Bone Pathology

As mentioned previously, there are several conditions which facilitate bone infection in the jaw. A summary of the most frequently involved pathological conditions enhancing the incidence of osteomyelitis of the jaws is given in Table 2.10; however, theoretically every pathological condition which alters bone physiology and/or vascularization of bone tissue may jeopardize host tissue defense mechanisms and hence may promote secondary infection. The unique location of the jawbones with their proximity to the heavily contaminated oral cavity makes them particularly vulnerable.

Depending on the nature of the underlying bone pathology, the clinical picture of succeeding secondary chronic osteomyelitis may differ from the average osteomyelitis infection established in "healthy bone." The initiation of infection is, like in regular acute and secondary chronic osteomyelitis, often a trauma such as extraction of a tooth or a dental infection leading to breakdown of the periodontal and/or mucosal barrier and promoting contamination and deep bone invasion of the jawbone. The further course of the disease is, however, strongly dependent on the reactive mechanisms of the host tissue (e.g., bone). In general, underlying bone pathology will reduce the defensive abilities of the host tissue and infection may spread faster than in healthy bone. Clinical and radiological signs reflecting suppurative infection, such as abscess and fistula formation, are similar to osteomyelitis cases without associated bone pathology. Bone reaction to infection, like osteolysis, sclerosis, sequester formation, and periosteal reaction, however, may strongly differ, making correct diagnosis and determining the extent of the infection more challenging (Fig. 2.21). In cases were necrotic bone is exposed to the oral cavity, secondary colonization of the bone and eventual deep bone invasion may occur (Fig. 2.22).

2.6.3.3.4 Laboratory Findings

In analogy to the clinical symptoms, the laboratory findings in secondary chronic osteomyelitis of the jaws are usually less prominent than in acute osteomyelitis. The overall moderate systemic reactions are reflected by these results and indicate a more localized infectious process, especially in secondary chronic osteomyelitis cases. This is especially true in cases with little or mild clinical symptoms where laboratory findings can be almost normal and hence are of little diagnostic or monitoring value. Examination of our own patient data is demonstrated in Table 2.16.

2.6.4 Primary Chronic Osteomyelitis

2.6.4.1 Definition

Acute and secondary chronic osteomyelitis of the jaw, as being the same disease at a different stage, share the same etiology, a bacterial or, in rare cases, a fungal infection. In the literature acute and secondary chronic

osteomyelitis are often summarized by the term "suppurative osteomyelitis," indicating a true bacterial infection with formation of pus.

The term "primary chronic osteomyelitis," as used in the Zurich classification of osteomyelitis of the jaws, refers to a rare inflammatory disease of unknown etiology. 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 represents a *conditio sine qua non* and 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 a rise de novo without an 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. In active periods dull to severe pain, limitation of jaw opening and/or myofacial pain, as well as variable swelling, may be observed. In certain cases

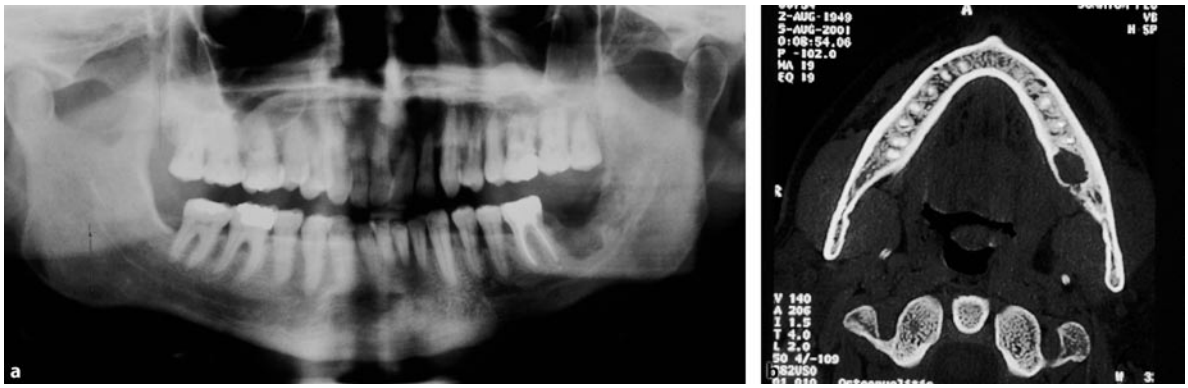


Fig. 2.19a,b Patient with a squamous cell carcinoma of the left lower jaw with concomitant secondary chronic osteomyelitis. The patient was referred to the maxillofacial unit approximately 1 month after surgical removal of the lower left second molar with chronic local fistula formation and pus discharge from the extraction site. The medical history, clinical appearance, and initial radiological work-up (OPG; Fig. 2.19 and corresponding axial CT scans in Fig. 2.20) were suspicious for secondary chronic osteomyelitis; however, initial bone and soft tissue biopsies revealed an invasive squamous cell carcinoma with a concomitant local bone infection

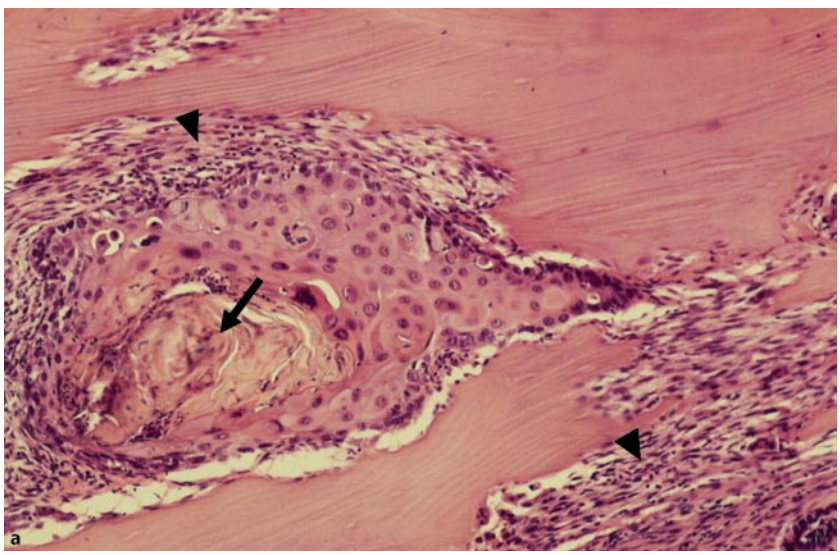


Fig. 2.20a,b Histology samples of the same patient shown in Figs. 2.19a and b. Hematoxylin and eosin stains. **a** Infiltration of bone by moderately differentiated squamous cell carcinoma. Keratinization in center of tumor cell islands (*arrow*). Peritumoral fibrosis and infiltration by inflammatory cells are present (*arrowheads*)

regional lymphadenopathy and reduced sensation of the inferior alveolar nerve (Vincent's symptom) are also accompanying symptoms.

Primary chronic osteomyelitis of the jaws almost always targets the mandible. In our patient data all but one case of primary chronic osteomyelitis involved exclusively the lower jaw. In the remaining case, the zygoma demonstrated the clinical, radiological, and histopathology findings as the mandible, indicating a possible spread of the pathological condition. The findings in the literature are similar to our data. Flygare et al. (1997) reported a case of primary chronic osteomyelitis with involvement of both jaws, which is considered to be a unique case.

2.6.4.2 Classification Problems of Primary Chronic Osteomyelitis of the Jaws

As mentioned previously, the classification of osteomyelitis of the jaws, and especially primary chronic osteomyelitis of the jaws, is somewhat confusing, mainly due to the wide variety of terms used to describe this disease entity. While diffuse chronic sclerosing or chronic sclerosing osteomyelitis are the favorite used terms in the

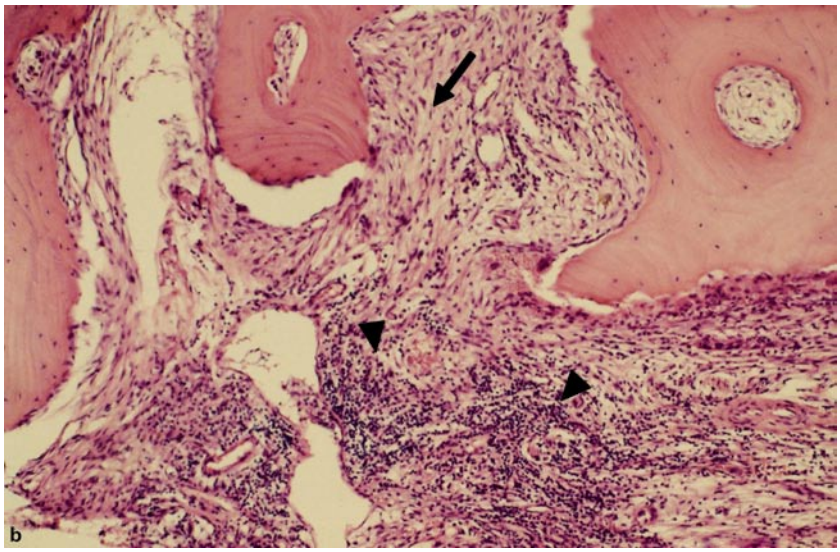
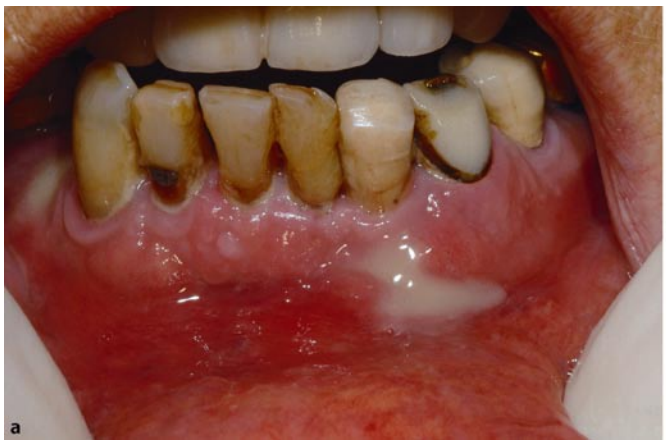


Fig. 2.20 (*continued*) Histology samples of the same patient shown in Figs. 2.19a and b. Hematoxylin and eosin stains. **b** Lamellar bone with preserved osteocyte nuclei is present besides signs of inflammation fibrosis of marrow spaces (*arrows*) and extensive infiltration by inflammatory cells (*arrowheads*)



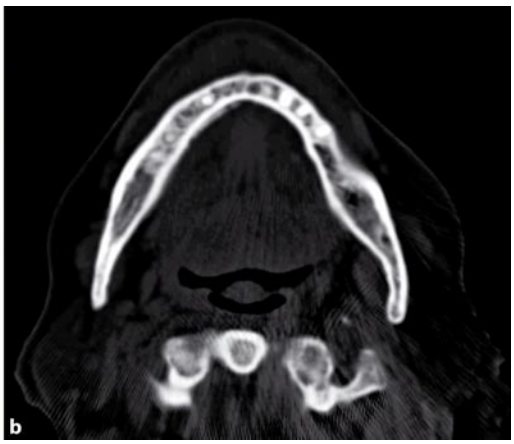


Fig. 2.21 **a** A patient with a clinically extensive secondary chronic osteomyelitis of the frontal region with multiple fistula and abscess formations. The patient was treated with i.v. bisphosphonates for metastatic breast cancer. (This case is described in detail in Chap. 12, case report 10.) **b** A CT scan corresponding to **a**: The bone and periosteal reaction is not as strong as would have been expected from the clinical picture and compared with cases of secondary osteomyelitis of the mandible with no underlying bone pathology. (This case is described in detail in Chap. 12, case report 10)