Cysts of the "Oro-Maxillofacial Region"

27

Neelima Malik

Learning Targets

1. Definition and classification of the Cysts of the Oro-maxillofacial region.
2. Etiopathogenesis, general features, and management of cysts in general
3. Pathogenesis, clinical features, radiological picture, histopathology, and surgical management of common cystic lesions.

27.1 Introduction

A cyst is essentially an enclosed sac formed by the cluster of cells, which group together. The unique characteristic of a cyst is that the cells that form the outer covering of the sac are abnormal from the surrounding normal cells of that specific region. There are various categories of cysts, which can occur almost anywhere within the human body's hard and soft tissues, and their occurrences are very common. They vary in size from tiny microscopic to huge macroscopic varieties, and the large cysts can displace the adjoining normal anatomical structures.

Once formed, sometimes, a cyst may resolve on its own, but in most cases, it keeps growing and needs surgical intervention depending on its type and location. Cysts are usually nonaggressive, but certain groups of cysts show aggressive behavior. The cysts of the oral and maxillofacial region are the commonest pathological entities. Historically, mummified specimens in Egypt (400 BC to 2800 BC) showed the presence of cysts [1].

Electronic Supplementary Material The online version of this chapter (https://doi.org/10.1007/978-981-15-1346-6_27) contains supplementary material, which is available to authorized users.

N. Malik (✉)
Department of Oral and Maxillofacial Surgery, Krishna Institute of Medical Sciences "Deemed to be University", Karad, Maharashtra, India

27.2 Definition

A cyst is explicitly defined as "A pathological (uni- or multilocular) sac that may or may not be lined by an epithelium and filled with a fluid, semifluid, or gaseous contents and not created by the accumulation of pus" [1, 2].

27.3 General Histopathological Common Components of a Cyst

Cysts can be found in the facial bones as well as in the soft tissues of the orofacial region.

Cysts lined by an epithelium are more common in both jawbones than any other regions of the body because of great many epithelial cell rests present in close proximity to the developing jaw bones, and they are called True Cysts, e.g., radicular cyst, dentigerous cysts, etc.

Pseudocysts do not have an epithelial lining, e.g., solitary bone cysts, Cysts of maxillary antrum, etc. [1] (Fig. 27.1).

A cyst is a tissue-space occupying lesion/sac with a cavity in the center known as a Lumen. There is an outer fibrous connective tissue wall that separates the cyst from surrounding normal tissues. On the inner aspect of this wall, there is a cystic lining of epithelium, mostly made up of stratified squamous epithelium (Fig. 27.2). In some cases, there can be lining other than squamous epithelium.

27.4 Etiopathogenesis

The etiopathogenesis of orofacial cysts basically originates from the remnants of the complex processes of embryonic tissue responsible for jaw and dental development. Such a conversion does not occur in any other part of the body.

All True Cysts have their genesis from the epithelial remnants along with strong proliferative impetus and capability for bone remodeling. Odontogenic cysts are derived from

K. Bonanthaya et al. (eds.), *Oral and Maxillofacial Surgery for the Clinician*, https://doi.org/10.1007/978-981-15-1346-6_27

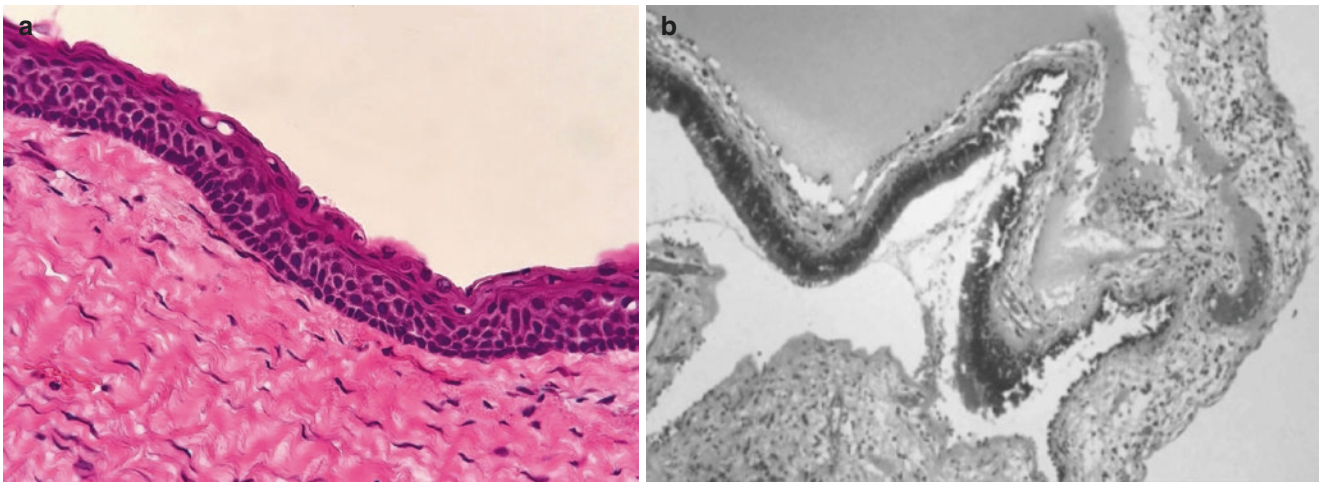


Fig. 27.1 Histological picture of a true (**a**) and pseudocyst (**b**)

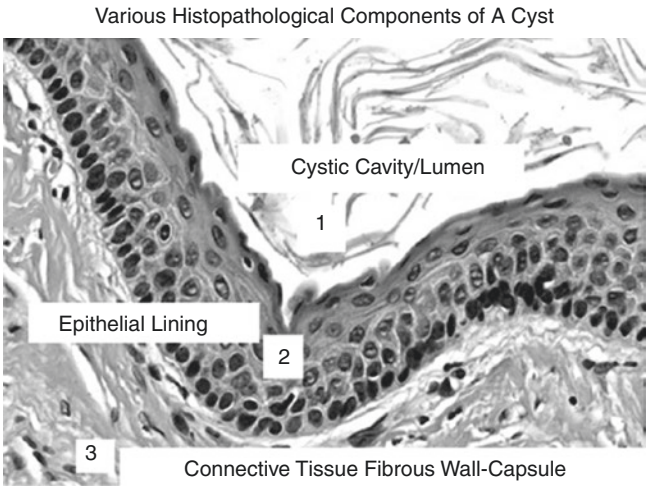


Fig. 27.2 General broad histopathological characteristic components of a Cyst; Epithelial lining-various types of epithelium can line a cyst

remnants of odontogenic epithelium of stomodeum, and inflammatory cysts are derived from infective process (Table 27.1).

Table 27.1 Classification of cysts based on the embryological derivation sources (modified from Regezi et al. [3])

Type	Source	Origin of cell rest	Cyst variety
Odontogenic rests	Cell rests of malassez	Epithelial hertwig's root sheath	Periapical (radicular) cyst
	Reduced enamel epithelium	Enamel organ	Dentigerous cyst
	Rests of dental lamina (rest of Serres)	Epithelial connection between mucosa and enamel organ	Glandular odontogenic cyst, Lateral periodontal cyst, Odontogenic keratocyst, and Gingival cyst of newborn & adult
Nonodontogenic Rests	Remnants of nasopalatine duct	Paired nasopalatine duct-vestigial	Nasopalatine canal cyst and Fissural cysts
	Remnants of maxillary sinus epithelium		Cysts of the maxillary sinus

Pathogenesis of a cyst is mainly divided into three stages:

(1) Cyst Initiation, (2) Cyst Formation, and (3) Cyst enlargement or expansion

1. *Cyst Initiation*—unknown stimulus promotes the rapid increase of epithelial rest cells via cytokine synthesis. The factors, which are suggested to be responsible for cyst initiation phase, are mainly genetics, loss of immunological surveillance, inflammatory mediators, or some local factors like decreased oxygen tension along with increased CO2 tension.

   The residual epithelial cells (Table 27.1) are implicated to initiate the process of cyst formation. Initiation is followed by the rapid growth of the epithelial cells and the development of a cystic lesion.

2. *Cyst Formation*—Nutritional deficiency theory
   After initiation, proliferating epithelial cells form a mass inside the sac and the innermost central cells become deprived of nutrients/blood supply, as they are far from the source of nutrients. The innermost cells do not get adequate blood supply, and so there is an ischemic liquefactive necrosis in the center, leading to a cavity for-

mation, which is surrounded by growing epithelial cells. Enhancement in intercellular edema and acid phosphatase activity leads to the formation of microcysts, which slowly start to form a larger cyst [4].

3. *Cyst enlargement or expansion*
   Once formed, the cyst continues to enlarge slowly, over the months.
   The process is similar for all epithelial lined cysts with some variations. Many debatable hypotheses have been put forward regarding the definitive mechanism of cyst enlargement.

27.4.1 Theories of Cyst Enlargement/ Expansion

27.4.1.1 Mural Growth & Peripheral Cell Division

(a) Epithelial proliferation-peripheral cell division, (b) Accumulation of the contents within the lumen.

Due to Proliferation or rapid increase in the number of cells and by the active division of peripheral lining epithelial cells, surface area of cystic sac increases and the enlargement of a cyst at the circumference is noted along with the accumulation of cellular contents [4, 5].

27.4.1.2 Hydrostatic Enlargement

Biomechanical Theory

Intraluminal concentration and pressure differences between the cystic cavity and the peripheral growth surroundings influence fluid movement into the cyst, bringing about an increase in size.

Cyst starts expanding and growing in size, with the increase in intracystic pressure due to the intake of fluids inside the cyst from the surrounding area. (The center of the cyst has higher concentration of sodium than the surrounding serum, and so it tends to absorb water.)

This increase in cyst size process is different from the true autonomous growth, which is found in tumor cells [5, 6].

Secondary proliferation of epithelial cells is, thus, a result of increased volume pressure within the cystic cavity, as a result of osmosis. An osmotic concentration gradient is created as a result of degradation and metabolic by-products, which are taken up inside the cyst.

Due to the rapid increase in the osmotic gradient, the fluid from the surrounding region diffuses in the cystic cavity, increasing internal hydrostatic pressure and thereby resulting in the expansion of the cyst (Fig. 27.3).

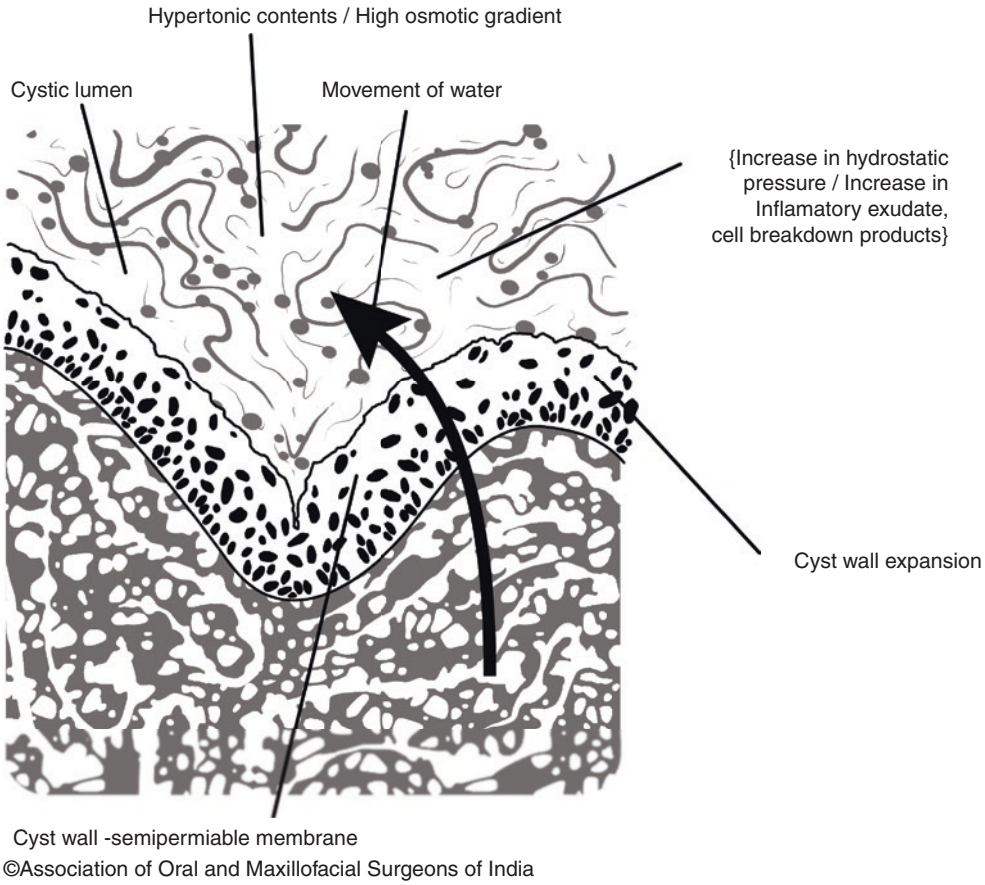


Fig. 27.3 The phase of enlargement of a cyst

27.4.1.3 Bone Resorbing Factor

In intraosseous cysts, resorption of the surrounding bone also increases the size of bony cavity.

Biochemical and Cellular Aspects of the Cyst Proliferation

Newer research points to the role of molecular biology in cyst proliferation, over older theories of bone loss resulting from osmotic gradient. The cystic capsule produces bone resorbing factors like prostaglandins, leukotrienes, and osteoclasts.

(A) Bone degeneration in the jaw bone is brought by Collagenase (breakdown of collagen), providing room for cysts to develop. Body's immune mechanism releases cytokines and growth factors due to the connective tissue breakdown, which contributes to the mobilization and proliferation of epithelial cells in the area.

Evidence-based studies showed that collagenase activities in cystic capsule result in bone degeneration by destruction of the collagen [6, 7].

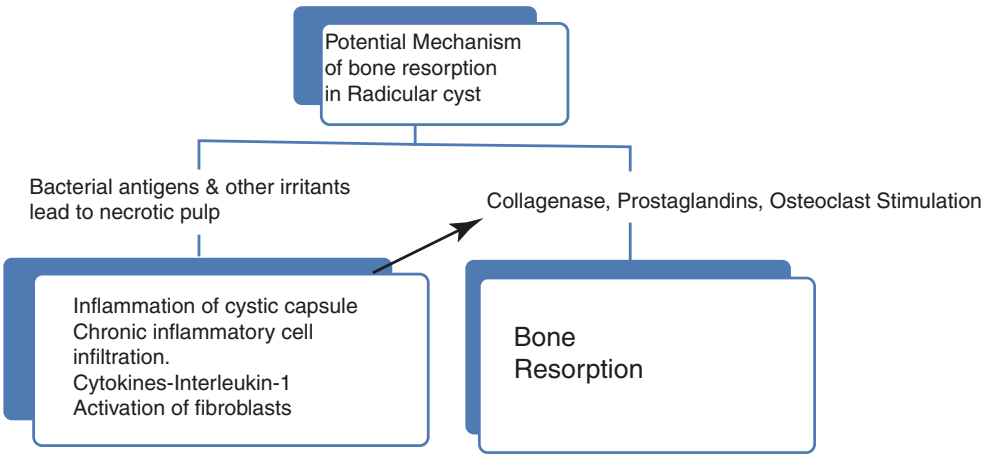
(B) Prostaglandin theory—Bone resorption caused by metabolism of acidic matter produced in the cysts lends to the cystic growth. These are the substances produced by the cyst itself, which include Prostaglandin-2 and Interleukin-1. Along with the epithelial cell division, the cyst enlarges within the jaw bone due to bone resorption caused by Prostaglandin-induced osteoclastic activity. Bone resorption is mediated as a result of production of PGE-2 and PGE-3 by dental cysts. Prostaglandin-2 and other by-products are part of arachidonic acid metabolism [8].

The production of prostaglandin-2 can be triggered by Interleukin-1. Meghji et al. [9] summarized that odontogenic cysts produce interleukin-1, which in turn triggers the production of Prostaglandin-2, resulting in osteoclastic bone resorption and cyst enlargement. Most dental cysts demonstrate a common growth mechanism though radicular and developmental cysts may be initiated by different factors (Flow Chart 27.1).

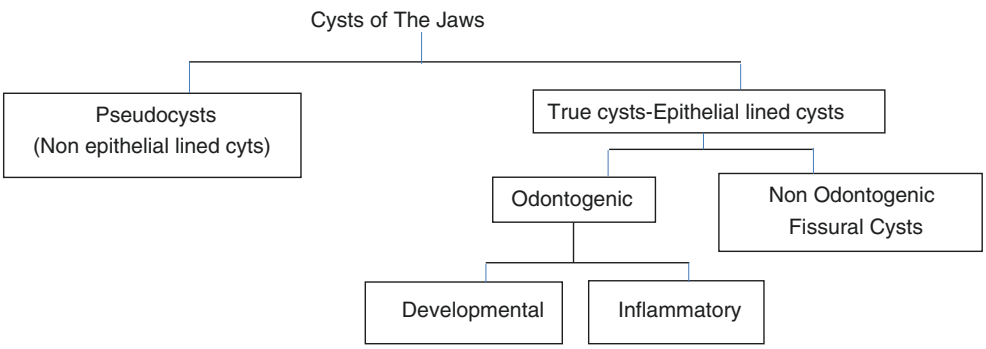
27.5 Historical Evolution of the WHO Classification Systems

Many researchers including WHO have tried to put forward a uniform, globally accepted nomenclatures and classifications for the cysts of orofacial region. But still there is a continuous debate going on, and therefore, various classifications are cited in the literature. WHO in 1992 [2] had classified cysts into two main categories as odontogenic and nonodontogenic, with further subsets as developmental and inflammatory (Flow Charts 27.2 and 27.3).

Flow Chart 27.1 Potential mechanism of bone resorption in a radicular cyst



Flow Chart 27.2 Basic classification of cysts of jaws



Flow Chart 27.3 Classification of pseudocysts

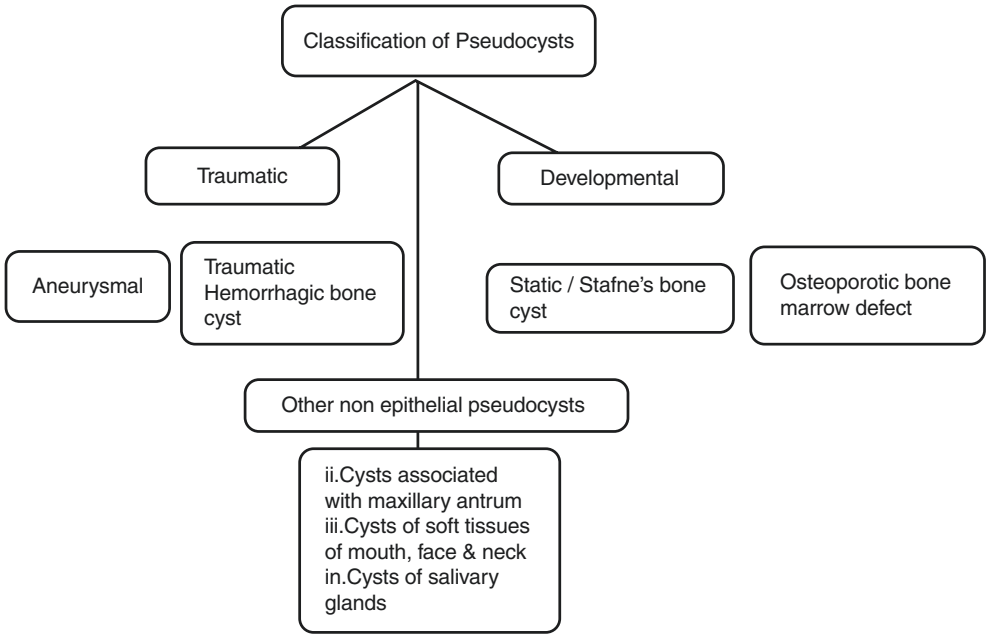


Table 27.2 According to Shear [1], cysts of orofacial region are categorized under three major groups:

I.	Cysts of the jaws
II.	Cysts associated with the maxillary antrum
III.	Cysts of the soft tissues of the mouth, face, and neck.

This simple classification did not include Calcifying odontogenic cyst (COC), cysts involving maxillary sinus and nonodontogenic soft tissue cysts. WHO in 2005 [10] reclassified the cysts into epithelial and nonepithelial varieties, which were further divided into odontogenic and nonodontogenic types. At this time, COC—calcifying odontogenic cyst—and Odontogenic Keratocysts (OKCs) were not considered as cystic entities, but they were listed as keratocystic odontogenic tumors—KCOT—and calcifying cystic odontogenic tumors—CCOT—respectively. The justification for this new OKC designation was the high recurrence rate and aggressive behavior along with association with mutations in PTCH gene. This reclassification led to a lot of confusion, and it was not accepted by many. But in 2017, the peer group of WHO did not think that there was sufficient affirmation for classifying both OKC and COC as neoplasms. Therefore, in 2017 again, both these lesions were put back in the cyst category [11].

Among so many classifications, Shear (2007) has suggested a comprehensive classification of cysts with good understanding of cystic lesions of mouth, face, and neck region [1] (Table 27.2).

The cysts of the jaws are divided into those that are:

I. Cysts of the jaws
  A. Epithelial-lined cysts
    1. Developmental origin
      (a) Odontogenic Developmental cysts
        (i) Odontogenic keratocyst
        (ii) Dentigerous cyst
        (iii) Developmental lateral periodontal cyst
        (iv) Gingival cyst of infants
        (v) Eruption cyst
        (vi) Gingival cyst of adults
        (vii) Glandular odontogenic cyst
        (viii) Calcifying odontogenic cyst
        (ix) Botryoid odontogenic cyst
      (b) Nonodontogenic Developmental cysts
        (i) Midpalatalraphé cyst of infants
        (ii) Nasolabial cyst
        (iii) Nasopalatine duct cyst
    2. Odontogenic Inflammatory origin
      (i) Radicular cyst, apical, and lateral
      (ii) Paradental cyst and juvenile paradental cyst
      (iii) Residual cyst
      (iv) Inflammatory collateral cyst
  B. Nonepithelial-lined pseudocysts
    (i) Solitary bone cyst
    (ii) Aneurysmal bone cyst
II. Cysts associated with the maxillary antrum
  (i) Retention cyst
  (ii) Mucocele

III. Cysts of the soft tissues of the mouth, face, and neck
  (i) Dermoid and epidermoid cysts
  (ii) Thyroglossal duct cyst
  (iii) Lymphoepithelial (branchial) cyst
  (iv) Anterior median lingual cyst (intralingual cyst of foregut origin)
  (v) Nasopharyngeal cyst
  (vi) Oral cysts with gastric or intestinal epithelium (oral alimentary tract cyst)
  (vii) Cystic hygroma
  (viii) Thymic cyst

27.6 Prevalence of Cysts

Quite a large number of studies are conducted on jaw cysts, but detailed information on demographic profiles in different populations is limited and most have focused on odontogenic cysts [12, 13] (Box 27.1 and Fig. 27.4).

Box 27.1 Prevalence of Dento-orofacial Cysts

Incidence:

- The jaw cysts are more common than cysts of other bones in the body [12].
- Prevalence of odontogenic cysts is higher (90%) than nonodontogenic cysts in the jaws [12, 13]
- The commonest varieties are periapical cyst (65%), dentigerous cyst (24%), and OKC (5–8%) [12, 13]
- Inflammatory cysts account for 36%, whereas developmental cysts represent 27% of all cysts. 4% cysts are either unclassifiable or nonepithelial (Lucas and WHO classification) [12, 13]

Age: Range from the 1st to 9th decades. Peak incidence is seen between 21 and 30 years of age.

Sex: More prevalent in males, with a male to female ratio of 1.4:1 [12, 13]

Site: Review of literature suggests mandibular preponderance and may imply a higher tendency for activation of cell rests to cystic degeneration in the mandible.

Box 27.2 Diagnosis of the Cystic Lesion Can Be Arrived by the Following Steps

A. History
B. Clinical Examination (signs and symptoms, site, inspection, palpation, percussion, teeth vitality check, and aspiration of the cystic content)
C. Radiographic examination
D. Biopsy (to ascertain histopathological features leading to final diagnosis)

Box 27.3 History

History: Duration of the complaints/progress is also important. History of pain, loose teeth, occlusion change, intraoral/extraoral swelling/discharge, or sinus track, missing teeth, and delayed eruption of teeth should be noted.

27.7 General Key Attributes Regarding an Oro-maxillo-Facial Cyst-Signs & Symptoms (Boxes 27.2 and 27.3)

Signs and symptoms of a cyst depend on its size and site. Small cysts are detected as an incidental finding during routine radiographic examination. Large cyst after enlargement can be noticed first by the patient himself, or there can be facial disfigurement noticed by others. Generally, cysts are symptoms free, unless they get infected secondarily.

If the cyst has not enlarged beyond its normal anatomical boundaries of the jaw bone, then its lump cannot be palpated intraorally or extraorally. The majority of cysts expand very slowly, and the surrounding bone gets time to form fresh subperiosteal new bony layer around the lesion, which isolates the lesion.

On Palpation

1. During early stage, smooth, bony hard, and painless prominence can be felt.

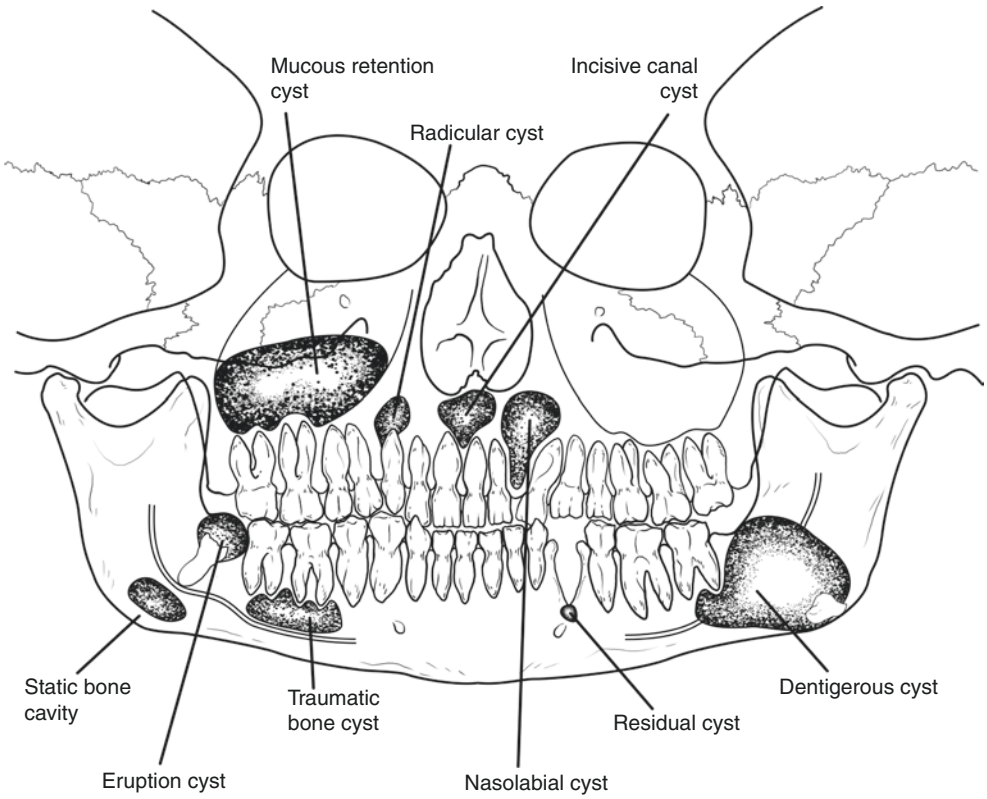


Fig. 27.4 Typical locations of odontogenic and nonodontogenic cysts

2. Later on "eggshell crackling" can be felt at the thinned out less mineralised *cortex*.
3. When the cyst grows in volume, the outer cortex is thinned out, due to the loss of bone mineral content and may show "Ping Pong/Table Tennis Ball" springy consistency, or
4. Fluctuation can be felt in its center, where the cyst has eroded the bone and the cystic sac fuses with oral mucosa. Cysts, which show buccal cortical expansion, are still mostly covered with a thin layer of the new bone. Cysts are typically slow growing and tissue space occupying lesions and have the capacity to displace or replace normal tissues. They form compressible, fluctuant swelling, if encroached into the soft tissues, and if they are very close to the mucosal surface, then bluish tinge is seen. A majority of cysts show buccal cortical expansion as the cyst grows in size, but in some aggressive cases, lingual or both buccal and lingual expansion can be seen, which produces facial disfigurement.

A cyst may become secondarily infected, and pus discharge may be seen into the oral cavity via a sinus tract. Examination of the sinus track and discharge from sinus track should be checked for cholesterol crystals or pus. Salty, sweet, or unpleasant taste of the discharge is noted.

At this stage, patient may complain of pain. Loosening of adjacent teeth or displacement of the teeth out of their normal arch alignment can happen. Very rarely, depending on the variety of cyst, as it enlarges to an enormous size, it may resorb adjoining teeth/roots, as well as bone, and may end up in pathological fracture of the jaw bone. As most cysts enlarge at a slow pace, and even in the large lesions, the inferior alveolar canal usually gets displaced and there will be no altered sensation (anesthesia or paraesthesia). Paraesthesia and/or anesthesia of the lower lip can exist in aggressive or acutely infected cysts. Percussion of involved teeth will produce a dull or hollow sound. Usually, high-pitched sound is obtained on the uninvolved teeth. Edentulous patient will complain of ill-fitting denture due to the bulge. Periapical cysts are always seen in relation to one or more nonvital teeth. A large maxillary anterior region cyst may cause distortion of nostril shape and show nasal congestion. Diagnosis can vary as per the site of the lesion,

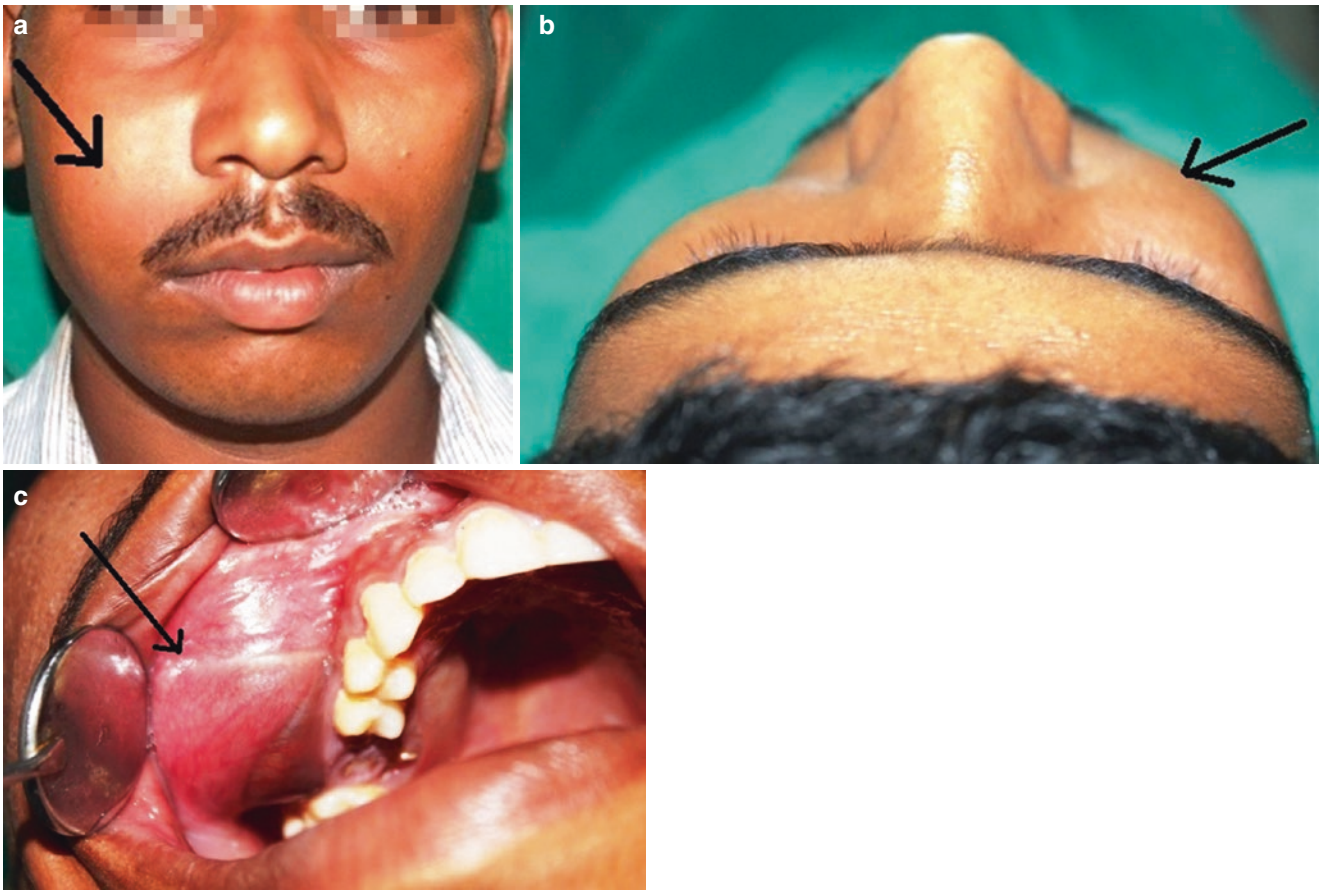


Fig. 27.5 Clinical examination: extraoral inspection; (**a**) extraoral swelling on the right cheek area, (**b**) head position for inspection of swelling and comparison with normal side, and (**c**) intraoral examination showing obvious bulge in right buccal vestibule. *(Courtesy Dr, Kumar Nilesh, SDS, Karad)*

age of the patient, clinical, radiological, and histopathological examination (Fig. 27.5).

27.7.1 Vitality Test of the Involved Teeth in the Lesion

In cysts other than radicular cysts or inflammatory periodontal cyst, there is no compromise in blood supply of the teeth, and so teeth vitality is preserved. Vital teeth are associated with odontogenic keratocyst, solitary bone cyst, lateral periodontal cyst, etc. In inflammatory cysts, the vitality of all involved and adjoining teeth should be checked.

27.7.2 Radiographic Examination

Radiographic picture of a cyst is not always pathognomonic. It will depend not only on cyst category, but also the variants related to its duration, location, and degree of expansion and the presence or absence of infection. When the patient is referred for X-rays, the type of film used will depend on the size of a lesion. Dental panoramic or maxillofacial Cone Beam CT provides good imaging for most of these cystic lesions. They help to define site, size, extent, and marginal outline of the lesion.

Intraoral film: For smaller lesions, minimum of two films are taken at right angles to one another. Periapical and occlusal views may be taken.

Extraoral film-used for larger lesions. Panoramic/Orthopantograms, Lateral oblique views, and Water's view may be taken.

Patient may be referred for CT scan or MRI in cases of extensive aggressive lesion or recurrent lesions to know the exact expanse, proximity to the important vital structures/adjacent anatomical structures, perforations, and multilobulated/multicystic character. If there is suspicious extraosseous lesion with soft tissue extension or malignancy, then it is also indicated. Postoperative imaging helps to assess the rate of regression and bone regeneration.

27.7.2.1 General Radiographic Picture

1. Radiographically, intrabony cysts, small or large, form sharply defined unilocular or multilocular radiolucency with or without cortication.

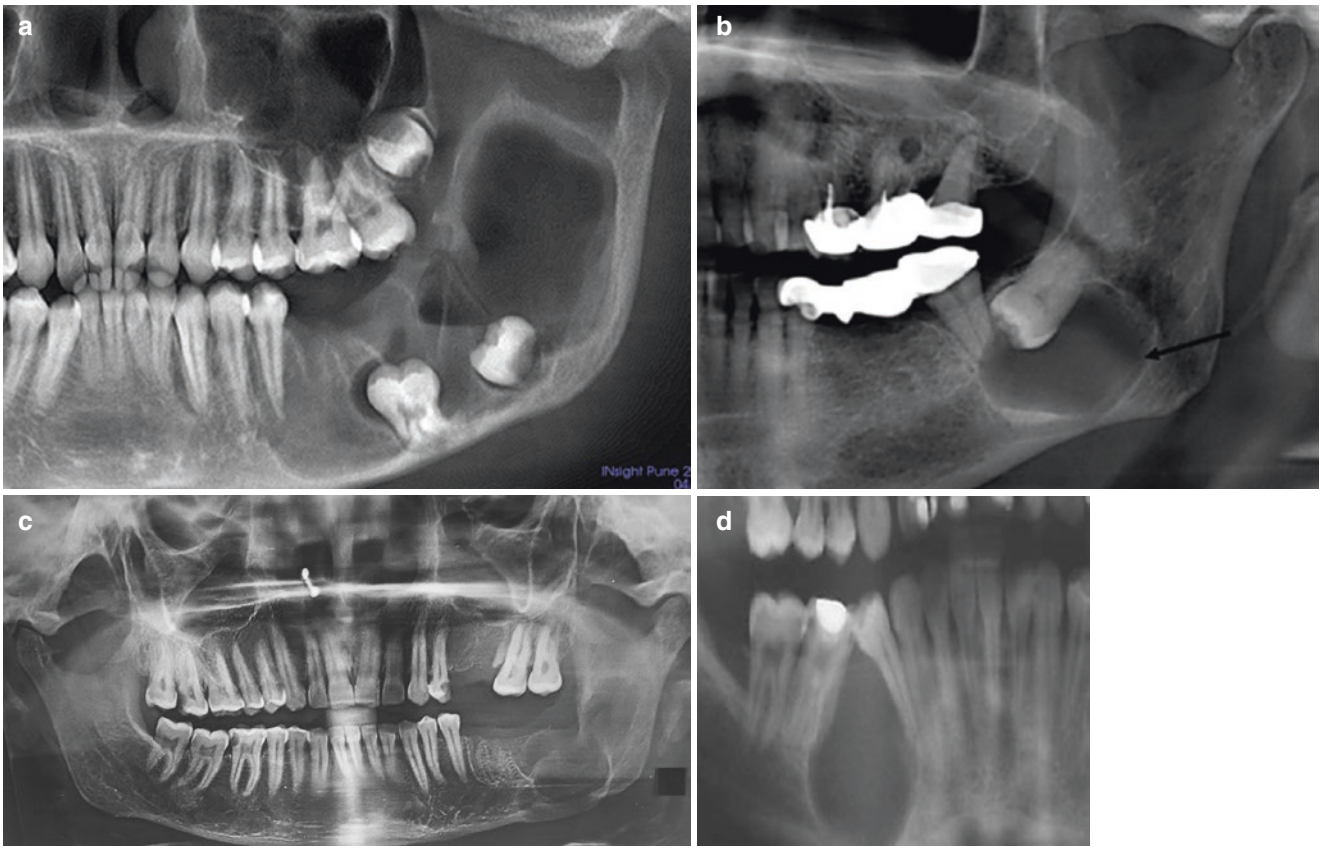


Fig. 27.6 Different radiological picture of the cystic lesions as per the types: (**a**) replacement type (cyst in place of third molar), (**b**) envelopmental type (cyst enveloping lower third molar), (**c**) extraneous type (ascending ramus cyst away from teeth), and (**d**) collateral type (adjacent to the roots of the teeth)

2. The presence of septae can be seen.
3. The shape of a cyst will vary, depending on the type; round or oval in radicular or dentigerous cysts, scalloped margins in odontogenic keratocyst, traumatic bone cyst, pear-shaped, heart-shaped in nasopalatine or incisive canal cyst.
4. Cortical expansion, perforations, or pathological fractures may be seen.
5. Displacement or compression may be noticed on the adjacent dentition, maxillary sinus, or neurovascular bundle.

27.7.2.2 Radiological Classification of Jaw Cysts (Shear) [1]

- Replacement type: cyst that forms in place of normal tooth
- Envelopmental type: cyst that embraces an adjacent unerupted tooth
- Extraneous type: cyst that occurs in ascending ramus away from the teeth
- Collateral type: cyst that occurs near the roots of the teeth (Fig. 27.6)

27.7.3 Aspiration

The orofacial cyst contains fluid in its cystic cavity, which varies in consistency, color, and protein content, and helps in differentiating and arriving at a provisional diagnosis based on these observations. These findings should be remembered to be able to diagnose any cyst, which may be encountered in the clinical practice. An aspiration biopsy of a cyst is the norm for initial diagnosis of all cysts.

- Aspiration with syringe is always positive for most of the odontogenic cysts. Aspiration can be carried out after the clinical examination is over or at the time of planned incisional biopsy. Aspiration and excision biopsy can be done in the same sitting for small lesions.
- Aspiration of Intralesional fluid is done using a wide bore needle of 18 gauge and 5 ml syringe under local anesthesia. It is a very valuable provisional diagnostic aid with simple procedure with least discomfort. Inability to retract the plunger may be due to a solid mass. Introduce a needle occlusally, as this area is usually thinner than buccal or lingual side (Fig. 27.7).

Fig. 27.7 Aspirated cystic fluid; (**a**) aspiration from infected radicular cyst, (**b**) aspiration from infected keratocyst

27.7.4 Cystic Fluids

Cystic contents are different ranging from clear yellow fluid to a creamy or cheese like semisolid liquid. The content can be examined for its color, consistency and for the existence shimmering cholesterol clefts or crystals (microscopic examination of cholesterol crystal shows an envelope with cut-corner appearance). Electron microscopic examination reveals the presence of various protein fractions like alpha and beta globulin , albumin, flecks of keratin, as well as total protein content along with inorganic phosphates [14] (Table 27.3).

27.7.4.1 Biochemical Analysis of the Cystic Fluid

Toller has opined that by an active cellular transport mechanism, the proteins are drawn into the cystic fluid by immunoglobulin (Ig) producing cells. Estimation of IgA, IgG, and IgM levels in cystic fluid can be done quantitatively [15]. Smith et al. [16] concluded in their study that the most of the cystic fluids show the presence of proteins with higher molecular weight. This is due to the fact that the semipermeable intraepithelial channels facilitate the passage of lactoferrin into the cystic lumen.

The cystic fluid, which is collected via aspiration biopsy, can be biochemically analyzed for their protein content estimation by Cellulose acetate membrane (CAM) electrophoresis. First, the cystic fluid is transferred to the centrifuge machine for the removal cell debris and deposits at 2000 rev/min for 5 min.

Since electrophoresis studies the movement of charged particles through an electrolyte, which is subjected to an electric field, and it separates different proteins as per their physical properties, the fluid free of debris is then studied qualitatively and quantitatively. The protein mixture is applied to the end of the CAM strip. Scanning of these impregnated CAM strips can be carried out using a densitometer for the quantitative estimation of protein fractions.

Table 27.3 Various cystic lesions and their aspirates

Types of cysts	Aspirate color	Aspirates' other findings
Dentigerous Cyst Inflammatory Cyst	Absolutely Clear and faint straw/golden color liquid	Shimmering Cholesterol crystals. Resembles serum. Aggregate Total protein >4 gm/100 ml.
Odontogenic Keratocyst	Dirty, creamy white, and viscoid/thick suspension	Floating of desquamated keratin flakes, Less than 4 gm/100 ml of Aggregate Total protein. The predominant presence of Albumin is seen, which is less soluble.
Periodontal Cyst	Absolutely Clear and faint straw/golden color liquid	Cholesterol clefts/crystals. Aggregate Total protein 5–11 gm per 100 ml.
Infected radicular Cyst	Presence of Pus or brown color fluid	Polymorphonuclear leukocytes and cholesterol crystals
Mucocele and Ranula	Sticky, viscous, and thick Mucus	Secreted by salivary glands
Gingival Cysts	Clear fluid	
Solitary Bone Cyst	Serous type of fluid; sometimes, blood is aspirated, or empty cavity is found	Necrotic material in blood clot
Stafne's Bone Cyst Idiopathic bone cavity	On aspiration air is drawn—Empty cavity	
Dermoid Cyst	Sebaceous thick material	
Fissural Cysts	Mucoid liquid	
Unicystic ameloblastoma	chocolate brown fluid	
Hemangioma-intramedullary cavernous	Syringe full of fresh venous blood	
A-V malformation Arterial or arteriovenous malformation	Bright red blood, pulsatile, pushes plunger	

27.7.5 Biopsy

Incisional (for large lesions) or excisional (for small lesions) biopsy and histopathological examination of the specimen is the gold standard to arrive at final diagnosis.

27.8 Various Surgical Treatment Modalities for Cystic Lesion

With all the investigation results in hand, the surgeon will have a clear idea of the type, the location, extent, and behavior of the lesion. A final diagnosis is then obtained, and a suitable surgical line of treatment is decided upon (Boxes 27.4, 27.5, 27.6, 27.7, 27.8, 27.9, and 27.10).

Box 27.4 Clinical Tips

Incisional Biopsy: For large lesions, a "representative" section of the lesion is incised with the help of a scalpel along with the normal tissue and sent for histopathological evaluation. An elliptical, wedge-shaped tissue is obtained with the "V" of the wedge converging into the deeper tissues. The depth of the biopsy should be enough to obtain a representative area of the lesion.

Excisional Biopsy: It is a combination of diagnostic and curative procedure and is suitably smaller for lesions <1 cm. In these cases, the entire lesion is excised in toto at the same sitting and sent for histopathological examination.

Box 27.5 Reasons for the Definitive Treatment

- Cysts continue to grow and show a tendency to increase slowly in size
- They can get secondarily infected
- Cyst can make the jaw bone weak, leading to pathological fracture
- Few cysts can undergo transformation to aggressive pathological lesions like ameloblastoma or squamous cell carcinoma
- Cysts prevent eruption of teeth (as in the case of a dentigerous cyst)
- Cysts can involve neighbouring structures like teeth, maxillary sinus, nasal cavity, inferior alveolar nerve, etc.

Box 27.6 Goals of Surgery

- Complete elimination of the pathology, minimizing the recurrence rate & morbidity for the patient, and improving the quality of life postsurgically
- Minimum trauma to the adjacent important structures like dentition and nerves
- Restore/Preserve/Maintain function & esthetics

Box 27.7 Factors for the Choice of Optimum Surgical Strategy/Treatment

Patient factors & lesion characteristics

- Patient's age & general health and coexistence of NBCCS-Nevoid Basal Cell Carcinoma Syndrome/ any other syndrome
- Patient's reliability to follow up
- Size of the lesion & whether solitary/multiple
- Uni/multilocular
- Location of the lesion-surgical access
- Cortical perforation/Soft tissue/adjacent structure involvement
- Presence or absence of infection
- History of recurrence/previous surgery
- Histological variant

Box 27.8 Conservative Surgical Treatment

- Decompression alone-placement of a drainage tube-palliative (decrease in lesion size)
- Decompression followed by Enucleation along with adjuvant therapy (two-staged procedure)
- Marsupialization Alone (creating a pouch)
- Marsupialization followed by Enucleation (Waldron's method) [17] (two-staged procedure)
- Enucleation Alone with packing, with primary closure, or with primary closure with bone grafting/ reconstruction
- Enucleation along with excision of overlying oral mucosa (Stoelinga protocol [18])
- Enucleation followed by various Adjuvant Therapies

Box 27.9 Enucleation with Adjunctive Modalities to Eliminate the Microscopic Pathologies

- Peripheral ostectomy (Mechanical/physical methods, Hand instruments like curettes, & use of rotary bur for removal of perimeter of investing bone)
- Chemical cauterization treatment with Carnoy solution (1.5 mm depth of bone penetration/5 min)
- Electrocauterization is used for buccal and lingual perforation area.
- Cryotherapy (use of liquid nitrogen after enucleation)
- Multidisciplinary Sequential treatment (MST) Approach (decompression, enucleation, peripheral ostectomy, and cauterizing bone cavity by carbolic acid) (Sun et al. [19])

Box 27.10 Aggressive Surgical Treatment

- Resection without causing a continuity defect-peripheral ostectomy
- Resection with a continuity defect–segmental resection
- Resection along with disarticulation of condyle

27.8.1 Conventional Surgical Options

The objective of the choosing any particular surgical method is to minimize patient morbidity and reduce the recurrence rate. Surgical procedures for treating cystic lesions are often put into two categories; conservative or aggressive (Boxes 27.8, 27.9, and 27.10).

Decompression and marsupialisation (cystotomy): Partsch I operation of the cysts is presumably the earliest treatment. Enucleation or cystectomy with primary closure is also known as Partsch II procedure (Partsch 1892, 1910) [17].

Decompression, marsupialisation: both methods achieve evacuation of the cystic contents by creating a surgical opening in the cystic wall. These procedures preserve the continuity of the cystic lesion with the oral/nasal cavity or maxillary sinus.

27.8.1.1 Decompression

Decompression of a cyst is achieved by a minor surgical procedure, which decreases the intracystic hydrostatic pressure, which is responsible for cyst expansion. Subsequently, decompression allows for the bone remodeling and bone fill.

Decompression can be achieved under L.A. by creating a small opening in the cystic wall and keeping it patent with a surgical drain. Acrylic tubes, Luer syringes, polyethylene tubes, nasopharyngeal airways, or nasal cannula or intravenous tubes have been used by fixing them with sutures or wires to keep the opening in the cyst patent, through which the cystic lumen is flushed twice/thrice everyday with saline/antiseptic wash.

Cysts of the lower jaw are normally evacuated through opening into the oral cavity, and maxillary cysts can be drained either into the oral cavity, the maxillary sinus or nasal cavity [17] (Fig. 27.8).

27.8.1.2 Marsupialization

It is a surgical procedure, whereby a cystic sac is modified or deroofed to convert it into a pouch. This results in a self-sustaining stoma/opening or outlet, which in turn reduces intracystic hydrostatic pressure. It is basically a surgical externalization of the cystic cavity by creating an opening in the superficial aspect of the cyst. The resected portion is sent for histopatholgical study. The remainder borders of the cystic wall are then sutured to the surrounding edges of the oral mucosa, thus converting an enclosed sac, into an open pouch, exposing the cystic lining or epithelium to the oral environment. This procedure decreases the volume and size of the lesion and promotes the speedy healing and new bone formation. This option is more precise compared to the decompression method. Marsupialization may be used as a solo treatment regime for a cyst or as a prior step to final second stage enucleation [17].

Surgical Procedure In Marsupialization, after locally anesthetizing the buccal/labial area, an oval/elliptical incision is taken to make a surgical window spanning 1 cm into a cyst; the window cover consisting of oral mucosa, thinned out bony cortex and cystic lining, is removed, and the boundaries of the cystic lining around the surgical opening are sutured to the surrounding oral mucosa. In the case of a thick bony cover over a cyst, an inverted U-shaped incision is planned with a wider base in the buccal sulcus, mucoperiosteal flap is reflected, and bony window is removed cautiously with burs or rongeurs. The excised tissue of the window created must be subjected to histopathological study. The contents of the cyst are sucked out, and the residual lining of the cyst is inspected. The remainder cystic cavity is irrigated thoroughly to lavage any residual debris. The residual cystic cavity is inspected carefully for any abnormal findings like ulcerative lesions or possible dysplastic/neoplastic areas.The cystic cavity is then packed with ribbon gauze strip soaked with tincture of benzoin or iodoform/white head's varnish or paraffin, or an antibiotic ointment, or bismuth iodine paraffin paste-BIPP, with its end protruding through the opening.

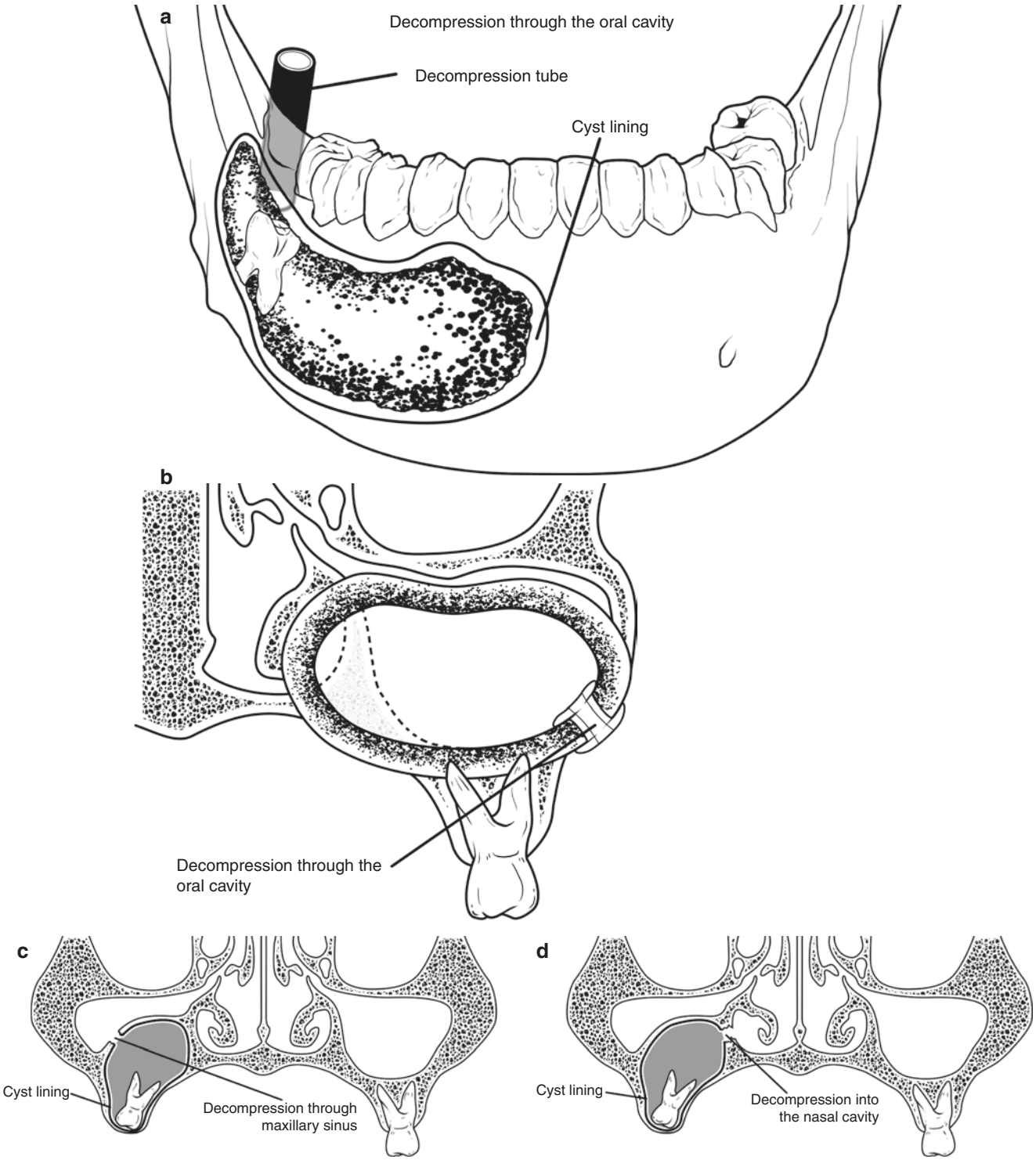


Fig. 27.8 Decompression of a cystic lesion by creating a small opening and keeping it patent by inserting a drain. (**a**, **b**) Decompression through oral cavity, (**c**) maxillary sinus, (**d**) nasal cavity

This packed gauze strip is left in situ for 2 weeks, until the line of junction between the cystic lining and oral mucosa is healed. After it is removed from the cystic cavity, the patient needs to irrigate/gargle with antiseptic mouthwash frequently in a day to prevent food accumulation. The flushing has to be continued for many following months, until the bone fill and complete healing is noticed.

Later on, acrylic plate or plug/obturator can be prepared to protect the healing cavity and used until it gets obliterated over a period of time, but as the healing progresses, the plug needs periodic adjustments (Table 27.4).

27.8.2 Modification of Marsupialization-Waldron's Method—Two-Staged Procedure [17]

Usually, once the cystic lesion regresses in size after initial marsupialization procedure, enucleation is carried out as a second stage surgery.

The larger or inaccessible cyst is initially marsupialized, and bony healing in progress is observed. As the cystic cavity decreases to a relatively small size, then complete surgical removal is possible by enucleation. The proper time for secondary enucleation is when bone covers adjoining vital structures. This protective shield of new bone prevents their injury during secondary enucleation, also provides adequate strength to the basal jaw bone, and prevents pathological fracture.

In a cyst associated with developing tooth bud, as soon as the tooth erupts into the dental arch alignment, there may not be any residual cystic lining left to enucleate. Decompression and/or marsupialization with less morbidity and preservation of adjoining vital structures has a good rate of success over many other aggressive treatments (Figs. 27.9 and 27.10).

Table 27.4 Indications, advantages & disadvantages of decompression & marsupialization

Indications	Advantages	Disadvantages
• Very large cyst in proximity to vital structures • When apices of many adjacent teeth are involved in large cyst • Guided Assistance for eruption of developing teeth- young children with developing teeth buds or unerupted teeth • Possibility of creating a pathological fracture of a jaw bone • Difficult Surgical access for large multilocular cyst • Medically compromised or debilitated patients • To detect any occult Pathology by visual inspection	• Very simple procedures, not much skill needed, and done under L.A. • Prevents iatrogenic injury to vital structures • Avoids pathological fracture • Gradually decreases the cystic cavity, preserving adjacent oral tissues • Maintains the pulp vitality, avoiding dental extractions • There is a change in the nature of the fragile cystic lining, which becomes thick or converts to normal mucosa, and thereby, secondary enucleation becomes easy. • Reduce the intracystic pressure and induce endosteal bone formation	• Leaves pathological tissue behind • It takes longer healing time • Needs patient commitments to maintain hygiene with repeated irrigations and for long follow-up • Second surgical intervention may be needed. • Not recommended for mentally challenged patients with multiple cystic lesions. • Inability to examine the whole cystic lining histopathologically is also a matter of concern sometimes and may miss out mural pathologic changes

27.8.3 Enucleation or Cystectomy or Partsch II (Videos 27.1 and 27.2)

Enucleation or Cystectomy or Partsch II with and without adjunct procedures has been validated as the most appropriate surgical modality for almost all cysts of the orofacial region, with various adjunct procedures as deemed fit for individual case.

To enucleate is "complete removal or excision in toto from its envelope without rupture." With this, no bone, other than required for surgically accessing the lesion, is removed.

It is the most versatile treatment modality, and many researchers have said that the surgical enucleation of a cyst in one piece has been known to reduce the rate of recurrence.

An enucleation procedure is possible because of the presence of a fibrous connective tissue layer in between the epithelial lining of a cyst and cystic cavity bony wall. This layer acts as a cleavage point for separating the cystic lining from the jaw bone and makes surgical procedure of enucleation easy, as we carry out stripping of periosteal layer from the jaw bone. The surgical cavity gets filled with the blood clot and eventually gets organized into bone formation.

27.8.3.1 Surgical Procedure

The small cysts can be treated with local anesthesia, but larger cysts need to be treated under general anesthesia. As per the size and site of the lesion, the mucoperiosteal flap is designed, following the right surgical principles. If the bone over the lesion is thinned out, access can be gained by removal of the cortical bone by rongeurs. But if the bony cortex overlying the access area is hard and thick, then the osseous window is created by using rotary burs.

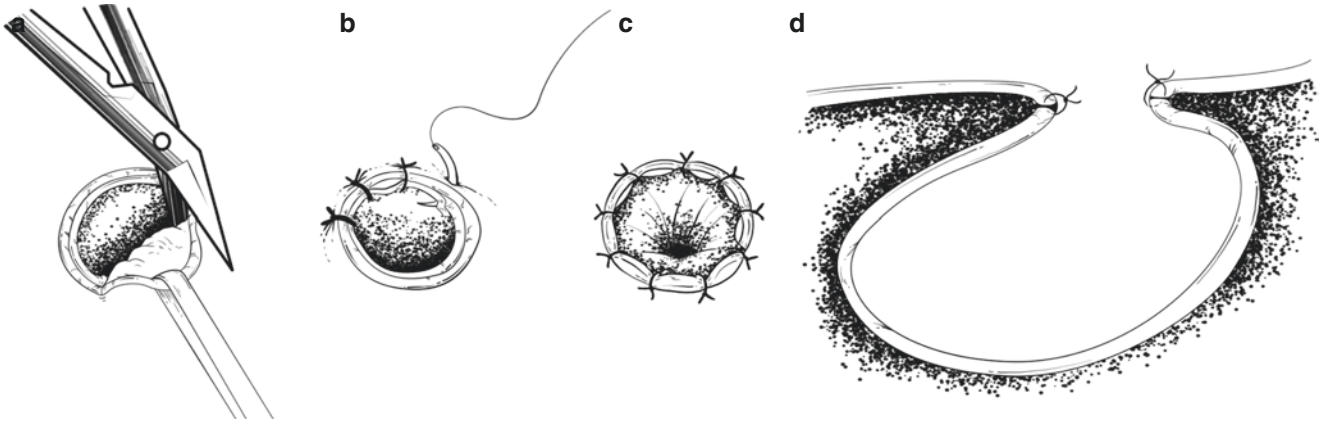


Fig. 27.9 Diagrammatic representation of Marsupialization procedure; (**a**) creation of opening on the buccal side of a cyst, (**b**) suturing remaining cystic lining to oral mucosa, (**c**) final suturing to keep the cystic cavity open into oral cavity, and (**d**) diagrammatic representation of Marsupialization procedure

After complete enucleation procedure is over, the entire cavity is inspected for proximity of the adjoining vital structures and for the remnants of the pathological tissues.. In large extensive cysts, usually the neurovascular bundle is pushed to one side by the slowly growing lesion, and in these cases, atraumatic enucleation should be carried out. Irrigation and cleaning of the entire bony cavity with saline will assist in visualising/inspecting it. The roughened bony edges of the cavity are then smoothened with a file or rotary bur before final suturing.

Cysts that include tooth roots or certain areas of the jaws, which are surgically inaccessible, require thorough curettage, in order to remove fragile cystic lining fragments. If devitalization of the teeth is brought about during enucleation, then the affected teeth should be treated with root canal fillings.

Clinical Tips: If the patient is young and the lesion is involving multiple anterior teeth, the teeth can be retained after root canal treatment and apicectomy, provided thorough inter-radicular curettage by using small periodontal instruments.

If the teeth show a great degree of mobility and in the case of recurrent lesion, they should be extracted.

Enucleation of a cyst is followed by watertight suturing over the sound bone. To achieve this, sometimes, mobilization of the soft tissue flaps with advancement is required. If complete surgical suturing is not possible, then the defect should be packed with stripped ribbon gauze soaked with an antibiotic ointment or BIPP/White head's varnish. Frequent change of this packing is advocated after irrigating the cavity, until new granulation tissue has filled up the cavity and complete epithelisation of the wound has taken place (Fig. 27.11).

27.8.3.2 Enucleation Along with the Adjunct Procedures

Enucleation with different adjuncts has been carried out since many years.

A. *Enucleation with Peripheral Ostectomy*

It is basically used as an additional adjunctive step for peripheral bone trimming for avoiding resection, as almost all hypotheses for recurrence point out toward the possibility of leaving residual pathological fragments behind, especially, in the large cyst with scalloped borders or cysts with difficult access. Here, a greater risk of incomplete excision may exist. Adjunct procedure of peripheral ostectomy may be carried out in cases of cysts, which have high recurrence rate, e.g., Odontogenic Keratocyst. A peripheral ostectomy with rotary bur with sterile irrigation helps to remove all the microscopic residual pathological tissue. The procedure is followed to remove the lesion in one piece along with an enveloping border of bone, and hence, the possibility of iatrogenic rupture of the cystic capsule or leaving its fragments behind is greatly reduced. A minimum 2–5 mm bony margin inclusion for peripheral ostectomy is supposed to be adequate. In the case of thin inferior border of mandible, reinforcement with reconstruction plate is advocated. This can also be accomplished by means of mechanical hand instruments like a sharp curette. The recurrence of the cyst can be prevented by this procedure.

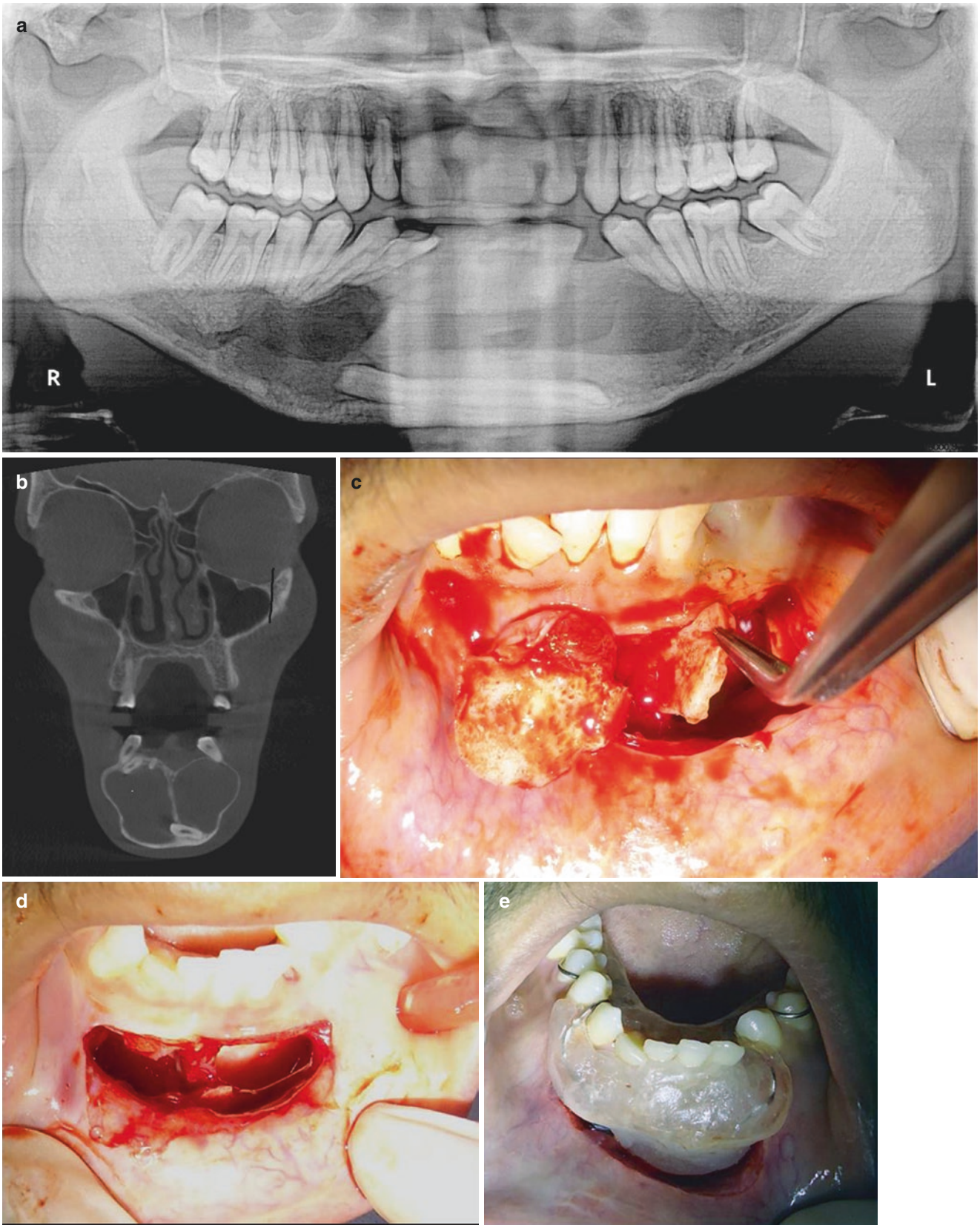


Fig. 27.10 *(CLINICAL CASE SCENARIO)*: (**a**) OPG showing the large radiolucent lesion extending in the mandibular body with impacted canine at the inferior border, (**b**) CT scan of the same patient showing multilocular radiolucent lesion with embedded canine, (**c**) a large opening was created in the anterior body mandible region, and roof of the cyst along with oral mucosa was removed along with the evacuation of the cystic content, (**d**) healing of the wound after marsupialisation, (**e**) acrylic plate was constructed to cover the wound, (**f**) 6 months follow-up, lesion reducing in size, and (**g**) OPG after six months showing the reduction in size of the cyst. The patient is advised to undergo second stage surgery for enucleation and extraction of impacted canine. *Courtesy-Prof.Vidya Rattan, PGI, Chandigarh*

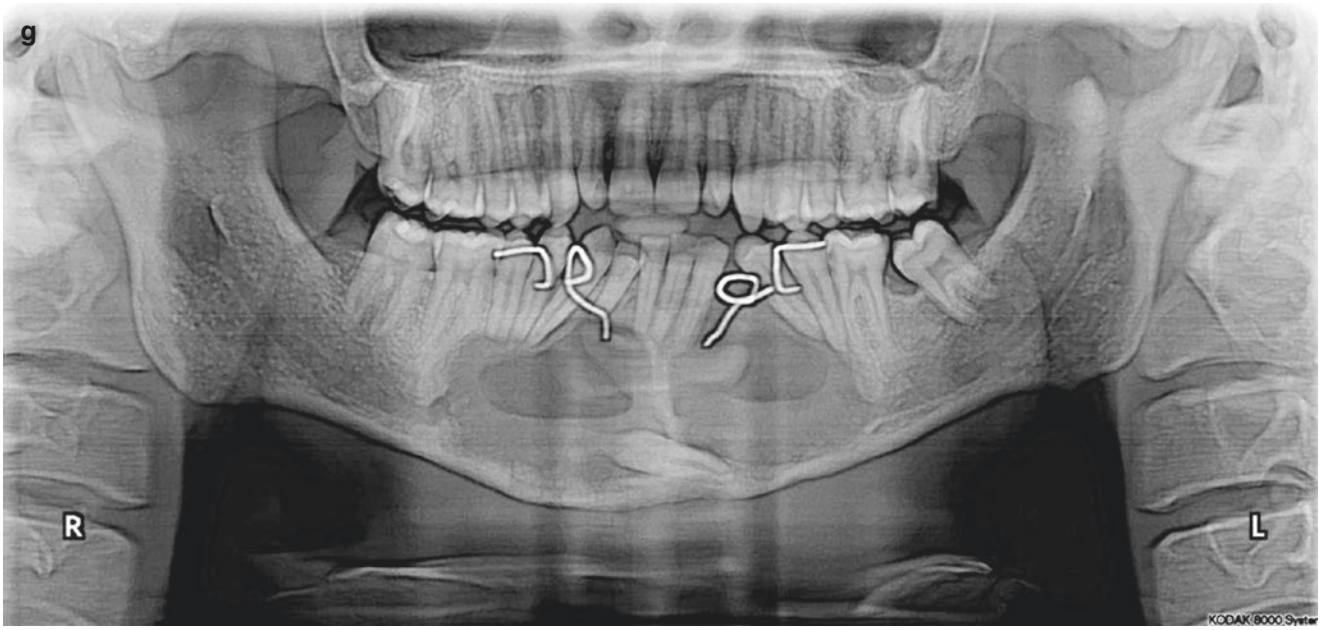


Fig. 27.10 (continued)

B. *Enucleation and application of Carnoy solution to the bony defect*
Many a times, due to the thin, friable wall and the presence of many small satellite cysts, there is a difficulty of enucleating it in one piece. Hence, the surgical treatment is focused on eliminating all residual epithelial fragments. In order to achieve this, a mild, judiciously penetrating, and cauterizing agent like Carnoy's solution is utilized. It has a mean bone penetration depth of 1.54 mm, with an application time of 5 minutes. (Carnoy's solution's composition is 3 ml of chloroform, 6 ml of absolute ethanol, 1 ml of glacial acetic acid, and 1 g of ferric chloride) [18, 20–22]. This is adequate to bring about chemical cauterization of the residual pathologic fragments. Literature shows the use of modified Carnoy's solution without chloroform, as it is currently listed as a carcinogenic agent.

The protocol of carrying out enucleation followed by the application of Carnoy's solution in the treatment of locally aggressive cysts, like OKCs, lowers the recurrence rate and morbidity. During the application of Carnoy's solution, the neurovascular bundle can be protected by using bone wax cover or wooden spatula or paraffin gauze.

Dashow et al. studied and compared the use of Carnoy's solution versus modified carnoy's solution in cases of OKCs and stated that the recurrence is almost eliminated, and the results are comparable to those of the resection without carrying out the morbid surgery [22].

C. *Enucleation followed by liquid nitrogen cryotherapy*
The aggressive cysts are best treated by enucleation followed by cryotherapy, using liquid nitrogen. This therapy is commonly used for the treatment of many locally aggressive jaw lesions, such as ameloblastoma, OKC, or ossifying fibroma [23]. Cryotherapy destroys the residual

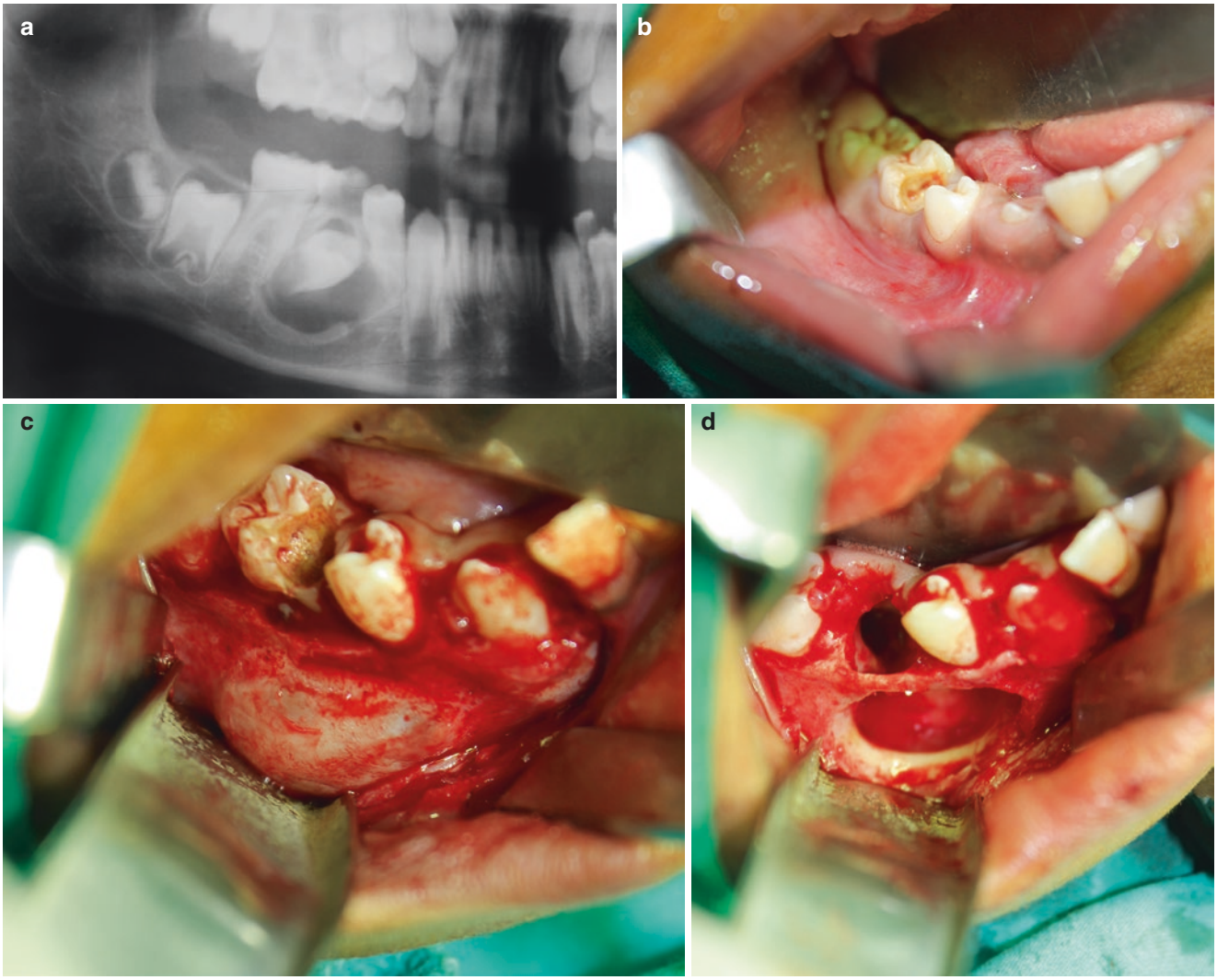


Fig. 27.11 *(CLINICAL CASE SCENARIO)* (**a**) OPG showing the presence of a dentigerous cyst in a 7 years old child, (**b**) clinical intraoral picture of the same, (**c**) reflected flap to expose the underlying expanded buccal cortex, and (**d**) enucleation of the lesion in toto. *Courtesy Dr, Kumar Nilesh, SDS, Karad*

epithelial lining cells or satellite cysts and leaves behind the inorganic bony matrix intact, which is helpful for osteoconduction. Liquid nitrogen causes bone devitalization due to direct effect/damage from ice crystal formation, which takes place in the cellular and extracellular compartments and due to the subsequent osmotic and electrolyte disturbances [23]. The routine first step in surgery of the lesion is enucleation of a cyst, followed by cryotherapy. The adjoining tissues are then shielded by sterile wooden spatula and gauze strip, and the residual cavity is treated with liquid nitrogen spray—two swipes for 1 min each, with a 5 min thaw break between two

spray freezes. After cryotherapy, it is possible to place the bone graft in the cystic cavity to strengthen the jaw bone. Finally, the wound is sutured in a watertight manner [23] (Box 27.11 and Table 27.5).

Box 27.11 The Advantages and Disadvantages of Liquid Nitrogen Cryotherapy After Enucleation

Advantages:

1. The matrix shell of basal bone is left behind, which acts as a scaffold and induces new bone formation.
2. In order to accelerate the bony healing and strengthening the jaw bone, immediate bone grafting can be done. This avoids pathological fracture.
3. It decreases bleeding and scarring.

Disadvantages:

1. Unpredictable results are usually due to utilization of uncontrolled spray of liquid nitrogen to the area. This may lead to bone necrosis and postoperative swelling.
2. If liquid nitrogen comes into contact with unprotected inferior alveolar nerve, there will be altered sensation/paraesthesia or total anaesthesia. In most of the cases,partial or total recovery of sensation is expected within 3 months [23].

27.8.3.3 Enucleation Followed by Bone Grafting

Indications

1. To avoid pathological fracture,
2. To avoid long-term esthetics and functional problems in larger cystic cavity, more than 4 cm.

Autogenous bone grafts possess characteristic osteoconductive and osteoinductive qualities due to the presence of abundant osteoprogenitor cells. The use of Autogenous cancellous bone grafts for large defects to obliterate the cavity and stimulate osteogenesis is the gold standard, but the issue of donor site morbidity is always there. The dead space elimination after enucleation of a large defect is recommended by packing the defect with autogenous bone graft or its synthetic substitute. Calcium phosphates, α- and β-tricalcium phosphate (TCP), bioactive glasses, calcium sulfate, glass ionomers, hydroxyapatite (HA), etc. are some of the synthetic graft materials available in the market, which can be used instead of autogenous bone grafts, for filling up the defect after enucleation. The blood clot in the cystic cavity is stabilized by these synthetic grafts, thereby minimizing the postoperative infection. These synthetic grafts are also osteoconductive in nature and promote new bone formation by facilitating the migration of osteoprogenitor cells [24, 25].

Table 27.5 Indications, advantages, & disadvantages of enucleation along with adjunct procedures

Indications	Advantages	Disadvantages
1. For smaller and accessible lesions. 2. Medically fit patients with larger lesions. 3. If it is possible to enucleate without jeopardizing the vitality & integrity of teeth & adjacent vital structures. 4. Enucleation as a second stage procedure after decompression or marsupialization. 5. Enucleation along with adjunct procedures.	1. Better alternative than radical treatment. 2. Cyst-oriented treatment 3. Entire pathological tissue is removed, which is available for histopathological examination. 4. Chances of recurrence are reduced with adjunct procedures. (Elimination of satellite cysts & epithelial remnants) 5. Healing period is reduced. 6. Maintainance of oral hygiene is easy. 7. Enucleation with water tight suturing eliminates the need for long postoperative treatment. 8. Good patient compliance. 9. Comfortable for patient.	1. After primary closure, it is not possible to observe the healing cavity. 2. In younger patients, erupting teeth have to be extracted. 3. Large cyst enucleation may end up in fracture or perforation/damage to adjoining soft tissues. 4. Possibility of damaging adjacent vital structures. 5. May lead to pulpal necrosis/devitalization of adjacent teeth. 6. Enucleation with fragmentation in inaccessible areas may end up in recurrence.

27.8.4 Block Resection, With or Without Preservation of the Continuity of the Jaw

Resection of a jaw bone can be done either as (1) marginal resection procedure or (2) segmental resection procedure. In marginal resection procedure, the lesion is smaller, which is excised in toto, and hence, it is possible to maintain the continuity of the jaw bone by preserving the portion of the uninvolved bone. In segmental resection procedure, since the lesion is extensive, the complete segment/portion of maxilla or mandible is sacrificed, and hence, continuity of the jaw bone is lost after this radical treatment. Since this procedure ends up in considerable morbidity, there is always a need for rehabilitating the patient functionally and esthetically by various reconstructive measures [26]. Many researchers felt that there is no need for aggressive therapy in the case of cystic lesions, as their management can be done by using relatively noninvasive means [26].

Blanas et al. [21] carried out a systematic review and found that following resection, there was 0% recurrence rate, but it is always associated with the high morbidity rate. Their study suggested that enucleation followed by the use of Carnoy's solution gives similar low recurrence rates, as resection, without unwarranted radical surgery. Complete resection of the mandibular/maxillary bone is considered as morbid overtreatment for large locally aggressive cysts. The only main disadvantage of a conservative treatment is prolonged therapeutic time [27].

In this chapter, we will be discussing only briefly Dentigerous and Keratocyst varieties prototypes.

27.9 Dentigerous Cysts or Follicular Cysts

Dentigerous Cysts or Follicular Cysts, The term dentigerous is a Latin word, literally means "tooth bearing/producing". Paget in 1853 first coined the term "Dentigerous cyst", in this entity, there is an enclosure of the crown of a tooth, which is unerupted, and cyst is attached to the CE junction and is formed by the enlargement of its follicle [1]. There is always an association of this cyst with the crown of fully or partially impacted or submerged tooth (Fig. 27.12).

Depending on the location and extent of the cystic degeneration in relation to the crown of an unerupted tooth, the cyst can have central, lateral, or circumferential variety [28]. In central type, initially, the crown may be enclosed by a cyst symmetrically, but as it expands, crown of the mandibular third molar may be shifted to the inferior border of the mandible or

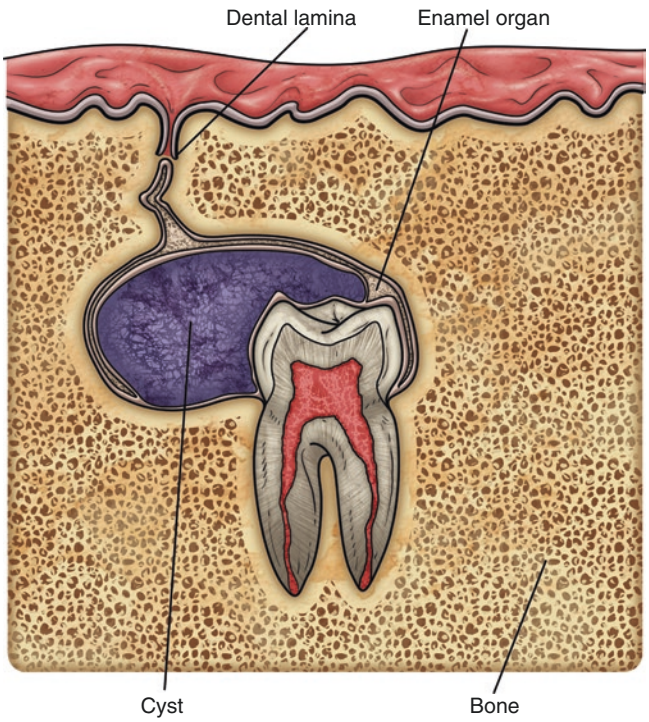


Fig. 27.12 Formation of a dentigerous cyst

migrated high up in the ascending ramus and similarly, maxillary canine or third molar may be seen at the orbital floor or high in maxillary sinus. The lateral type will be because of expansion of cyst only on one particular side of the crown, and it will be seen in cases of partially erupted mandibular third molars. In circumferential type, the radiograph will show a radiolucency enveloping the entire tooth (Fig. 27.13).

27.9.1 Differential Diagnosis

Hyperplastic follicle-Normal follicular space size is 2–3 mm; if it exceeds 5 mm, then dentigerous cyst should be suspected.

Differential diagnosis of unicystic ameloblastoma, an odontogenic keratocyst, Calcified odontogenic cyst, Ameloblastic fibroma, Adenomatoid odontogenic tumor, or radicular cyst must be considered in such cases comparable to the radiographic details, but the incidence of all the above lesions is rare in the first decade of life. Since radiographs alone cannot differentiate the above-mentioned lesions, a histopathological examination should be performed.

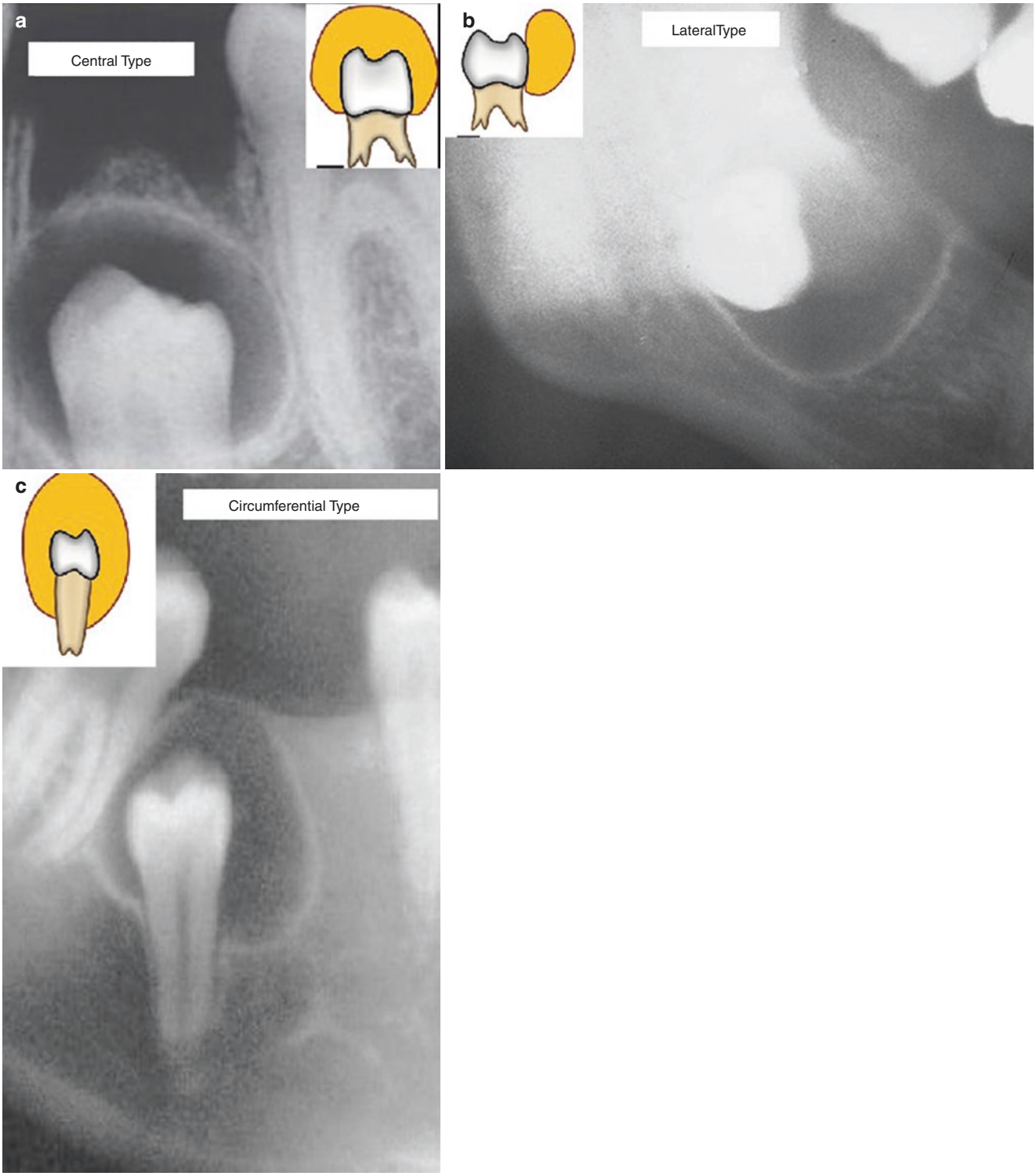


Fig. 27.13 Types of dentigerous cysts and their radiological picture of central, lateral, and circumferential type (**a**–**c**)

Fig. 27.14 Arrow pointing to a thin lining in dentigerous cyst resembling reduced enamel epithelium histologically

27.9.2 Histology

Thin layer of nonkeratinizing stratified squamous epithelium lining the lumen is seen, and no rete ridges are seen. Connective tissue wall shows bundles of collagen fibers; sometimes, many odontogenic epithelial islands are seen. The cystic lumen contains thin, watery, and yellowish fluid (Fig. 27.14).

27.9.3 Potential Complications of Dentigerous Cyst

1. As it is known that dentigerous cysts have potential for neoplastic proliferation in the form of cystic or mural ameloblastoma, in these cases, there is a nodular thickening at some places in the cystic wall, which cannot be discerned clinically, but is a tumor manifestation itself, and therefore, histopathologist is requested to carry out thorough gross and microscopic examination of the whole specimen for nodular thickening, etc. in the cystic wall.
2. Epidermoid carcinoma—cyst lining, which shows long-standing keratin metaplasia, should be considered as a marker for the initiation of carcinomatous changes.
3. Mucoepidermoid carcinoma—dentigerous cyst may contain cells with the potential of mucus secreting ability, which may transform into mucoepidermoid carcinoma [28].

27.10 Odontogenic Keratocyst

OKC has got its name because it exhibited keratinization of cystic lining. Its lumen contains a cheesy material resembling keratin debris and clear fluid. It is a Dilemmatic, Distinctive, Odontogenic Developmental, and Intraosseous cyst of epithelial origin of Oral & maxillofacial region, with specific characteristics, such as rapid Infiltrative growth, aggressive nature, high recurrence rate and defined histopathological features [26, 27]. Since 1956, for the last six decades, many researchers started focusing on this entity. Journey of this changing nomenclature is pretty interesting (Box 27.12).

Box 27.12 History of OKC

1774	Dental cyst (John Hunter)
1876	Dermoid cyst (Mikulicz) identified & described as a part of familial jaw condition
1926	Cholesteatoma (Hauer)
1945	Primordial cyst as per origin
1956	Odontogenic Keratocyst (OKC) (Philipsen first coined the word)
1963	Aggressive growth/high tendency for recurrence rate (described by Pindborg & Hansen)
1967	Regarded OKC as a benign tumor (Toller)
1992	OKC as preferred term for keratinized cysts (WHO)
2004	Keratinizing Cystic Odontogenic Tumor(KCOT) (Reichart & Philipsen)
2005	Keratocystic Odontogenic Tumor (KOT) (WHO working group)
2017	Odontogenic Keratocyst (WHO)

In 2004, Reichart and Philipsen suggested a new classification for the odontogenic tumors, redesignated OKC as Keratinizing cystic Odontogenic Tumor (KCOT), and put it under the subcategory of "benign neoplasm of odontogenic epithelium with mature, fibrous stroma "due to its propensity for local destruction, aggressive biological behavior, and high recurrence rate and mitotic figures seen in the suprabasal layers [29]. Shear had re-emphasized that OKC shows increased proliferative activity & high recurrence tendency and stressed on association of OKC with the Gorlin-Goltz syndrome/Nevoid Basal Cell Carcinoma syndrome (NBCCS). Some of these OKCs had association with the PTCH 1 gene mutation and increased immunohistochemical expression of proliferation markers Ki 67 and presence of PCNA (Proliferating cell nuclear antigen marker of cell rep-

lication) and p53 in KCOT. All this evidence led to change in nomenclature by WHO in 2005 [10].

This shift in tumor category suggested change in management protocol for OKC, which created a lot of skepticism, and the concept was not widely accepted, with the reason being not all OKCs possess identifiable PTCH mutation. There were no clear-cut suggestions such as neoplastic title was to be applied to all OKC or to just a small subset. All relevant sequencing data on the odontogenic keratocysts has not yet been presented and still under research.

Researchers have suggested that marsupialization can revert the fragile cystic lining epithelium to normal oral mucosa or from parakeratin to orthokeratin type [30, 31].

Extensive debate (for 12 years) over putative neoplastic nature of the lesion took place. So, in 2017, a WHO expert panel declared that there is no strong affirmation to rationalize to label OKC as a neoplasm, and therefore, Odontogenic Keratocyst-OKC should be put back in cyst category and the term keratocystic odontogenic tumor (KCOT) was eliminated from the new classification (Boxes 27.13, 27.14, 27.15, 27.16, 27.17 and 27.18).

Box 27.13 Epidemiology of OKC

Incidence: Second most prevalent cysts of odontogenic origin (10–12% of all odontogenic cysts) [32].

Age: Wide age range. Range of occurrence between the 1st and 9th decades of life. Bimodal age distribution (first peak at 20–30 & second at 50–60 years of age) and Predominantly in younger patients in syndromic cases.

Sex: Male predilection (1.6:1 ratio), More Female predilection in syndromic cases.

Race: predominantly in white population.

Box 27.14 Site Predilection of OKC

Central intraosseous Lesion—Thrice more prevalent in mandible. Seen more at various sites in following order-angle-ascending ramus, maxillary third molar region (*may involve sinus, nasal floor premaxilla, presence of impacted third molar seen, and occasionally floor of orbit involvement*), mandibular, premolar area, and maxillary canine.

Peripheral OKC in buccal gingiva (female predominance 2.2:1 ratio [33])

Box 27.15 Number of Cysts in OKC

- Usually solitary/sporadic/nonsyndromic lesions
- *Syndromic*: Multiple OKCs are often one of the manifestations of genetically inherited Nevoid Basal cell Carcinoma Syndrome (NBCCS), Gorlin-Goltz syndrome, etc. [In syndromic cases, multiple cysts can be seen in one patient at a time or during lifetime occurrence, many cysts can happen at different times [34].
- *Nonsyndromic multiple cysts* [34]

Box 27.16 Syndromic Associations of OKC

- Basal cell nevus syndrome, Nevoid Basal cell Carcinoma Syndrome (NBCCS), or Gorlin-Goltz syndrome
- Marfan syndrome
- Noonan syndrome
- Orofacial Digital Syndrome
- Simpson–Golabi-Behmel syndrome

Box 27.17 Latest Histopathological Groups of OKC

As per the occurrence of satellite/daughter cysts & squamous islands found in the cystic wall (Kahraman et al. [35]) (Fig. 27.17)

Group I: Unicystic, without any satellites (63%)

Group II: With few satellite/microcysts & squamous islands in the cystic lining less than (10–27%)

Group III: Abundant presence of satellite/daughter cysts and squamous islands (6–10%)

27.10.1 Etiology and Pathogenesis

Various origins—Two sources are implicated.

1. Remnants of dental lamina and
2. It can originate from downgrowth or implantation following trauma of the offshoots of epithelial basal layer of the oral gingiva and mucosa [27]. Islands of Epithelium and/or daughter cysts are seen in 50% of the cases, in overly-

Box 27.18 Reasons for Recurrence of OKC (13–62%; Nakamura et al. [36])

1. Thin walls and fragile epithelial lining
2. Epithelial lining is weakly attached to capsule
3. Extension of the cyst into cancellous bone
4. Dental lamina remnants in bone/overlying mucosa
5. In the case of perforation of the cortex, cyst lining adheres to adjoining bone or buccal or lingual mucosa (especially, lingual perforation is difficult to access during enucleation)
6. In dentate area (residual remnants in intraradicular areas)
7. Scalloped margins in multilocular variety
8. Desire to preserve adjacent vital structures
9. Location with difficult access
10. Extensive lesion involving coronoid/ascending ramus (difficult access)

ing mucosa. (In the past designated as basal cell hamartias). Genetic factors are also always key players, especially PTCH gene aberration.

27.10.2 Unique Growth Pattern—Peculiar Behavior—Pattern of Bone Involvement in OKC

Unlike other cysts, lesion grows by extension in medullary space in anteroposterior direction, compared to osmotic expansion.

Finger-like projections are seen in marrow spaces, and enlargement goes on relentlessly along the path of least resistance. When it reaches a considerable size, it expands buccolingually also (Figs. 27.15 and 27.16).

27.10.3 Radiographic Differential Diagnosis

OKC is a great mimic; many times, the radiographic picture is nonpathognomonic. Radiographically, the following differential diagnosis for Odontogenic Keratocyst has been suggested:

Dentigerous cyst, residual cyst, radicular cyst, lateral periodontal cyst, Nasopalatine cyst, Unicystic/multicystic ameloblastoma, A-V malformation, fibro-osseous lesion at initial stages, Benign intraosseous neoplasms, traumatic cyst. Patients with multiple jaw cysts should always be evaluated for basal cell nevus syndrome.

27.10.4 Aspiration

- Cheesy, straw color, caseous, dirty milky white semifluid, and viscoid content-Keratin-varying consistencies reflect various densities of keratinous debris.
- Protein content less than 3.5/4 g per 100 ml by electrophoresis, mostly albumin is present.
- Protein-53 is positive in NBCC Syndrome, indicating active proliferation of cells.
- Exfoliative cytology/smear is stained & examined for keratin cells, and Estimation of Keratocyst Antigen (KCA) and Lactoferrin levels is helpful.
- Immunohistochemistry for cytokeratin is also a useful diagnostic tool

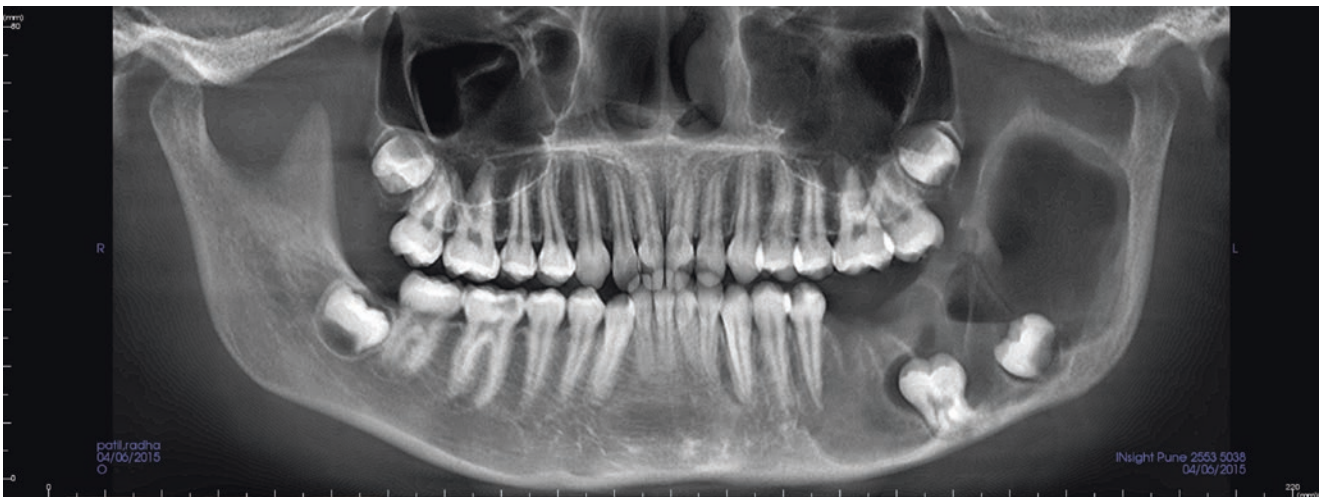


Fig. 27.15 OPG showing how lesion grows in medullary space (in anteroposterior direction), multiloculated radiolucency in left angle, and ascending ramus with impacted teeth diagnosed as OKC

27.10.5 Surgical Treatment

Incidence of these lesions is seen more in younger age group and the supportive evidence of success of conservative treatment options like marsupialisation for large expanding OKCs or two-staged surgical procedures, plus the fact of alteration of the remaining epithelium, i.e., return to more normal oral epithelium after decompression/marsupialisation has prompted many to opt for these procedures. The lesions, which are easily accessible, can be enucleated by adjunctive methods.

27.10.5.1 Resection

- It should be used as a last alternative method
- Resection of the jaw bone results in morbidity and requires extensive reconstruction/rehabilitation, which is unwarranted in the treatment of benign lesions, and hence, most of the times, more conservative approaches are sought.

Absolute indications

- Multiple recurrences

Fig. 27.16 Multiple cysts in the same individual, involving both maxilla and mandible

HISTOPATHOLOGIC CRITERIA OF OKC-SHEAR & PINDBORG (1960–62)

- Thin, collapsed and folded, corrugated lining
- Zone of uniform parakeratinized stratified squamous epithelium 5–8 cell layers with no rete pegs
- Picket fence / tombstone appearance of hyperchromatic palisaded basal cells with reversed polarity
- Weak epithelial connective tissue interface
- Presence of daughter satellite cyst

Fig. 27.17 Typical histopathological picture of OKC showing all the features

- Extensive soft tissue invasion and multiple large perforations
- Resection is used only in aggressive extensive cases or under extraordinary situations
- Condylar involvement or lesions that have undergone ameloblastomatous/malignant transformation

Follow-up

- After surgery, yearly follow-up till 5 years postoperatively
- After 5 years of follow-up, once in 2 years as long as patient cooperates
- Lifelong follow-up is a must-more than 10–20 years

27.10.6 Basal Cell Nevus Syndrome/Nevoid Basal Cell Carcinoma Syndrome

It is also known as bifid rib syndrome or Gorlin and Goltz syndrome or multiple jaw cyst syndrome. This is a genetically inherited uncommon affliction with autosomal dominant trait/inheritance and high penetration.

This syndrome's complex manifestations include relative frontal bossing, Ocular hypertelorism, brain tumors, midface hypoplasia, mandibular prognathism, mental retardation, schizophrenia, multiple basal cell nevi/epitheliomas on the skin, calcification of the falx cerebri, bifid ribs and vertebral anomalies, palmar pitting (the pits later develop into basal cell carcinoma), ovarian tumors, CNS disturbances, hypogonadism in males,cleft lip and palate, etc., and 50% of cases show multiple KCOT-now OKCs. Multiple KCOTs (OKCs) are indicative of basal cell nevus syndrome until diagnosed otherwise. 5% of the patients with KCOT/OKC are diagnosed having basal cell nevus syndrome. Early identification of these patients with their associated manifestations along with proper treatment planning and long-term follow-up will improve the long-term survival rate and quality of life.

27.11 Conclusion

Cysts of the jaw bones are considered as one of the most common pathologies in the oral and maxillofacial region. Various tumors mimic the clinical features of cysts and, thus, can be confused with the same. Radiography alone cannot be the diagnostic tool to distinguish various jaw cysts. Cysts are benign lesions, but few will show locally aggressive and destructive behavior. The detailed present and past history of the patient accompanied by a thorough clinical examination along with aspiration biopsy will lead to probable differential diagnosis. Both conservative and aggressive surgical treatment modalities have been used in the past to treat orofacial cysts with variable results, depending on the type of cyst. Correct final diagnosis, thorough planning, meticulous surgery with stringent protocols, and watchful long-term postoperative follow-up will ensure high success rate.

References

1. Shear M, Speight PM, editors. Cysts of the oral and maxillofacial regions. 4th ed. Oxford: Blackwell Munksgaard; 2007.
2. Kramer IRH, Pidborg JJ, Shear M. Histological typing of odontogenic tumors. Berlin: Springer-Verlag; 1992.
3. Regezi J, Sciubba J, Jordan R. Oral pathology: clinical pathological correlations. 4th ed. St. Louis: Elsevier Health Sciences; 2016. p. 244–54.
4. Browne RM. The pathogenesis of odontogenic cysts: a review. J Oral Pathol. 1975;4(Suppl 1):31–46.
5. Harris M, Toller P. The pathogenesis of dental cyst. Br Med Bull. 1975;31(Suppl 2):159–63.
6. Shrestha P, Yamada K, Higashiyama H, Takagi H, Mori M. Epidermal growth factor receptor in odontogenic cysts and tumors. J Oral Pathol Med. 1992;21(Suppl 7):314–7.
7. Sakamoto S, Sakamoto M, Goldhaber P, Glimcher M. Collagenase and bone resorption: isolation of collagenase from culture medium containing serum after stimulation of bone resorption by addition of parathyroid hormone extract. Biochem Biophys Res Commun. 1975;63(Suppl 1):172–8.
8. Harvey W, Guat-Chen F, Gordon D, Meghji S, Evans A, Harris M. Evidence for fibroblasts as the major source of prostacyclin and prostaglandin synthesis in dental cyst in man. Arch Oral Biol. 1984;29(Suppl 3):223–9.
9. Meghji S, Harvey W, Harris M. Interleukin 1-like activity in cystic lesions of the jaw. Br J Oral Maxillofac Surg. 1989;27(Suppl 1):1–11.
10. Barnes L, Eveson JW, Reichart P, Sidransky D. Pathology and genetics of head and neck tumours: WHO classification of tumours. 3rd ed. Lyon: IARC Press; 2005. p. 107–62.
11. Wright JM, Vered M. Update from the 4th edition of the World Health Organization; classification of head and neck tumours: odontogenic and maxillofacial bone tumors. Head Neck Pathol. 2017;11(Suppl 1):68–77.
12. Martin L, Speight PM. Mini-symposium: pathology of the jaws. Odontogenic cysts. Diagn Histopathol. 2015;21:359–69.
13. Olojede O, Adisa AO, Effiom O, Warith AA. Cysts of the orofacial region: a clinicopathologic review of 403 Nigerian cases. East Afr Med J. 2017;94(Suppl 2):116–24.
14. Das AK, Prajapati VK. Concentration of proteins in intra osseous jaw cysts as an adjunct to diagnosis. Int J Sci Stud. 2015;2:150–5.
15. Toller PA, Holborow EJ. Immunoglobulins and immunoglobulin containing cells in cysts of the jaws. Lancet. 1969;2(Suppl 7613):178–81.
16. Smith AJ, Matthews JB, Mason GI, Browne RM. Lactoferrin in aspirates of odontogenic cyst fluid. J Clin Pathol. 1988;41(Suppl 10):1117–9.
17. Pogrel MA. Treatment of keratocysts: the case for decompression and marsupialization. J Oral Maxillofac Surg. 2005;63(Suppl 11):1667–73.
18. Voorsmit RA, Stoelinga PJ, van Haelst UJ. The management of keratocysts. J Maxillofac Surg. 1981;9:228–36.
19. Sun J, Wu J, Zhou N, Meng N, Lin Y. A prospective study of jaw odontogenic keratocyst treated by multidisciplinary sequential treatment. Int J Oral Maxillofac Surg. 2009;38(Suppl 5):537.

20. Morgan TA, Burton CC, Qian F. A retrospective review of treatment of odontogenic keratocyst. J Oral Maxillofac Surg. 2005;63(Suppl 5):635–9.
21. Blanas N, Freund B, Schwartz M, Furst IM. Systematic review of the treatment and prognosis of the odontogenic keratocyst. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2000;90(Suppl 5):553–8.
22. Dashow JE, McHugh JB, Braun TM, Edwards SP, Helman JI, Ward BB. Significant decreased recurrence rates in keratocystic odontogenic tumour with simple enucleation and curettage using carnoy's versus modified carnoy's solution. J Oral Maxillofac Surg. 2015;73(Suppl 11):2132–5.
23. Schmidt BL, Pogrel MA. The use of enucleation and liquid nitrogen cryotherapy in the management of odontogenic keratocysts. J Oral Maxillofac Surg. 2001;59(Suppl 7):720-5–6-7.
24. Ochandiano CS. Bone cavity filling with alloplastic material in maxillofacial surgery. Rev Esp Cir Oral Maxillofac. 2007;29(Suppl 1):21–32.
25. Ettl T, Gosau M, Sader R, Reichert TE. Jaw cysts—filling or no filling after enucleation? A review. J Craniomaxillofac Surg. 2012;40(Suppl 6):485–93.
26. Stolinga PJ. Long term follow-up on keratocysts treated according to a defined protocol. Int J Oral Maxillofac Surg. 2001;30(Suppl 1):14–25.
27. Giuliani M, Grossi GB, Lajolo C, Bisceglia M, Herb KE. Conservative management of large odontogenic keratocyst: report of a case and review of the literature. J Oral Maxillofac Surg. 2006;64(Suppl 2):308–16.
28. Neville BW, Damn DD, Allen CM, Bouquot JE. Oral and maxillofacial pathology. 3rd ed. Philadelphia: WB Saunders; 2004.
29. Reichart P, Philipsen H. Odontogenic tumours and allied lesions. 3rd ed. New Malden: Quintessence Publishing; 2004.
30. Wushou A, Zhao YJ, Shao ZM. Marsupialization is the optimal treatment approach for keratocystic odontogenic tumour. J Craniomaxillofac Surg. 2014;42(Suppl 7):1540–4.
31. Maurette PE, Jorge J, de Moraes M. Conservative treatment protocol of odontogenic keratocyst: a preliminary study. J Oral Maxillofac Surg. 2006;64(Suppl 3):379–83.
32. Chirapathomsakul D, Sastravaha P, Jansisyanont P. A review of odontogenic keratocysts and the behaviour of recurrences. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101(Suppl 1):5–9.
33. Chuong R, et al. The odontogenic keratocyst. J Oral Maxilllofac Surg. 1982;40:797–802.
34. Auluck A, Suhas S, Pai KM. Multiple odontogenic keratocysts: report of a case. J Can Dent Assoc. 2006;72(7):651–6.
35. Kahraman D, Gunhan O, Celasun B. A series of 240 odontogenic keratocysts: should we continue to use the terminology of "keratocystic odontogenic tumour" for the solid variant of odontogenic keratocyst? J Craniomaxillofac Surg. 2018;46(6):942–6.
36. Nakamura N, et al. Marsupialization for odontogenic keratocyst: long term follow up analysis of the effects and changes in growth characteristics. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2002;94(Suppl 5):543–53.