

In The Name Of  
God

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THESIS FOR D.M.D. DEGREE

LATEST METHODS IN  
TREATMENT OF  
ODONTOGENIC  
KERATOCYST

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*Dedication:*

*This thesis is dedicated to all of my  
teachers and professors  
in appreciation for all they have taught me  
and  
their unfailing support.*

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## INTRODUCTION

A cyst is a pathological cavity having fluid, semifluid or gaseous contents and which is not created by the accumulation of pus (Kramer, 1974). It is frequently, but not always, lined by epithelium

Pindborg and Hansen described the main features of odontogenic keratocysts in 1963, although Philipsen had already used the term in 1956. Nevertheless, there are great controversy about such important aspects as whether they are really odontogenic in origin and what factors account for their peculiar behavior. This survey reviews the recent literature on odontogenic keratocyst and reports the latest methods for its treatment.

Because the origin and the main features that characterize a keratocyst have been clarified, statistics on the incidence of the lesion vary, depending on the criteria used. It has been reported that they account for anywhere from 3.0 to 10.5% of jaw cysts. According to some investigators half of these cysts derive from patients who have a permanent dentition or who are edentulous, but there is no known reason to exclude their occurrence in persons who have a mixed dentition or deciduous teeth. and in fact there have been such cases associated with basal cell nevus syndrome. Although persons of any age can be affected, it appears that they are more frequently found between the ages

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of 20 and 40 years. Some authors believe that males are affected, more frequently than females, while others have not found any sex predilection.

It is unanimously accepted that the maxilla; 60 to 80% of cases have occurred in the lower jaw, with the majority having been found in the molar, angle, and ramus areas. When associated with basal cell nevus syndrome, the cysts are usually multiple and the age of the patient, younger.

In the past, terms such as cholesteatoma and epidermoid cyst were used to describe the odontogenic keratocyst. With few exceptions, however, the majority of investigators now seem to agree with the World Health Organization classification according to which primordial and odontogenic keratocyst are considered synonymous terms. It is true, however, that keratinization can be found in some other categories of cysts, such as fissural and the dermoid cyst.

Odontogenic keratocyst are thought to derive from the enamel organ or from the dental lamina and are probably not related to any kind of infection. Clinically, they do not present any characteristic features. There are similarities, however, with the ameloblastoma as to the age of the patient, the localization of the lesion, the radiographic picture, and the tendency for recurrence. Although they grow to reach a larger size than any other cyst, they may remain asymptomatic. When they do not, intraoral drainage and swelling are the most common findings. It is of interest that these cysts more often penetrate bone rather than expand it and they grow in an anterior-to-posterior direction rather than buccally to lingually.

Radiographically, keratocysts appear as unilocular or, more frequently, multilocular radiolucencies with well-defined borders that indicate osseous reaction. There is extension along the medullary bone rather than cortical expansion, and cortical resorption rather than expansion. They may often displace teeth (particularly unerupted teeth) rather than cause their resorption. There is some difference of opinion as to whether the unilocular or the multilocular variety is more common. The multilocular type, which radiographically resemble the ameloblastoma, is often associated with basal cell nevus syndrome and is characterized histologically by parakeratinized epithelium. In the unilocular type, the epithelium, the epithelium is orthokeratinized. The difference in the pattern of keratinization may be of prognostic significance. In both instances, the

epithelium is very thin unless it is infected, with no more than five to ten cells (the basal layer may include columnar or cuboidal cells), occasionally arranged in a wavy manner, and showing a high degree of differentiation. Rete pegs are very rare.

The epithelium is clearly separated from the connective tissue, the latter containing islands of similar epithelium, some of which are in fact daughter cysts. The connective tissue is composed of thin irregular collagen bundles that are not as well-arranged architecturally as in the walls of other cysts. The lumen of the cyst may contain a thin, straw-colored fluid or thick, creamy material. Occasionally it contains various amounts of keratin. Hyaline bodies and cholesterol crystals are rare and are usually found in sites of inflammation.

Electrophoresis of the aspirated fluid usually shows a soluble protein content lower than 4.8-g/100 ml. Another frequent finding is keratinized squamous cells. Lack of osmotic pressure within the cyst has been mentioned so that their expansion may be attributed active growth, although an increased osmotic pressure, compared with that found in other types of cyst has also been reported. The levels of acid phosphatas and oxidative enzymes have been found to be increased in keratocysts in comparison with other types of cysts, where the activity is equivalent to that of the skin, a fact that indicates higher metabolic activities in the keratocyst. It has also been reported that leucine aminopeptidase activity in the thin fibrous capsule is increased in keratocysts, as are the phospholipids in the keratinized and parakeratinized layers. Increased acid phosphatas activity is an indication of increased lysosome activity, while elevated aminopeptidase activity, is an indication of collagenolysis; all of these findings have been associated with the separation of epithelium from connective tissue and invasive behavior of keratocyst in general. The mere presence of keratinization has been interpreted as biologic indication of active and persistent growth of epithelium. Prostaglandin-induced bone resorption has also been mentioned as possible cause.

Odontogenic keratocysts are characterized by a high rate of recurrence, which has been estimated to be between 6-60%. Some cases have recurred in soft tissues. Possible explanations for this recurrence, apart from what has already been stated, are the collagenase activity in the cyst wall and the increased fibrinolytic activity have also been viewed as indicators of an unusual growth potential. Others underline features of the



cyst's behavior such as the epithelial proliferation in connective tissue; the infiltration of soft tissues and adherence to periosteum and adjacent muscles after the cyst perforates the bone; the residual dental lamina, which may generate new cysts; and the pattern of keratinization (it has been found that orthokeratinized keratocysts are less aggressive, while parakeratinized cysts have a higher tendency to recur).

Finally, another group of investigators proposed that some clinical and technical features related to the treatment of keratocysts cause their recurrence, such as the existence of undetected microcysts and daughter cysts (a fact not unanimously accepted). Also mentioned are their size and location, which render their extirpation difficult and the thin cyst wall, which is easily ruptured and detached and renders complete removal difficult. On the basis of these factors, it has been proposed that the cysts persist after attempted removal rather than recur and that they should be treated as benign tumors rather than cysts. Very rarely, ameloblastomatous and malignant transformation has been reported to occur.

Because of the high frequency of recurrence (recurrence has even been reported in a graft placed following surgical removal of a cyst,) most authors advocate complete removal, with meticulous curettage of surrounding tissues, which may then be followed by cauterization. It has also been suggested that the overlying mucosa should, in some cases, be removed, and that marsupialization should not be the treatment of choice. Nevertheless, a more conservative approach has recently been proposed in an attempt to preserve the teeth in the area. Long-term follow up, ranging from at least five to ten years, has also been suggested.



## HISTORY

Jaw cysts are not lesions confined to modern man. Ruffer (1921) in his studies on the palaeopathology of Egypt has described lesions in the jaws of three mummified specimens, which appear to be radicular cysts. The first, from a predynastic era, Naga el Deir (*circa* 4500 BC), shows a root remnant in the right second premolar region of the maxilla. A cavity is present in the bone at its apex.

In the second specimen, which is thought to be from the same period, the mandibular teeth show marked attrition and there is a cystic area in the bone around the first permanent molar. The third specimen is from Cleopatra's period, Ras el Tin. An oval opening with smooth borders measuring 12 × 18 mm is present in the outer wall of the alveolar bone in the premolar region. An aperture artificially made through the external wall of the mandible lead into a smooth-walled cavity, 36 × 20 mm, in which the roots of the canine, lateral incisor and anterior root of the second molar were exposed.

Salama and Hilmy (1951) reported on two specimens from a collection of skulls excavated at Sakara. All belonged to the period of king Unas of the fifth dynasty (*circa* 2800 BC). One was an adult skull showing a large radicular cyst in relation to teeth 234. The teeth in relation to the cyst were missing but sockets are present, suggesting that the teeth were lost post mortem. The remaining teeth show marked attrition. The cyst had expanded almost to the midline of the palate. The second specimen showed a large multilocular cyst in the left body of an edentulous mandible. There was expansion of both

the inner and outer plates of bone. A skull thought to be from the Hellenistic period has been examined by Dascoulis (1960), who found that it contained a radicular cyst.

Lufkin (1938) quotes Cleucus, writing in the early part of the first century AD:

*It also happens, that from an ulcer of the gums.... One may have for a long period a discharge of pus, on account of a broken or rotten tooth, or else on account of a disease of the bone; in this case there often exists a fistula.*

*Then the latter must be opened, the tooth extracted and if any bony fragment exist, this should be removed; and if there be anything else diseased, this should be removed; and if there be anything else diseased, this should be scraped away.*

Lufkin also pointed out that alveolar and perialveolar abscesses are commonly seen in palaeopathological studies, particularly in Egyptian mummies.

Neiburger (1977) has described a cystic lesion in the angle of a mandible excavated from a burial mound (Dodge County, Wisconsin) of the middle Woodland cultural period, AD 700-1100. The lesion is described as being composed of three depressed areas grouped around an elevation of bone. The radiograph shows a 'multicystic' defect. The subject was thought to be a 24-to 38-year-old female. Neiburger suggested a diagnosis of 'multilocular cyst or ameloblastoma'. It might also, however, be an odontogenic keratocyst (primordial cyst) of the variety, which presents radiologically with scalloped margins.

A photograph of a skull housed in the Abelholt monastery museum in Denmark of a subject buried in the Middle Ages, shows a cystic cavity involving the apices of the left maxillary central and lateral incisors. The incisal edge of the central has been notched, possibly for ritual purposes (*FDI Newsletter*, 1983).

Fauchard (1746), having described the dentoalveolar abscess and its treatment, wrote:

*I have seen many very considerable tumors, which could only have been caused by carious teeth... Nothing is more frequent than to see these sort of large tumors, of which the results are insignificant or troublesome according to the exciting causes or the treatment applied to dissipate them and to cure radically when they have formed. I have treated a great number with success.*

*When incisions in the gums have to be made, for the tumors or to keep them open, sufficient dilation is made with sharp instrument and the incision held open so as not to allow it to close too soon. Not to frighten the patient by the introduction of a fresh cutting instrument, recourse must be had to use of dossils and tampons of charpie or cotton or to properly made tents covered with wax of some ceriate or convenient plaster which should*

*not be disgusting by its taste or smell ...A prepared sponge will do as well. But the tents must be gradually reduced in size as the wound heals for if used too long it may be very dangerous, as I know from experience, and it happens too often*

*Sometimes it is necessary to take away, to file and remove some portion not only of the gum but even of the alveolus carious or otherwise to procure sufficient aperture for the discharge of matter and for the introduction of medicaments.*

Fauchard's 'Sixth Observation' in Chapter 35 of the same work appears to be a case report of a radicular cyst, although he does not give any specific name to the condition he describes.

*On the effect of caries of two roots of a tooth which gave rise to a tumor and abscess on the left side of the lower jaw.*

*On the 6th December 1723 the wife of M. Brossard Concierge and keeper of furniture of the Hotel de Conti having two roots of a second large molar of the left side of the lower jaw carious for some years, this caused a considerable tumor on the same side. I was called to examine this tumor and to extirpate the two roots, which I did in the presence of M. Finot (a) and M. Darmagnac (b). The gap, which was left by this, enabled me to insert my stiletto into the tumor. By this means I ascertained the depth which extended to the base of the maxillary bone. I knew then that the bone was exposed. I made a sufficient incision in the upper part of the gum to give vent to the matter and, to prevent the opening of the wound being closed too soon, I dressed this lady with a tent of lint covered over with a little white wax. I renewed this tent night and morning and syringed out the wound every time that I dressed it with a lotion made of two ounces of water of ound wort, barley water with cinnamon, balsam of Fioravanti and honey of roses of each one ounce, the whole mixed together, The fourth day I ceased to use the tents and continued to syringe the wound as formerly until the twenty-fifth day when the patient was perfectly cured.*

## Reflexion

If one deferred at first to draw the carious roots and to open up the abscess sufficiently the lodgement of the matter would have formed a new sinus and made greater progress: when it would not have been perhaps possible to end thus happily the cure of this patient.

John Hunter, writing in about 1780 of diseases of the jaw bones, described a type of lesion which appears to be a cyst.

The second of these diseases in the bone.... Is an accumulation of curdly substance; probably it is coagulable lymph, and may be reckoned among the encysted tumors. The ossific inflammation often goes on here, till the bone acquires great size, but in these the outer ossific accumulation is not in proportion to the absorption, and therefore, being only a thin shell, it gives way.

The lingual mandibular bone defect, or Stafne cavity, which is sometimes mistaken for a solitary bone cyst on radiographs, has been identified in archaeological studies and the literature on the subject has been reviewed by Keene (1990).

Early work on the nature and treatment of jaw cysts appears in the English literature in papers by Spence (1853-54), Harvey (1855), Moon (1877-78), Heath (1880, 1887), Pedley (1886), Baker (1891), and Turner (1898).

## **Classification.**

Numerous classifications have been published of cysts of the jaws. Most of these are perfectly satisfactory and the reader is advised to use any classification, which he finds valuable as an aid to memory and understanding. The classification of the epithelial lined cysts used in this survey is based on that recommended in the World Health Organization's publication *Histological Typing of Odontogenic Tumors* (Kramer, Pindborg and Shear, 1992). An exception is that we include the calcifying odontogenic cyst there, whereas this entity is classified as an odontogenic tumor in the WHO work. There is also merit in Main's proposal (1985) that the midpalatal cyst (midpalatal raphe cyst) of infants be given a place in a classification of jaw cysts. The remainder of the classification shown below is the one, which we use in this survey.

The order in which the various entities are dealt with in this survey does not strictly follow their order in the classification.

### **Classification:**

#### **I. Cysts of the jaws**

##### *A. Epithelial*

#### **I. DEVELOPMENTAL**

##### **(A) Odontogenic**

- i. Gingival cyst of infants
- ii. Odontogenic keratocyst (primordial cyst)
- iii. Dentigerous (follicular) cyst
- iv. Eruption cyst
- v. Lateral periodontal cyst
- vi. Gingival cyst of adults
- vii. Botryoid odontogenic cyst
- viii. Glandular odontogenic cyst (sialo-odontogenic cyst; mucoepidermoid odontogenic cyst) cyst
- ix. Calcifying odontogenic cyst

### **(B) Non-odontogenic**

- i. Nasopalatine duct (incisive canal) cyst
- ii. Nasolabial (nasopalveolar) cyst
- iii. Midpalatal raphe cyst of infants
- iv. Median palatine, median alveolar and median mandibular cysts\*
- v. Globulomaxillary cyst\*

## **2. INFLAMMATORY**

- i. Radicular cyst, apical and lateral
- ii. Residual cyst
- iii. Paradental cyst and mandibular infected buccal cyst
- iv. Inflammatory collateral cyst

### **B. Non-epithelial**

1. Solitary bone cyst (traumatic, simple, haemorrhagic bone cyst)
2. Aneurysmal bone cyst

## **II. Cysts associated with the maxillary antrum**

1. Benign mucosal cyst of the maxillary antrum
2. Postoperative maxillary cyst (surgical ciliated cyst of the maxilla)

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\* These cysts, previously regarded as developmental non-odontogenic cysts, are of debatable origin.

**III. Cysts of the soft tissues of the mouth face and neck**

1. Dermoid and epidermoid cysts
2. Lympho-epithelial (branchial cleft) cyst
3. Thyroglossal duct cyst
4. Anterior median lingual cyst (intralingual cyst of foregut origin)
5. Oral cysts with gastric or intestinal epithelium (oral alimentary tract cyst)
6. Cystic hygroma
7. Nasopharyngeal cysts
8. Thymic cyst
9. Cysts of the salivary glands: mucous extravasation cyst; mucous retention cyst; ranula; polycystic (dysgenetic) disease of the parotid .
10. Parasitic cysts: hydatid cyst; *Cysticercus cellulosae*; trichinosis







## ODONTOGENIC KERATOCYST (PRIMORDIAL CYST)

There has been a great deal of interest in the Odontogenic keratocyst (primordial cyst) since it became apparent that it may grow to a large size before it manifests clinically and that, unlike other jaw cysts, it has a particular tendency to recur following surgical treatment.

In the earlier literature, the keratocyst was described as a cholesteatoma (Hauer, 1926; Kostecka, 1929). In his detailed study of the cyst, Forssell (1980) concluded that the first account of this lesion was that of Mikulicz who, in 1876, described it as a dermoid cyst.

The term 'odontogenic keratocyst' was introduced by Philipsen (1956) and is now very widely used. In this and in a subsequent paper (Pindborg, Philipsen and Henriksen, 1962), and in a paper by Pindborg and Hansen (1963), the designation 'Keratocyst' was used to describe any jaw cyst in which keratin was formed to a large extent. Some dentigerous, radicular and residual cysts were therefore included in the category of odontogenic keratocyst. Moreover, keratocysts may give an erroneous radiographic impression that they are dentigerous, lateral periodontal, residual, or even so-called fissural cysts, thus giving rise to the view that these latter entities are lined by keratinized epithelium (Forssell, 1980).



Although a few radicular and residual cyst linings may become keratinized by metaplasia (**Figure 2.1**), these linings are distinctly different from the characteristic lining epithelium of the odontogenic keratocyst (Browne, 1971a; Forssell and Sainio, 1979). There are however other histological features that distinguish them and it is these which are responsible for their biological behavior, rather than the presence of keratin. Lucas (1972) has made the point that the emphasis that has been placed on keratinization is to some extent misleading, in that there is the implication that cysts of widely differing types may all keratinize and that if they do they are then liable to recur. There is now a great deal of evidence that the cyst under discussion here is a distinct entity of developmental origin, arising from primordial odontogenic epithelium, and it is for this reason that we have tended to prefer the term 'primordial cyst' to the non-specific histological term 'keratocyst; a preference which have been emphasized in other articles. However, the designations 'odontogenic keratocyst' or 'keratocyst' are now so firmly established in the literature that they will be used in this survey.

Browne (1969, 1972) has shown that keratinizing cysts have a significantly ( $P < 0.01$ ) different age distribution (mean age 32.1 years; peak in second and third decades) from dentigerous (mean age 36.6 years; peak in fifth decade) and radicular cysts (mean age 40.2 years; peak from third to sixth decades). He concluded from this that the three types of cyst arise from different populations and that the keratocyst is therefore a distinct lesion in its own right. The fact that it occurs at a younger age than the others makes it unlikely that it has arisen in long-standing dentigerous or radicular cysts.

Browne (1969) and HjØrting-Hansen, Andreasen and Robinson (1969) have demonstrated, moreover, that the site distribution of keratinizing cysts differs significantly ( $P < 0.01$ ) from that of non-keratinized cysts; a fact which has been confirmed by Rud and Pindborg (1969) who believed that this supported the assumption that keratocysts are actually primordial cysts. Forssell and Sainio (1979), who also had a preference for the term 'primordial cyst', have shown that in these lesions ('genuine keratocysts') the epithelium was distinctly parakeratotic with cuboidal or columnar palisaded basal cells, and occasionally orthokeratotic. Cysts which show local orthokeratinization in otherwise non-keratinized epithelium; cysts with epithelium similar to that seen in parakeratotic oral mucosa; and cysts with scanty areas of thin parakeratinization, should not be regarded as primordial cysts. None of these varieties, moreover, has accentuated basal cells.

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Despite agreeing that these cysts are distinct entities, Browne (1969) argued that they cannot be primordial cysts because he defines a primordial cyst, according to the original description of Robinson (1945), as one which arises by breakdown of the stellate reticulum of the enamel organ before any mineralized tissue is formed and hence develops in place of a tooth which may be one of the normal series or a supernumerary. Despite an extensive literature on the subject of primordial cysts and odontogenic keratocysts over the 47 years since Robinson published his paper, there has been no convincing evidence to support the theory which he postulated. Later in this discussion, we shall however present the evidence supporting origin of the keratocyst from primordial odontogenic epithelium, i.e. dental lamina or its remnants (Soskolne and Shear, 1967; Toller, 1967), or odontogenic basal cell hamartias (Stoeltinga, 1971a, 1973; Voorsmit, 1984).