Inborn or acquired changes in children under three years of age – a review of the literature

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Abstract

This study aimed to discuss some inborn and acquired changes in the oral cavity in young children under three years of age. Based on current literature, eruption cyst, Riga-Fede disease, natal and neonatal teeth, congenital epulis, Epstein pearls, Bohn’s nodules, and gingival cyst of the newborns have been described. The symptoms, clinical presentation, and histological features of these changes, their epidemiology, prevalence, etiopathogenesis, differential diagnosis, and management were taken into consideration to present them accurately. Described oral normal findings and anomalies are not very common, so they require precise diagnosis and management properly. Having relevant knowledge on issues is important both for the pediatricians and pediatric dentists who always cooperate to distinguish the pathology or anomaly and start dealing with it. To our knowledge, this is the first literature review presenting comprehensive and thorough specification of abnormalities occurring in children’s mouth, basing on the most recent scientific literature between 1999 and 2022.

Keywords: mouth abnormalities, newborn, early childhood development, neonate

Introduction

During early childhood, the oral cavity might seem relatively uncomplicated; however, it is a complex organ subjected to major diversification with growth. Moreover, it performs various physiological activities, some of which, characteristic for adulthood, are not fully developed but are suitable for young organisms; while others, typical for a child under three years of age, disappear naturally with the development progression [1–3].

At the early childhood, considerable diversification of the tissues and organs occurs, which is related to the functional activities of a developing organism. Tissues, which are not fully formed, begin to develop based on external cues [1,2]. Histological underdevelopment of the mucosal membrane can be observed. The lining epithelium is thin and delicate, rich in glycogen, loosely connected to lamina propria mucosae. Typically, there are large amounts of glycogen and scarce fibrous elements that can increase with age. It contains only two layers: stratum basale and stratum spinosum, instead of the fully developed epithelium with an additional layer of stratum corneum and stratum granulosum occasionally occurring [1,3].

Despite the underdevelopment, a child’s oral mucosal membrane is subjected to various pathological factors, both: internal, which are related to the overall health condition, and infectious agents and factors originating from the external environment, including chemical, physical and mechanical. The influence of detrimental factors can directly damage oral mucosa or indirectly influence it by increasing susceptibility to other harmful factors [2].

Morphological and functional immaturity of the oral mucosal membrane predisposes it to changes related to mastication organ development and mechanical damages—children under the age of three present unique and transitional anatomical structures typical to that age. According to Padovani et al. [4], the prevalence of soft tissues abnormalities during early childhood was 34.8%.
Most of the changes are innocuous, resolve with age, and do not require treatment. Among the most common are: oral inclusion cyst (which include Epstein pearls, Bohn’s nodules, and Gingival cyst), congenital epulis, melanotic neuroectodermal tumors; while the milk teeth eruption period can give rise to Riga-Fede disease, eruption cyst, eruptive gingivitis, natal or neonatal teeth, and oral mucosa damage, triggered by inserting hard or soiled objects into the mouth causing damages or secondary infections.

The ability to recognize, diagnose, and implement correct treatment in cases of congenital and acquired changes in the oral cavity is necessary for dentists and pediatricians. Proper diagnosis of oral mucosa abnormalities allows calm and reassure parents, often very concerned upon discovering changes in their child’s mouth—additionally, accurate diagnosis sanctions prompt treatment implementation. Therefore, this review aimed to describe these inborn or acquired changes in the oral cavity in young children based on the current literature.

Method

The selection of articles was performed using Scopus and PubMed databases, and included works published in English between the years of 1999 and 2021. The following keyword phrases were used for the searches: "eruption cyst" OR "Riga-Fede disease" OR "Natal and Neonatal Teeth" OR "congenital epulis" OR "Epstein pearls" OR "Bohn’s nodules" OR "Dental Lamina Cyst" OR "gingival cyst" AND "mouth abnormalities" AND "newborn" OR "pediatric dentistry". Out of 478 retrieved articles, 69 records were qualified for this review, including all types of papers such as: narrative reviews, systematic reviews, meta-analyses, observational studies, and clinical studies. The exclusion criteria were set to reject: publications unrelated to the focus of this work, animal studies, papers unavailable in full-text version, and articles written in languages other than English. Table 1 summarizes the inborn or acquired changes in children under 3 years of age including main characteristics such as alternative names, clinical characteristics, size, correlation with gender, localization, symptoms, diagnosis and treatment.
### Table 1. Summary of inborn or acquired changes in children under 3 years of age.

<table>
<thead>
<tr>
<th>Eruption Cyst</th>
<th>Riga-Fede Disease</th>
<th>Natal and Neonatal Teeth</th>
<th>Congenital Epulis</th>
<th>Epstein Pearls</th>
<th>Bohn’s Nodules</th>
<th>Dental Lamina Cyst</th>
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<tr>
<td>Alternative names</td>
<td>hematomai</td>
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<td>-</td>
<td>congenital granular cell tumor; Neumann tumor; congenital granular cell lesion; gingival granular cell tumor of the newborns</td>
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<td>gingiva 1 cyst of newborns; alveolar cyst</td>
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<td>Clinical characteristics</td>
<td>smooth reddish ulceration [20] with bite marks made by incisors [16,20-22], on palpation well indurated [16,20], sometimes with infiltration deep under the muscle [22]; during palpation, usually painful [16,20,21,23,25]; may be covered with a yellowish [18,26] or glistening grey exudate [17,23]</td>
<td>Conical [34, 37, 38], or typical for a normal tooth [35, 39]; brownish, yellowish[35, 38], or opaque white [40.41] enamel; poorly formed root [33, 40]; mobility in grade 2 [39, 41, 42], grade 3 43–45] or total stability [36]</td>
<td>usually single lesion exophytic, elastic, smooth-surfaced pedunculated, same color as healthy gingiva; benign and non-hemorrhagic; d or lymphadenopath upon palpation [45, 66, 68, 69, 71–77].</td>
<td>small, whitish, raised, rigid nodules, usually arranged in groups of three, filled with keratin[4, 93–95]</td>
<td>small, yellowish-white, nodules, filled with keratin [4, 93, 95, 98]</td>
<td>multiple rounds or/and solid small white or pink oval nodules [98, 100–104]</td>
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<td>Size</td>
<td>diameter of about 2 cm [5,6]</td>
<td>diameter from 12 mm [16] to 40 mm [18]</td>
<td>typical like teeth erupted in the time or smaller [35,39]</td>
<td>few centimeters [45, 67, 73–75, 77, 80] to considerable sizes [66, 69, 70, 72, 76, 77, 80, 81]</td>
<td>1 mm to 1 cm [4, 93–95].</td>
<td>variable [4, 93, 95, 98]</td>
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<tr>
<td>Correlation with gender</td>
<td>not observed [14]</td>
<td>higher incidence in males [22, 27], or no correlation with gender [31]</td>
<td>more common in females [33, 38, 50], or no correlation with gender [34, 37, 39, 49, 57]</td>
<td>much higher incidence in females at ratio of 8:11 [66, 67, 73, 82]</td>
<td>no correlation with gender [4]</td>
<td>no correlation with gender [4, 93]</td>
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<td>Symptoms</td>
<td>Diagnoses</td>
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<td>rarely discomfort; no food intake problems, no damage to deciduous teeth underneath [5,6,8,12]; possible breastfeeding concerns [14], bleeding, pain, symptoms of infections, or significant increase in size [5,11]</td>
<td>clinical examination; radiological examination, in stand-alone eruption cyst not recommend [5,7,15]; histopathological examination not essential [6,11]</td>
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<td>hypersensitivity, anxiety, fever, crying, feeding problems [16, 29]; may also be asymptomatic [17, 22, 26].</td>
<td>physical examination; excisional biopsy not necessary [16, 17, 20, 25, 29]</td>
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<td>pain, anxiety, and difficulty in food intake leading to dehydration, malnutrition, and underdevelopment caused by traumatic injuries (Riga-Fede disease) [34,40, 43, 51].</td>
<td>interview with the child's parents, clinical examination, and X-ray scans [36, 39, 40, 51, 53, 62].</td>
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<td>no pain, discomfort upon palpation [73, 75]; large lesion, causing difficulty in eating [66, 69, 70, 72, 76, 77, 80, 81] and breathing [72, 74].</td>
<td>clinical examination, location, and characteristic appearance at birth; in lesions with atypical morphology, [66, 70, 73, 75, 82], identification of the immunohistochemical profile of neonatal granular cell tumor [45, 66, 68–70, 77, 82, 85].</td>
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<td>asymptomatic and transient [93, 95].</td>
<td>clinical examination; radiological examination not recommend [93, 95].</td>
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<td>asymptomatic and transient [4, 93, 95, 96].</td>
<td>interview with the child's parents, clinical examination but X-ray scans not recommend [93, 95, 96].</td>
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<tr>
<td>asymptomatic and transient [4,93,94].</td>
<td>clinical examination, characteristic appearance, and location [98, 100–102, 104].</td>
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<td>Treatment</td>
<td>In majority of cases: spontaneous retreatment [5,6,8,12]; in cases of pain, bleeding, infection symptoms, increase in size, or breastfeeding problems: surgical exposition of erupting tooth and hematoma drainage essential [5,11,12]</td>
<td>smoothing sharp incisal edges of lower incisors with finishing bur [16, 21, 22]; using bottle with bigger teat hole and teething ring [19]; covering lower incisors with composite [19, 27], eliminating pain with topically corticosteroids [22,28], teeth extraction if conservative treatment options fail [20, 23, 24, 26]</td>
<td>most commonly: spontaneous regression - small lesions not obstructing breathing or nutrition [73, 75]; complete surgical excision under local [66, 70, 79, 88] or general anesthesia [45, 66, 68, 71, 72, 74, 77, 80–82, 88] when lack of spontaneous regression, or when eating and breathing issues</td>
<td>surgical intervention or pharmacological treatment not required [93, 95]</td>
<td>surgical intervention or pharmacological treatment not required [4, 93, 95, 96]</td>
<td>surgical intervention or pharmacological treatment is required [98, 100–102, 104]</td>
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</table>
Eruption Cyst

Eruption cyst occurs as a soft translucent elevation of the gums mucosal membrane above the crown of the cutting tooth, permanent or deciduous [5–8]. According to Bodner et al. [9], this pathology was observed in about 50% of cases of children with neonatal and deciduous teeth compared to permanent teeth. The abnormality coloration can range from pink, blue-black, to brown and depends on the volume of blood present in the cyst's liquid [5,6,10]. Among newborns, it is most commonly yellowish [5,6], pinkish [10,11], or bluish [7,8]. According to Oliveira et al. [5] and Navas et al. [6], the diameter of this anomaly is about 2 cm. The predisposed location of eruption cyst emergence in newborns is the anterior sector of the mandible [5–7,9,12]. According to the study by Şen-Tunç et al. [8], maxillary primary first molars are most frequently affected. Gaddehosur et al. [11] described a case of eruption cyst associated with primary molars in both jaws. The etiology of this hematoma is not fully recognized [5–7]. However, specific characteristics indicate that it can develop from degenerated cystic changes in the reduced enamel epithelium following the completion of amelogenesis. Another hypothesis postulates that the hematoma might develop from remnants of dental lamina covering an erupting tooth [11]. A study by Kuczek et al. [13] demonstrated that administration of cyclosporin A in children at the time of tooth eruption might result in eruption cyst formation, thus delaying tooth eruption.

The connection of this abnormality with sex is controversial; some authors [8,9] concluded more common eruption cysts among males, while others [14] did not find any correlation. However, issues reported with relation to the occurrence of eruption cysts are rare. In most reported cases, no food intake problems were reported among newborns, nor damage to the deciduous teeth located below the hematoma [5,6,8,12]. Nevertheless, there could be concerns about breastfeeding [14], bleeding, pain, symptoms of infections, or a significant increase in size [5,11].

The diagnosis of this pathology is based on clinical examination. Radiological examination, in cases of stand-alone eruption cyst, is not recommended due to the typical lack of bone fragments in the area of this aberration. However, X-ray imaging does offer an opportunity to examine the morphology of the tooth located below the abnormality and possible pathology within the surrounding bone [5,7,15]. Similarly, histopathological examination is not considered essential for diagnosis. A needle aspiration biopsy reveals crystals of cholesterol present in the cyst's fluid, characteristic of hematoma-like abnormalities [6,11]. It allows to form a conclusive diagnosis, simultaneously rejecting: hemangioma, melanoma, unicystic, ameloblastoma, keratinizing cysticodontogenic tumor, mucocele. It is particularly important when the treatment plan requires marsupialization or surgical extraction [6,11]. Navas et al. [6] also noted that performing diagnostic biopsy reduced the pressure around the hematoma, therefore reducing the size of the aberration, while the tooth underneath became palpatively perceptible.

The treatment of eruption cyst depends on the clinical symptoms. In the majority of cases, it retreats spontaneously [5,6,8,12]. According to Navas et al. [6] and de Oliveira et al. [5], change of color, from yellowish to the hue of surrounding gum and decrease in size, was noted after a month of observation, while total decline, after four months.
In case of pain, bleeding, infection symptoms, increase in size [5,11], or problems with breastfeeding, surgical exposition of the erupting tooth and hematoma drainage is essential. According to Weber et al. [10], after six months from the intervention in a ten-month-old female child, the eruption of the bottom right incisor was observed [12]. Similarly, in a case report by Gaddehosur et al. [11], after surgical exposure of teeth covered by cystic lining, the 22–month-old male was under observation for four months, and normal eruption of primary molars was clinically observed.

While researching 24 cases of eruption cysts, Bodner et al. [9] found two cases of instances related to neonatal teeth. In these situations, the intervention was dictated by the condition of neonatal teeth; in the first case, the tooth was removed alongside the abnormality, in the second, after performing needle aspiration biopsy and palpable examination, which showed significant stability of the tooth as well as no problems with food intake, it was decided that that the abnormality should remain in child's mouth. However, the cyst had declined, and the tooth started erupting, and when the child reached four months, the tooth took up the correct position in the mouth.

Muraleekrishnan et al. [7] presented a male infant with a congenital eruption cyst associated with natal teeth. In this case, the cyst was enucleated, and the hypermobilited natal teeth were extracted. However, the diagnostics and treatment of eruption cyst is not unambiguous and requires an individual approach in each case, based on knowledge, detailed medical history, examination, and cooperation with the child's parents.

**Riga-Fede Disease**

The Riga-Fede disease is also referred to as eosinophilic ulcer of the oral mucosa, sublingual fibrogranuloma, sublingual growth in infants, sublingual ulcer, reparative lesion of the tongue, (neonatal) traumatic lingual ulceration, traumatic atrophic glossitis, traumatic granuloma of the tongue [16].

The disorder was first identified in 1881 by the Italian pediatrician Antonio Riga, and Francesco Saverio Fede carried out a histological study in 1890, thus deriving the name Riga-Fede disease [17–19]. This lesion is defined as a reactive traumatic injury to the mucous membrane caused by the erupting lower teeth. It appears around two months of age and, in these cases, is associated with the natal or neonatal teeth, while from 6 to 24 months of age, it correlates with the deciduous lower incisors [2].

The lesion is smooth reddish ulceration [20] with the bite marks made by the incisors [16,20–22], which can cause bleeding [18,21,23]. Alamankany [21] described ulceration with fungal infection. On palpation, it is well circumscribed [16,20], indurated [24], sometimes with infiltration deep under the muscle [22]. During palpation, it is usually painful [16,20,21,23,25], although some authors [20,22] failed to observe palpable tenderness. It may be covered with a yellowish [18,26] or glistening grey exudate [17,23]. The diameter of the described lesions ranges from 12mm [16] to 40mm [18].

In the histopathological structure, the ulcerated mucosa with the granulation tissue and mixed inflammatory infiltrate consisting of lymphocytes, macrophages, mast cells, and an abundant number of eosinophils can be distinguished, the latter being the most typical of this entity [18,27].
The typical location is the ventral surface of the tongue [16,17,19,20,22–28], although it may appear on the mucosa of the upper anterior region [29], on the lower jaw [30], on the lip, on the dorsal part of the tongue [21] and the tongue tip [18].

The symptoms reported by the child's parents connected with an appearance of the lesion are hypersensitivity, anxiety, fever, crying, feeding problems [16,29], but the ulceration may also be asymptomatic [17,22,26]. Some authors [22,27] found a higher incidence of ulceration in the male sex, while Joseph and Sundaram [31] found no correlation with gender.

Significantly, ulceration occurs in children suffering from various diseases; among others, cerebral palsy and lack of spasticity control of the tongue can be linked to it [17]. The Riga-Fede disease can also occur in Lesch-Nyhan syndrome (a disorder of purine metabolism), familial dysautonomia (disorder in automatic and peripheral sensory functions), congenital indifference to pain [17], cerebral palsy [27], Down syndrome [24,28,30], syndactyly and oligodactyly [26]. At the same time, Alamankany [21] presented Riga-Fede disease associated with Fabry’s disease and Niemann-Pick disease type C (NPC) in a boy with microcephaly. Although, as a result of the analysis of 35 cases, one-fourth of the children were suffering from concomitant diseases, the rest were healthy [22].

The diagnosis of the ulceration usually comes down to a parent interview and a physical examination [16,17,20,25,29]. An excisional biopsy is not necessary for conclusive identification, but its performance gives a definitive confirmation of diagnosis. According to Slayton [28], a histopathological examination is indicated when the lesion persists upon extraction of deciduous teeth, potentially responsible for the ulceration. This examination also enables to exclude other lesions unequivocally [22]. During the differential diagnosis, the following should be considered: ulcerative candidiasis, fungal and bacterial infections, primary syphilis, tuberculosis, lymphoma, sarcoma, agranulocytosis, agranulocytosis, recurrent aphthae [18,32].

Management of ulceration should eliminate a trauma factor and the pain and discomfort of the child and mother during breastfeeding. It is recommended to smooth the sharp incisal edges of the lower incisors with a finishing bur [16,21,22], as a result of which the lesions healed within a period of 1 month, in the case presented by Slayton [28] to 3 months in van der Meij report [22]. It is also worth using a bottle with a bigger hole in the teat for feeding and sometimes recommending a teething ring [19]. The sharp edges of the lower incisors could also be covered with a composite [19,27]. With this method, a lack of cooperation from the patient, the difficulty of keeping the treatment field dry, and the risk of swallowing the composite by the child should be considered. Corticosteroids can be administered topically to eliminate pain [22,28]. In the case reported by Çavuş and Özmen [29], the recommended application of an analgesic and autoinflammatory gel was sufficient, and upon four months, there was complete healing of the mucosa. Machuca et al. [25], as a treatment for very painful Riga-Fede disease in a patient with hypoxic-ischemic encephalopathy and uncontrollable tongue thrusting reflex, used a custom-made acrylic mouthguard that covered the lower incisors (mandibular primary incisors) and the alveolar ridge, reducing contact with the dorsum of the tongue.
An application of the cicatrizing gel on the surface and mouth guard for the maximum amount of time was recommended [25]. However, where the conservative treatment options fail to achieve the intended result, extracting the teeth that cause mucosal injury is necessary. Those mentioned above mainly refers to a situation where there is a connection with loosened, atypical natal or neonatal teeth [20,23,24,26].

In the ulceration resulting from the Riga-Fede disease, a rapid proper evaluation and diagnosis are necessary. Delayed or incorrect diagnosis and ineffective treatment will result in deformities of the tongue, nutritional insufficiency, and growth retardation.

**Natal and Neonatal Teeth**

Natal teeth are the teeth with which the child is born, while neonatal teeth erupt in the first month of life [33–36].

Natal and neonatal teeth are usually small and conical [34,37,38], but they can have the size and shape of teeth erupted in time [35,39]. They are covered with brownish and yellowish [35,38] or opaque white [40,41] enamel. The root is usually poorly formed [33,40], resulting in grade 2 [39,41,42] or 3 [43–45] mobility, although they may show total stability, and the root then features a greater degree of development [36]. In histological terms, natal teeth are covered by a thin layer [39] of hypoplastic or hypomineralized enamel [38], and in some cases, absence of this tissue has been observed [46]. The dentine layer has a thickness comparable to that of teeth erupted at the right time [39]. The dentinal tubules have a regular course near the incisal edge, while ostodentin and large interglobular areas are irregularly arranged [39]. In the study by Anegundi et al. [38], the dentin demonstrated irregular dentinal tubules, a neonatal line, a change in the direction of the primary or secondary dentinal tubules, and a Y-shaped branching of dentinal tubules towards a dentin-enamel junction. The pulpal chamber of neonatal or natal teeth is larger, and the primitive mesenchymal pulp contains many cellular elements and vascular channels lined with endothelial cells [38].

The prevalence rate of prematurely erupted teeth is rare, ranging from 1:2000 to 1:3,500 [47,48]. According to a study by Yen and Kuppuswami [37], out of 4,341 newborns examined, only four newborn babies were born with neonatal teeth within seven months. Study by Bulut et al. [39] shows that out of 17,829 newborns examined, only 17 had teeth that came in prematurely. Natal teeth appear more frequently than neonatal teeth [34,39,49,50]. In 56-76% of cases, they occur in pairs [38,49,51], although Bulut et al. [39] found two prematurely erupted teeth in one of 27 newborns, one of which was natal and the other neonatal. Portela et al. [52] described the case of a male neonate in whom an examination at 24 days of age revealed three neonatal teeth and eight were extracted promptly upon the birth due to significant mobility, risk of aspiration, or swallowing during feeding. Among neonatal or natal teeth, 95% of cases are prematurely erupted deciduous teeth, while only 5% are supernumerary teeth [35,39]. While in a study by Samuel et al. [49], all the natal and neonatal teeth were found to be primary mandibular central incisors. The most common location where natal and neonatal teeth can be observed is the mandibula, in the region of the central incisors [33–38,43,44,47,49,50,53–56], less frequently the maxilla in the anterior segment [33,34,38,53], and the region of the canines, upper or lower molar teeth is where they appear very infrequently [33,34,38,53].
Kumar et al. [40] presented a case of a 3-month-old female child with posterior neonatal teeth: deciduous maxillary right first molar and deciduous maxillary left first and second molars.

This anomaly is more common in female neonates [33,38,50], although other studies fail to confirm this correlation [34,37,39,49,57]. The etiology of natal or neonatal teeth remains unknown. A familial pattern like the hereditary transmission of an autosomal dominant gene was mentioned as a predisposing factor [54]. Portella et al. [52] described a case of a 24-day-old child with 11 neonatal teeth, whose father and grandfather were also affected by this anomaly, but in their case, the number of teeth was significantly lower. According to Samuel et al. [49], a positive family history of natal and neonatal teeth was present in eight cases (out of 33 babies with natal and neonatal teeth), including one set of monozygotic twins. Dahake et al. [55] presented a case of two natal teeth in both premature dizygotic twin female babies.

Other causes included: endocrine disturbances in the mother [51], a high position of tooth germs [51], osteoblastic activity within an area of the tooth germs [51], infections, malnutrition, an eruption accelerated by febrile incidents or hormonal stimulation, hypovitaminosis [51], congenital syphilis [34], and toxic factors; polychlorinated biphenyls (PCBs), and dibenzofurans (PCDFs) [58]. In addition, according to Samuel et al. [49], the majority of mothers (72%) of children with natal and neonatal teeth had some antenatal complications such as twin gestation (35%), intrauterine growth retardation (30%), gestational diabetes mellitus (22%), pregnancy-induced hypertension and eclampsia (26%).

Neonatal teeth may be associated with some genetic conditions and certain disorders, which include: Hallermann-Streiff syndrome (HHS) [59], Ellis van Creveld syndrome (EVCS, chondroectodermal dysplasia) [60], cleft lip and cleft palate [53,56,61], cyclopia, pachyonychia congenita, Pierre-Robin, Pallister-Hall, short rib-polydactyly syndrome of type II (SRPS), Aicardi-Goutières syndrome (AGS) with hypothyroidism [49], Wiedemann-Rautenstrauch syndrome (WRS, neonatal progeroid) [53,61], Down's syndrome [46,49]. Triches et al. [54] describe two cases of neonates, one male, and one female, with leukoderma.

Although the appearance of natal or neonatal teeth can be correlated with varied factors or systemic disorders. As presented in the literature [39,50], most children were found to have prematurely erupted teeth that were healthy and unaffected by any harmful factors. For example, in the study by Basavanthappa et al. [53], out of 17 cases, only one child suffered from cleft lip and cleft palate.

The diagnosis of prematurely erupted teeth consists of an interview with the child's parents, a clinical examination, and X-ray scans. Diagnostic imaging enables the evaluation of the position of the tooth in relation to the surrounding structures and indicates the presence or absence of deciduous teeth. Thus, answering whether this is an additional structure or perhaps a final and only deciduous tooth that erupted in this place. The correct diagnosis allows for correct therapeutic decisions and avoids misjudged/unnecessary tooth extractions [36,39,40,51,53,62].
When a medical interview and an examination are carried out, there is no doubt that correct therapeutic management may be refrained from not exposing a child to unnecessary radiation [43]. Sometimes radiographic examination of natal teeth can be difficult due to the very small mouth opening and excessive crying of the infants [55]. In some cases, parents have not consented to X-ray imaging [41,42].

Natal or neonatal teeth should be distinguished from Bohn's nodules, which are whitish in color, resemble grains of rice and appear in large quantities on the lingual or buccal surface of the alveolar mucosa of the mandibular and maxillary ridges. They do not present any clinical symptoms and disappear spontaneously within a few weeks [33,35]. Congenital epulis grows from the gingiva and can be sessile or pedunculated. X-rays are decisive in case of the aforementioned changes as these anomalies do not have any bone structure. Prematurely erupted teeth may also be similar to lymphangioma, which can occur in the posterior mandibular region and hamartoma of the alveolar ridge [33].

The most common symptoms related to congenital or neonatal teeth are traumatic injuries to the ventral part of the tongue, causing Riga-Fede disease [34,43,51]. Such injury can cause pain, anxiety, and difficulty in food intake [40], leading to dehydration, malnutrition, and consequently underdevelopment of the child. Kamboj and Chougule [63] described a case of a 15-day-old inborn baby in whom eruption of a neonatal tooth in the anterior mandibular region was extremely severe, occurring with a high temperature, formation of an abscess in the chin area, and difficulty in breathing. The child required drainage of the abscess and extraction under general anesthesia on an urgent basis. In addition, prematurely erupted teeth frequently have a high degree of mobility, which presents a risk of swallowing or aspiration into the airway [34,39,40,42,51]. Finally, sharp incisal edges can injure the maternal nipple during feeding [35,50,53].

Management in the event of prematurely erupted teeth should be well-advised, with all factors being taken into account, ensuring the safety of the child and reducing parental anxiety. Extraction is the most common method of managing natal or neonatal teeth [39,49,51,53], although Moura et al. [57] performed the extraction procedure only in 9 newborns out of 23 children with prematurely erupted teeth, due to the significant degree of mobility. Other indications for extraction may include a clear diagnosis that it is a supernumerary tooth [61] and severe pain causing feeding difficulties [40]. In ulceration in Riga-Fede disease, it is not always advisable to perform surgery [35]. However, tooth extraction is the only solution when the ulceration is extensive, does not regress after smoothing the incisal edges or covering with composite material, and makes a food intake difficult [43].

An optimal time frame for extraction is after the child's 10th day of life. However, if it is necessary to perform the procedure before the 10th day of life, a consultation with the pediatrician is advisable [63] and an intramuscular vitamin K supplementation [62,64] is necessary due to the risk of hemorrhage.

The extraction procedure is usually performed under local anesthesia [37,38,41,43,54,57,61] with the application of a topical anesthetic using forceps [43,44] or a gauze [57] when the tooth shows significant mobility. It is recommended to perform a curettage of the alveolus to remove the dental lamina and avoid tooth re-development [43,62,64].
However, Moura et al. [57] did not perform a curettage of the alveolus upon the extraction due to a complete lack of root development in the extracted teeth.

If the extracted tooth is a premature deciduous tooth, keeping it in the mouth should be considered. A premature extraction may contribute to crowding within the permanent teeth and cause underdevelopment of the dental arch [49]. In a study by Cho et al. [51], two out of four children observed after the tooth extraction noted a lack of space. The determining factor for keeping a tooth is primarily lack of its mobility; the primary factor against extraction is the lack of tooth mobility [36, 54]. If a prematurely erupted deciduous tooth in a correct position causes pain or ulceration of the tongue in the child and wounds the mother's breast, a sharp incisal edge should be smoothed or covered with a glass ionomer material [42].

When a prematurely erupted deciduous tooth is left in the oral cavity, it is extremely important to instruct the parents [42, 55, 65] on the hygienic recommendations, the use of fluoridated toothpaste [42], and a necessity of follow-up visits [36]. In addition, breastfeeding on request (when infants have ad-lib access to breastfeeding) may be a risk factor for the development of early childhood caries. Another cause of early childhood caries of prematurely erupted teeth is an underdevelopment of the enamel [39].

**Congenital Epulis**

Congenital epulis (CE) is also known as congenital granular cell tumor, Neumann tumor, congenital granular cell lesion, and gingival granular cell tumor of the newborn [66–72].

Congenital epulis is an exophytic, elastic, smooth-surfaced tumor characterized by the same color as healthy gingiva [45, 66, 68, 69, 71–77]. It is benign and non-hemorrhagic [73]. Epulis is a pedunculated lesion [66, 70–74, 76–81]; upon palpation there is no pain, discomfort or lymphadenopathy [73, 75]. It can measure a few centimeters [45, 67, 73–75, 77, 80] or reach considerable sizes, causing difficulty in eating [66, 69, 70, 72, 76, 77, 80, 81] and even breathing [72, 74]. It occurs as a single tumor [45, 66, 69, 71, 73, 75, 76, 79, 81]. However, Bawazir et al. [67] described 10 cases in newborns, of which three children had two lesions occurring simultaneously, similarly, Sharma et al. [78], Saki and Araghi [80], and Liang et al. [77] presented cases of multiple congenital epulis in alveolar ridges of maxilla and mandible.

The etiology of this granular cell tumor is uncertain [67]. However, there are hypotheses assuming its origin derived from myocytes, neurocytes, fibroblasts, histiocytes, mesenchymal cells, and neurogenic cells [67].

Histologically, epulis is the mass comprised fibrous connective covered by a parakeratotic, stratified, squamous epithelium. It also contains elongated rete ridges and thickening of the stratum spinosum. An enlarged image of the tumor reveals proliferation of large cells with oval hyperchromatic nuclei and granular or clear cytoplasm [45, 66, 68–71, 74, 76–82].

A typical location is the anterior portion of the alveolar process of the maxilla [70, 71, 73–76, 83], but it may appear in the anterior region of the mandible [45, 68, 81]. According to Bawazir et al. [67], out of 13 cases of epulis, seven were located in the maxilla and 6 in the mandible; there was one male infant with two lesions: one on the anterior portion of the mandible and the other on the upper portion.
Epulis is much more common in females at a ratio of 8:1 [66,67,73,82] an endogenous hormonal influence has been proposed to explain the gender bias [73]. CE is commonly detected in healthy children [45,66,68–74,76,78–81], although it has also been found in newborns with polydactyly [83], goiter [84], triple X syndrome [83], polyhydramnios [75], maxillary hypoplasia [75], neurofibromatosis [75].

The lesion is usually diagnosed at birth, based on clinical examination, location, and characteristic appearance [66,70,73,75,82], due to the fact that histological examination would involve surgical intervention with the possible risks of hemorrhage in the neonate [73]. Identification of the immunohistochemical profile of the neonatal granular cell tumor is helpful in the diagnosis of lesions with atypical morphology. A postoperative immunohistochemical examination can reveal tumor cells that are diffusely and strongly positive for vimentin and negative for S100-protein, actin, desmin, laminin, creatine, estrogen, and progesterone receptors [45,66,68–70,77,82,85].

In a situation where the lesion is of significant size, its presence may be revealed by a 3D ultrasound and magnetic resonance imagining (MRI) performed prenatally in the third trimester (diagnosed in utero). Observations of fetuses with CE revealed that the tumor was shown its maximum growth potential just at the end of the 3rd trimester, presumably due to fluctuations in hormones at the end of pregnancy. This examination also allows the assessment of fetal swallowing and fetal airway patency and planning delivery, which in these cases requires a polyhydramnios multidisciplinary team to be present at the time of delivery [84,86,87].

In some cases [69,74,80], despite the considerable size of congenital, epulis ultrasound performed in the third trimester did not reveal any abnormality, suggesting the tumor may have become apparent only at a later stage.

Computer tomography (CT) and magnetic resonance imaging (MRI) performed after birth may be key for a thorough diagnosis. In particular, accurate mapping of the lesion with an MRI was able to rule out maxillary and intracranial extension and was thus a crucial part of preoperative planning [72,74].

Congenital epulis should be distinguished from haemangiomas and lymphangiomas, which are spongy on palpation and have a dark blue surface, unlike CE, which covers normal oral mucosa. Ultrasonography (USG) allows distinguishing granular cell tumor (GCT) from a cystic lesion, in which the fluid flow is visualized on USG [81]. Teratoma, congenital dermoid cyst, congenital fibrosarcoma leiomyoma, rhabdomyoma, and gastrointestinal cyst differ in morphology from granular cell tumors [74,88]. Malignant alveolar sarcoma shows a remarkable resemblance to CE, while there is no characteristic malignant cytological feature and evident vascular invasion that would allow differentiating these changes. X-ray examination allows for GC differentiation, which does not have a bone structure, from solid tumor lesions visualized in the image. CE is very similar to GCT; differentiation is performed on a histological level. Congenital epulis has no single-cell infiltrating clusters of solid growth pattern, also termed neuroid spindle cells, specific to GCT. In order to differentiate lesions from neuroectoderm, urine analysis is performed to test vanillylmandelic acid. In the case of congenital epulis, the result will be negative [75].
If there are different pathologies diagnosed in the oral cavity of a fetus or a newborn, then encephalocele, dermatoid cysts or teratoma, and benign and malignant neoplasms including hemangioma, the lymphatic tumor should be excluded [74,89].

Congenital epulis in newborns may undergo spontaneous regression. This applies to small lesions that do not obstruct breathing or nutrition [73,75]. Spontaneous regression of the tumor is presumably due to the lack of influence of maternal estrogen, which may lead, if not to the disappearance of the lesion, as observed by Kokubun et al. [45], to a reduction of size within five months of observation. Bhatia et al. [73] described spontaneous regression of congenital epulis after ten months of observation, and the eruption of anterior maxillary teeth remained unaffected without hypoplasia.

Traditional therapeutic strategy in case of lack of spontaneous lesion regression [73] or a large granular cell tumor in infants, causing problems in eating and breathing, is reduced to complete surgical excision under local [66,70,79,88] or general anesthesia [45,66,68,71,72,74,77,80–82,88]. The lesion resection time ranges from several days [66,72,74,83,88] to several months after birth [45,79,88].

The tumor is removed traditionally with a scalpel [90,91], laser [66] or cautery [70,72,76]. Pathak and Narula [76] used local anesthesia and cautery excision in two patients, which presented difficulty to intubate due to the size of the lesion. After the surgery, there may be some minor bleeding [66,74,76,90]. The ability to eat will return to normal on the day of surgery [74,88,90] or the day after surgical intervention [66,76,77,82]. The wound may need to be re-epithelialized within ten days [76].

In many cases [71,77,85,88,90,92] no recurrence or malignancy [81,88,92] was observed, even after incomplete resection and post-operative dentition was described as uneventful [79,88].

Epstein Pearls

Epstein pearls are the inclusion cyst present in newborns. They develop from epithelial remnants that became trapped during the fusion of the palatal process. Epstein pearls are small, whitish, raised, rigid nodules, usually arranged in groups of three. Their size ranges between 1 mm and 1 cm and are filled with keratin [4,93–95]. Surgical intervention or pharmacological treatment is not required due to the fact that these lesions are asymptomatic and transient [93,95]. Their most common location is the midline of the hard palate, confirmed in the study by Perez-Aguirre et al. [93] and George et al. [94]. However, this abnormality can also be identified near the junction of the hard and soft palate. Epstein pearls were recorded in 66% and 35.2% of neonates by Perez-Aguirre [93] and George et al. [94], respectively; making them the second most frequent lesions described.

Conversely, further studies found that Epstein pearls were the most common abnormality in the oral cavity of infants and were observed in 27.4% [96] or 14.8 % [4] cases. These abnormalities appear in the first month of life in 43.2% of cases [4]. They have not been observed during the examination of 3-year-old children [4]. No significant differences in the prevalence of Epstein pearls were related to child’s sex [4], preterm births [93], maternal characteristics like age [93], systematic disease [93], and habits (smoking, consuming alcohol).
Results of the study by Perez-Aguirre et al. [93] suggest that taking folic acid could be related to the prevalence of Epstein pearls. Further longitudinal studies are needed to explain this correlation because folate deficiency has been associated with abnormalities in both mothers (anemia, peripheral neuropathy) and fetuses (neural tube defect prevention and congenital heart defect) and suggest that folic acid consumption during pregnancy may also protect against preterm birth [97].

Bohn’s Nodules

Bohn’s nodules, similarly to Epstein pearls and gingival cysts, are classified as inclusion cysts [93,96]. These nodules were first described by Henrich Bohn in 1866 as "mucous gland cysts" derived from the epithelial remains of developing palatine salivary glands [95]. Nowadays, Bohn’s nodules can also be found along the buccal and lingual surface of the maxillary and mandibular dental ridges and are considered reminiscent of glandular mucosal tissue [4,95]. Their most common location is the buccal posterior in the maxilla (52.4%) and mandible (50.1%) [93]. Histologically, Bohn’s nodules are usually covered with three layers of paved epithelium and filled with keratin. These malformations are small, yellowish-white in color, transient in nature, and asymptomatic; they vary in size and thickness [4,93,95,98]. The presence of these abnormalities does not inhibit breastfeeding nor causes discomfort to the child [4,93,95,96]. Literature states that they have occurred most commonly among Mexican newborns [93], where their frequency reached 70% of cases and Indian newborns with the prevalence of 47.2%. At the same time, another study among Indian children [99][94] showed a very similar prevalence between Bohn's nodules (38.8%) and Epstein pearls (38.3%). Moreover, two Brazilian studies found Bohn’s nodules in 26.3% and 24.1% of cases [4,96] and are the second most common abnormality observed.

These nodules decline after the primary tooth eruption. [4,93]. Folic acid consumption during pregnancy can increase the probability of Bohn’s nodules significantly. Furthermore, preterm newborns were observed to be less likely to experience Bohn’s nodules. No significant associations with the intake of calcium or intake, mother’s age, preeclampsia, urinary tract infection, and low birth weight were noted [93].

Dental Lamina Cyst

Dental lamina cyst (also termed Gingival Cyst of Newborn or Alveolar Cyst) manifest clinically as multiple round or/and solid small white or pink oval nodules. The lesions size ranges between 1 and 4 mm [98,100–104], or according to Benni and Sirur [98] and Moda [104], even up to 6 mm diameter. They arise from remnants of the degenerating dental lamina (rests of Serres) and consist of the keratin-producing epithelial lining. During the bell stage of tooth development, the dental lamina disintegrates into the discrete island of epithelial cells. Usually, these clusters degenerate and resorb. However, occasionally, they persist as islands within the jaw known as the "rest of Serres" [98,100,102].

Microscopic evaluation has shown that the cystic lumen is lined with parakeratinized stratified squamous epithelium with flat basement membrane and low cuboidal cells with flat basement membrane [103]. Gingival cysts can be incorrectly diagnosed as a natal tooth, particularly if they are found in the newborn’s mandibular anterior ridge [101].
With regards to the prevalence of oral cyst in newborns, Padovani et al. [4], in the study of 199 Brazilian babies age 0 to 1 month, found the gingival cysts in 11 neonates (5.6%), while Perez-Aguirre et al. [93] in the study of 2216 Mexican newborns diagnosed the gingival cysts in 991 babies (44.7%). The lesions were predominantly located on the posterior maxilla (85.3%) and anterior mandible (84.3%). The majority of these cysts degenerate and involute or rupture into the oral cavity within two weeks to five months of postnatal life, demonstrably study by Padovani et al. [4] found the alveolar cysts only in the group of babies of 0–1-month-old. The diagnosis of this abnormality is based on clinical examination, characteristic appearance, and area [98,100–102,104]. Some studies reported female predisposition [105], while others found no gender specificity [4,93]. In a study by Perez-Aguirre et al. [93], no association between dental lamina cyst and maternal factors including age, systematic diseases, habits, and preterm births have been found. Donley and Nelson [106] demonstrated a correlation between gestational age and weight birth

Folic acid consumption during pregnancy increased lamina cyst prevalence significantly; however, no significant association with calcium and iron intake, mother’s age, preeclampsia, and urinary tract infections were observed [93]. Marini et al. [101] presented a case of multiple inclusion cysts localized on the alveolar ridge of this maxilla and mandible in newborns causing pain in sucking and bleeding. In this situation, surgical removal under local anesthesia was performed.

Summary
Because of many different inborn or acquired changes, which can be present in the oral cavity in young children, it is important for pediatricians and pediatric dentists to be aware of this problem and to have depth knowledge about different identification of the changes. Early and thorough diagnosis and management of these findings are crucial and protect against pathology development or unneedful treatment when the anomaly is recognized.

References


