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Supernumerary teeth: A pictorial review and revised classification

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ABSTRACT

Current literature regarding supernumerary teeth poses the risk of confusion as ambiguity in the terminology and classification of supernumerary teeth permits differing interpretations.

Uncertainty in this regard distorts data on the true incidence and prevalence of supernumerary teeth. This pictorial review provides an overview of the current understanding regarding the development of supernumerary teeth, their positional and morphological classification, and eruptive alterations. We highlight the ambiguity in defining supernumerary teeth and propose an updated classification for the description of these teeth.

1. Introduction

Human tooth development progresses over a number of years. It commences prenatally with calcification of the first teeth beginning around 5 months in utero, and concludes by the mid-twenties with closure of the root of the third permanent molar. ¹⁻³ The human dentition is diphyodont, having first a deciduous set of teeth which is lost and replaced by an increased number of permanent teeth. The deciduous dentition, also referred to as the primary dentition, is comprised of twenty teeth with five teeth in each quadrant of the oral cavity. Growth of the jaws and timing of eruption accommodates the additional 3 molar teeth per quadrant with the permanent premolars replacing the primary molars and the permanent molars found distal of the second permanent premolar. This results in the permanent dentition complement comprising of thirty-two teeth.

Both dentitions are heterodont, comprising of different tooth morphologies. Incisors, canines and molars constitute the primary dentition and in the permanent dentition, there is the addition of premolars. The developmental process however, be it for primary or permanent teeth, follows the same sequence and phases. Initiation of odontogenesis results in an epithelial outgrowth, referred to as the primary dental lamina, that extends into the adjacent condensed ectomesenchyme. The terminal portion of this lamina undergoes morphological changes designating the bud, cap and bell stages of development. For those primary teeth that are replaced by a successional permanent tooth, the permanent tooth begins its development late in the primary tooth's bell

stage as an additional extension of the primary tooth's lamina. The additional three permanent molar teeth, that do not have primary predecessors, develop from a dental lamina extending into the ectomesenchyme posterior of the second primary molars.

The determination of tooth position is closely related to the eruptive sequence. Teeth begin development at different times and consequently erupt into the oral cavity at different ages. Both the developmental and eruptive processes are regulated by a number of pathways. 4-6 Any error in these pathways can result in altered development or eruption.⁷ The timing and sequence of eruption of the primary and permanent dentition have been investigated by many studies.^{8–17} It has been observed that the order of eruption is similar when comparing opposite sides of the same jaw, but differs slightly when comparing the maxilla and mandible. 18 Additionally, discrepancies in the eruption times of different population groups have been found in age estimation studies, with some populations showing either an advanced or delayed eruption. $^{17,1\hat{9}-2\hat{1}}$ Although largely genetically regulated, tooth eruption can be affected by local factors like the available space in the jaws, trauma or the early loss of primary teeth. 22,23 Systemic disorders and syndromes can furthermore influence both the developmental and the eruptive processes. 22,

The determination of tooth morphology, also referred to as patterning, is regulated by molecular mechanisms. Two theories, the field and the clone theory, have been implicated in establishing the pattern of the dentition and should be viewed as complementary. The field theory is based on localised and overlapping regions regulated by

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different combinations of homeobox genes that yield teeth of similar morphology. ^{29,30} The premise of the clone theory is that teeth of a specific type all develop from a solitary pre-programmed clone of ectomesenchymal cells receiving instructive signals from the epithelium. ³¹ This theory provides a possible explanation for the development of the permanent molars where the one dental lamina sequentially generates all 3 molar teeth.

Anomalous tooth development can affect the number of teeth developing and the position of the affected tooth and the morphology of the teeth. The final outcome is dependent on the stage at which tooth development is affected. Deviation from the normal dental complement where the number of teeth is increased is referred to as hyperdontia. The additional tooth that develops is termed a supernumerary tooth.

The exact aetiology of hyperdontia is not completely understood. Multiple theories have been proposed in an attempt to explain the different types of supernumerary scenarios. These include atavism, dichotomy (split of tooth germ), and hyperactivity of the dental lamina. ^{32–34} Currently, the most widely accepted theory of supernumerary tooth development is the hyperactivity of the dental lamina. ^{35,36} The aetiology of this hyperactivity is believed to be multifactorial, attributed to both genetic and environmental factors. ³⁷ The supernumerary tooth can develop from either an additional tooth germ originating from the epithelial band/epithelial cord, or it can develop from the remnants of epithelial cells that persist during disintegration of the dental lamina. ³³

Supernumerary teeth are classified according to their position in the jaws and their morphology. Positionally, supernumerary teeth are generally classified as a mesiodens, paramolar and distomolar or distodens. The term mesiodens refers to a supernumerary tooth developing between the maxillary central incisors^{38–40} and a posterior supernumerary tooth lying buccal or lingual to a molar tooth is termed a paramolar. Al, A distomolar or distodens refers to a supernumerary tooth developing behind the last molar tooth in the dental arch. Another term, parapremolar has been used in the literature to describe a supernumerary tooth developing between or in relation to the permanent premolar teeth. This term however, does not form part of the general descriptions of supernumerary teeth. A fair amount of discrepancy is observed in the literature regarding the descriptions and terminologies used to describe supernumerary teeth occurring in the respective regions of the oral cavity.

Supernumerary teeth are furthermore classified according to their morphology. In the primary dentition, they usually resemble the normal anatomy considering the associated tooth class in the affected region or they present with a conical shape. ⁴⁴ In the permanent dentition however, the morphology can be classified into two broad categories: supplemental and rudimentary. Supplemental refers to teeth of normal size and shape whereas rudimentary would include teeth with an abnormal morphology, displaying differences in size and/or shape. Rudimentary teeth are further described as conical/peg, tuberculate (having more than one cusp or tubercle) or molariform (small premolar or molar-like) in shape. ⁴⁵

Supernumerary teeth are most often seen as incidental findings and even though generally asymptomatic, surgical removal is required in some instances. Worldwide prevalence of supernumerary teeth has been reported to range between 0.1 and 3.6 %. ^{45–51} However, some populations show an increased prevalence. African Americans are almost nine times more likely to have additional teeth compared to Americans with Caucasian background. ⁴³ A study on skeletal remains in South Africa also documented a significantly higher prevalence of supernumerary teeth in their population (6.7 %). ⁵² Generally, males show a higher predilection compared to females, however, a recent South African study showed the prevalence of supernumerary teeth to be 2.48 % with no difference in the number of supernumerary teeth between

Supernumerary teeth are more frequently located in the maxilla than in the mandible. $^{34,54-56}$ Supernumerary teeth mostly present as singular, unilateral and impacted. 57 However, various cases of multiple

supernumerary teeth have been mentioned in the literature, both in association with or without a syndrome. ^{47,58-61} One meta-analysis study noted a slightly increased frequency of supernumerary teeth in the mandible, however, they defined non-syndromic multiple hyperdontia as the presence of five or more supernumerary teeth which would not have accounted for fewer multiple supernumerary teeth in other regions. ⁶² It has been noted that dental anomalies are less frequently observed in the primary dentition. ⁶³

The purpose of this review is to provide a pictorial overview of the current understanding regarding the positional and morphological classifications of supernumerary teeth with reference to developmental and eruptive considerations. We propose an altered description of supernumerary teeth to simplify the classification and minimise ambiguity.

2. Positional considerations of supernumerary teeth

Supernumerary teeth present most commonly in the anterior maxilla. ⁶⁴ A mesiodens typically refers to an additional tooth located between the two maxillary central incisors ^{39,65} (Fig. 1A). The presence of supernumerary teeth in the anterior maxillary region, as observed in Fig. 1B and C, therefore differs from this mesiodens description. These two examples of supernumerary teeth in the anterior maxilla represent supplemental teeth not located between the central incisors and are distinctive entities to that of a mesiodens. These supernumerary teeth therefore need to be differentiated as such. The importance of the distinction between supernumerary teeth in the anterior maxillary region was highlighted by Mossaz et al. ⁴⁰ These authors referred to the term mesiodens only when an additional tooth is present in the midline between the central incisors. When the supernumerary tooth is positioned lateral to the midline Mossaz et al. described these teeth as supernumerary lateral incisors.

Supernumerary teeth presenting in the canine region are typically referred to as supernumerary canines (Fig. 1D). They are rare, but when present are generally supplemental. These teeth are more frequently located in the maxilla and have been found in both the primary and permanent dentition. Ge-70 Supernumerary canines are often impacted as seen in Fig. 1D and can frequently cause impaction of the permanent canine or adjacent teeth. The possibility exists that supernumerary canines could also develop as rudimentary supernumerary central or lateral incisors that are conical in shape.

Supernumerary teeth found in the premolar region that lie interproximal, palatal/lingual or buccal of the first and second premolars have been described in the literature as parapremolars. ⁴³ Figs. 1B, 2A and 2B represent examples of such parapremolars. The term parapremolar did not form part of the general supernumerary classification and is not consistently used to describe supernumerary premolar teeth.

Supernumerary premolars have been proposed to represent a third series of teeth, also referred to as a post-permanent dentition.^{72,73} They are thought to develop from the proliferation of the remnants of the dental lamina after the permanent dentition is complete.⁷⁴ Fig. 2A, B, and C may all represent examples of the hyperactivity of the dental lamina and post-permanent dentition. Eruption of the first mandibular premolars normally occurs at around 10-12 years and for the mandibular second premolars at around 11-12 years. The roots of the permanent premolar are normally complete between 12 and 14 years of age. In Fig. 2A, supernumerary premolars can be seen developing in both the right maxilla and mandible and Fig. 2B is similar, with the exception that the first permanent mandibular premolar on the left is impacted as a result of a developing supernumerary tooth. The age of the patient in Fig. 2B was 10 years old and the first and second mandibular permanent premolars already exhibited advanced/completed root development. This could be attributed to advanced dental development being associated with supernumerary teeth. 75 As supernumerary teeth develop quite late, they are not often found in the primary dentition. If they do develop in the primary dentition they are usually seen after 3 or 4 years of age. In

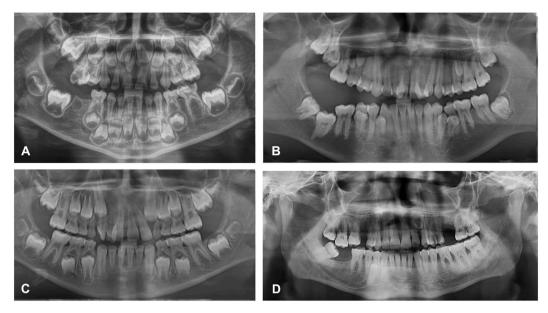


Fig. 1. Panoramic radiographs of supernumerary teeth in the anterior maxillary region. A: Mesiodens visible between the maxillary central incisors. B: Two fully formed supernumerary maxillary central incisors can be observed. C: A supernumerary lateral incisor can be observed in the upper right maxilla. D: An impacted supernumerary canine visible in the upper left maxilla.

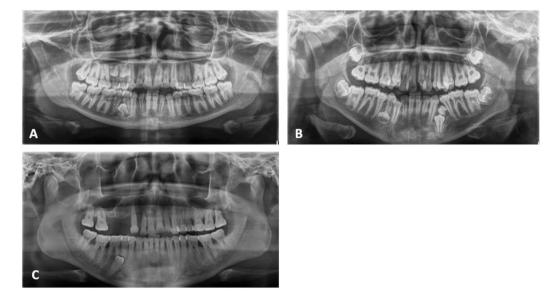


Fig. 2. Panoramic radiographs of supernumerary teeth in the premolar region. A: Two developing supernumerary teeth of premolar crown morphology in the right maxilla and one in the mandibular premolar region (associated with teeth FDI 14, 15 and 44). B: Developing supernumerary teeth can be observed on the right and left mandibular premolar regions. C: A fully developed, impacted supernumerary tooth of premolar morphology located between the lower right second premolar and first molar.

the permanent dentition, they can generally be observed radiographically in children older than 9 years. 76 Further supporting their development as a post-permanent dentition.

An alternative theory of supernumerary tooth development is the progress zone theory. This theory proposes that additional teeth result from the progress zone of a proliferating tooth series that then continues to form teeth at the end of that series. This theory is similar to that of the hyperactivity of the dental lamina and the post-permanent dentition. Fig. 2C provides such an example. The supernumerary tooth is found at the end of the series and has a similar morphology to the type of tooth class in series. A case report by Prasad et al. used the term parapremolar to describe a supernumerary tooth located between the first and second premolars. However, they used the term paramolar to describe the supernumerary tooth located adjacent to the first molar even though the

morphology was almost identical to that of the parapremolar. Considering the theories of supernumerary development, this paramolar could have developed from the hyperactivity of the dental lamina of the premolars, especially as it was positioned lingually.

Supernumerary teeth found in the premolar region differ from the normal supernumerary tendencies as they are more likely to be located in the mandible and are mostly supplemental. A recent publication on hyperdontia in a Sub-Saharan African sample found that supernumerary premolar teeth are more common in this population compared to the global prevalence. In this study, males were more likely to present with supernumerary premolars, and one individual presented with seven additional premolars, five of which were in the mandible.

Supernumerary teeth occurring in the posterior regions lying buccal or palatal/lingual of a molar tooth are referred to as paramolars. If the supernumerary tooth is located posterior to the third molar tooth, it is referred to as a distomolar (Figs. 1B and 3A and B). Distomolars, like paramolars, can present with a molar-like morphology or can be smaller in size compared to the adjacent molars and are then referred to as a microdont. 41

The development of a distomolar/distodens can also be linked to the progress zone theory mentioned earlier. The supernumerary tooth located adjacent to the third molar in the first quadrant in Fig. 3A is a good example of this theory, as the morphology is similar to the molar tooth class. In Fig. 3B, the supernumerary tooth distal of the third molar in the first quadrant has a different morphology, which questions the mechanism of development. This supernumerary tooth has a more rudimentary morphology and may represent the dichotomy theory where the division of the tooth bud, forms either two similar-sized teeth or one normal sized tooth and a smaller supernumerary tooth. If the supernumerary tooth developed due to proliferation of an additional dental lamina, a tooth with a more molar-like morphology would form in this region. Distomolars can either fully erupt into the occlusal plane or can be partially or completely impacted.⁷⁸

3. Morphological considerations of supernumerary teeth

Supernumerary morphology is characterised as either supplemental or rudimentary. Supplemental refers to supernumerary teeth that are of normal size and shape. Rudimentary on the other hand refers to supernumerary teeth that are often smaller with altered shape. The terms conical/peg-shaped, tuberculate and molariform are used to describe rudimentary supernumerary teeth. The word rudimentary refers to an entity being immature and underdeveloped, which is not necessarily always the case with supernumerary teeth that are not supplemental. The multiple scenarios observed regarding the morphology of supernumerary teeth may be the reason why some authors include odontomas as part of the classification of supernumerary teeth. 40,46,79,80 However, odontomas and supernumeraries are classified as distinct entities. 81

The morphology of the human dentition is largely genetically regulated through a number of pathways. $^{4.5,82}$ The morphology of teeth, including supernumerary teeth, is related to the developmental location as explained by the patterning theories. Teeth that develop closest to a key tooth or in the most anterior region of a homeobox field are proposed to have a similar morphology to the teeth in that field. However, teeth that develop more distally in a field, will show a greater morphological variation. 29,83,84 Supernumerary teeth that develop at the boundary of two fields can present with morphological features of teeth from both tooth classes. 85 Although this morphological regulation is proposed, different types of morphologies of supernumerary teeth can be observed.

Most permanent supernumeraries have a conical morphology (Figs. 1A and 4) which is small and peg-shaped. ^{39,40,78} Supernumerary teeth with a tuberculate morphology refer to teeth that have more than one cusp or tubercles and are typically barrel-shaped. ³⁶ Additionally,

the other term that is used is molariform which also denotes a small premolar or molar-like shape. Both these terms encompass both the premolar and molar-like morphology and therefore do not differentiate between these two different tooth classes.

Supplemental teeth generally display a similar morphology to the teeth in the series in which they are located. This links their development to both the hyperactivity of the dental lamina and progress zone theories depending on their position. Fig. 2A and B and C provide such examples. Interestingly, in our presented cases of supernumerary premolars, all showed a premolar-type morphology and none displayed a molar-like morphology regardless if they were located between the premolar teeth or at the distal aspect of the premolar region (Fig. 2A and B and C).

A discrepancy in the morphology of the supernumerary teeth was observed in Fig. 3A. The supernumerary tooth in the upper left maxilla was more premolar-like and the upper right supernumerary was of molar morphology. The supernumerary in the upper right maxilla showed a similar morphology to the series of teeth in which it was located and can be considered supplemental. The supernumerary in the left maxilla however can be considered under the general classification as rudimentary. This is in agreement with Cassetta et al. who found that supernumerary molar teeth are mostly of tuberculate shape. ⁷⁸

Our selection of cases does not include rudimentary tuberculate or molariform anterior supernumerary teeth. These supernumerary teeth have been described as rare and the developmental mechanism of such morphologies in the anterior region has not yet been clarified. ^{87,88}

4. Associations with other anomalies

Supernumerary teeth can occur as isolated cases or can be associated with other anomalies. ⁴⁷ Simultaneous occurrence of supernumerary teeth with other dental anomalies can be explained by the unified aetiology theory which is based on the cumulative effect of genetic and environmental factors. ³³

In Fig. 1A, a mesiodens can be observed together with congenitally absent second premolars in all four quadrants. This is an example of hypodontia associated with hyperdontia. Although supernumerary teeth present more commonly in the maxilla with the mesiodens being the most frequent, supernumerary premolars are more likely to be located in the mandible. ^{89,90} Fig. 2B provides an example of developing supernumerary teeth in the mandible together with enamel pearls on the lower second molars.

Khalaf et al. stated that it is difficult to determine if supernumerary teeth in the molar region with premolar morphology, originate from the premolar series and are transposed to the molar area, or if they originate from the molar region and present with altered morphology from the molar field. This phenomenon, however, could be considered as transposed supernumerary premolars. Tooth transposition is defined as the positional interchange of two teeth or the disturbance of tooth order and eruptive position. The aetiology of transposition is not clear, but the disturbance of tooth order and eruptive position.



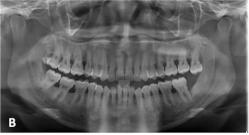


Fig. 3. Panoramic radiographs of supernumerary molars. A: Fully formed supernumerary maxillary molars (FDI teeth 19 and 29). In the maxillary left region, the third molar (tooth 28) is impacted in the maxillary sinus region and the supernumerary tooth (tooth 29) is located distal of the second maxillary molar. This supernumerary tooth displays a premolar-like morphology whereas the distomolar in the right maxilla has a molar-like morphology. B: A distomolar can be observed behind the third molar in the first quadrant. This supernumerary tooth is smaller in size compared to the adjacent molars and fully erupted.



Fig. 4. Conical-shaped microdontic supernumerary tooth in the right posterior premolar region between the second premolar and first molar.

there seems to be a strong genetic influence within a multifactorial inheritance model. 33,91,92 Transposition is often associated with other dental anomalies and seems to have a female predominance. 93,94 Fig. 5A and B both show supernumerary teeth transposed into the molar region.

5. Genetic regulation of supernumerary teeth and future prospects

Ethical considerations render it challenging to study human odontogenesis. For this reason, tooth development is often studied in animal models; most commonly mice and rats. The human and mouse dentition differs, with mice having one continuously growing incisor anteriorly and 3 molar posteriorly in each quadrant. A toothless region or diastema separates the incisors and molars. Non-functional tooth germs have been identified in these regions. These tooth germs have been shown to exhibit development up till the bud stage and then regress. 95 They are considered remnants of ancestral teeth prior to evolutionary reduction. 96,97 Rudimental successional laminas have further been identified on the lingual aspect of the mouse incisor and molar teeth indicating the potential for the development of a supplemental dentition. 95,98,99 Supernumerary teeth in mice are said to develop from these non-functional tooth buds and the teeth that develop are usually standalone. $^{100-102}$

Anh et al. demonstrated that Sostdc1 inhibits Wnt signalling which suppresses the non-functional tooth buds in the diastema and incisor regions in mice. 103 Inhibition of Sostdc1 increases the proliferation and development of the arrested tooth buds leading to supernumerary tooth formation. Interaction between developing tooth germs may also influence the occurrence of supernumerary teeth. Retarded growth of first

molar tooth germs in mice, leads to overgrowth of the dental lamina resulting in additional tooth germs in the diastema space anterior to the molar. 104 Studies exploring the reactivation of vestigial pathways could provide insight into creating artificial replacement teeth for the advancement of tissue engineering and regenerative dentistry. 105–107

Supernumerary teeth may present as isolated cases, but more commonly can occur in families of affected individuals. ^{34,108,109} Heredity is therefore an important factor. ¹¹⁰ Multiple supernumerary teeth are considered rare and are most often associated with other systemic conditions or syndromes indicating an underlying genetic cause. ^{46,47,110} The presence of multiple supernumerary teeth should highlight the need for further investigation of a possible underlying syndrome. Fig. 1B represents an example of multiple supernumerary teeth in a child without a diagnosed syndrome. Even though great advancements have been made in the field of odontogenesis, complete understanding regarding the genetic control of successional tooth initiation is still restricted.

Five conserved signalling pathways; the Wnt (Wingless), BMP (bone morphogenic protein), FGF (fibroblast growth factor), Shh (sonic hedgehog), and Eda (ectodysplasin) have all been implicated in tooth development. Genetic studies have shown that Wnt/ β -catenin seems to be the most upstream signal initiating tooth development. Both the stabilization of β -catenin and activation of Lef1 are important in regulating normal tooth development. Tooth-like structures have been observed in non-tooth regions of mice with an over expression of Lef1. Elevated levels of Wnt/ β -catenin protein seem to be associated with abnormal teeth and ectopic invaginations of the dental epithelium which could result in supernumerary tooth formation. BMP4





Fig. 5. Panoramic radiographs of transposed supernumerary teeth. A: Bilateral premolar-shaped supernumerary teeth are evident distal to the first mandibular molars. This resulted in impaction of the second molars bilaterally. B: Fully developed impacted supernumerary premolars distal to the first mandibular molars.

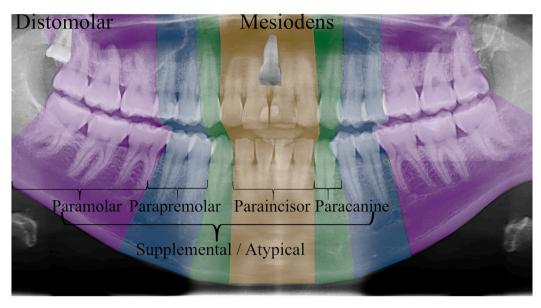


Fig. 6. Proposed classification considering both the position and morphology of supernumerary teeth. The different colours indicate the respective positions including paraincisor (orange), paracanine (green), parapremolar (blue) and paramolar (purple). The terms mesiodens and distomolar are restricted to the extremities of the four quadrants. The descriptive terms for the morphology of supernumerary teeth would include supplemental or atypical. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

supresses tooth development inhibitors and together with Msx-1 can activate supernumerary tooth development. Mutation in the adenomatous polyposis coli (APC) gene, which negatively regulates Wnt signalling, has also been shown to initiate supernumerary tooth formation. This can be observed in patients with Gardner's syndrome, where these individuals present with a mutation in the APC gene. The presence of multiple supernumerary teeth can therefore be valuable in identifying underlying rare diseases or syndromes.

Mutations in Runt-related transcription factor 2 (RUNX2) have been implicated in inherited cleidocranial dysplasia, characterised by hyperdontia. 120 Mice lacking the RUNX2 gene demonstrate tooth agenesis and lack bone development. The antagonist effect between RUNX2 and uterine sensitization-associated gene-1 (USAG-1) and CCAAT/enhancer binding protein beta (CEBPB) has been described. 123-125 CEBPB and RUNX2 have demonstrated a synergistic effect in supernumerary tooth development. 123 The USAG-1 gene, a regulator of BMP and Wnt pathways, neutralises BMP activities. 126 It has been demonstrated that USAG-1 can partially rescue arrested tooth development in Runx2-deficient mice. 127 This group of researchers affirmed the role of the third dentition in human supernumerary tooth formation 128 and described an antibody against USAG-1 for tooth regeneration in mice. 127 Furthermore, a novel mutation of the fer-1-like family member 6 (FER1L6) gene was identified in non-syndromic familial multiple supernumerary teeth. The function of the FER1L6 protein in human organogenesis and tooth development, however, has not yet been specified. 129 Supernumerary teeth are also found in cleft lip and palate patients, attributed to the fragmentation of the dental lamina during cleft formation. However, this is not the most common presentation, as hypodontia is most often observed in this region. 130-1

6. Proposed supernumerary classification and descriptions

Forming a clear-cut supernumerary classification system is complex as both positional and morphological characteristics require consideration, and the developmental aetiologies and outcomes are diverse. The current traditional classification and description of supernumerary teeth is at times ambiguous and deficient. Zhang et al. stated that the features of supernumerary teeth lack descriptive consistency. ⁸⁰ Furthermore, Alvia-Gonzalez and Gay-Escoda refer to bias when studying

supernumerary teeth due to the lack of unanimity in diagnosis in the classification. ⁶² The true prevalence of supernumerary teeth cannot be obtained until the classification system thereof is improved and standardised. Furthermore, epidemiological studies on multiple supernumerary teeth should not be restricted to specific numbers as this distorts the total incidence. The consideration of both positional and morphological presentations of supernumerary teeth should be included in any comprehensive classification system.

Positional considerations for supernumerary teeth can be based on the regions separated naturally by the differing tooth classes. Transitional zones can be found between the different tooth classes which could allow for some overlap in morphology. Morphological considerations of supernumerary teeth should be described as supplemental for supernumerary teeth having the same size and morphology as the series of teeth in which they are found. The term rudimentary is typically used to describe an entity as underdeveloped or immature. Under the rudimentary term, teeth were classified as conical, tuberculate, or molariform. Conical describes teeth that show a conical or more pointed shape. The distinction between tuberculate and molariform is currently confusing as tuberculate refers to teeth that have more than one cusp or tubercles and molariform describes a small premolar or molar-like shape. A premolar-like morphology may then fit into both the tuberculate and molariform descriptions. We propose that the term rudimentary be discarded for describing supernumerary teeth and replaced with atypical. The term atypical is more appropriate to describe supernumerary teeth that present with an altered size and/or altered shape compared to the morphology of the adjacent tooth series. Atypical can therefore encompass differing shapes and sizes including conical, tuberculate, molariform, microdontic and macrodontic morphologies.

The following classification and descriptions, considering both the position and morphology of supernumerary teeth, are proposed. The term mesiodens should be limited to supernumeraries in the midline of the maxillary or mandibular central incisors. In this description, bilateral mesiodens or mesiodentes as previously described is not plausible. ¹³⁴ Supernumeraries found lateral to the midline in the anterior maxilla or mandible can be referred to as paraincisors. If the morphology is altered or smaller, it should be referred to as an atypical paraincisor. The term parapremolar would include a supernumerary tooth in the premolar region, and if the morphology is altered, they can be termed

atypical parapremolars. The canine area is a transitional zone between the anterior and posterior regions of the jaws. If a supernumerary tooth is located in association with the canines and is conical in shape, it should be referred to as a paracanine. If a supernumerary tooth is located in this transitional zone and resembles an incisor or a premolar and is not conical, it should be referred to as a paraincisor and parapremolar respectively. Paramolars would include supernumerary teeth in the molar region and if their morphology is altered, they would be referred to as atypical paramolars.

In agreement with de La Dure-Molla et al. (2019), one should refrain from using the term distodens as this term could include any supernumerary distal to any given tooth class regardless of morphology. ⁴² Even though these authors discouraged the use of distomolars, this term would be more acceptable as the location and morphology are clear in being located distal of the third molar tooth. An additional transition zone can be found between the premolar and molar regions. Classification of supernumerary teeth in these regions should be considered according to both the morphological and the positional descriptions. A suggested visual representation of the amended classification considering both the position and morphology of supernumerary teeth can be seen in Fig. 6.

7. Conclusion

Although epidemiological studies on supernumerary teeth are relevant for early clinical diagnosis, ambiguity in the classification and terminologies used in the literature complicates and obscures the true prevalence of this anomaly. Improved and standardised definitions are therefore important. Continued efforts to investigate the genetic regulation and pathways driving hyperdontia will guide proper description and classification of supernumerary teeth. It will further provide valuable information for the development of tooth regeneration therapies. This proposal aimed to clarify and simplify the classification of supernumerary teeth.

Patient's/Guardian's consent

Not applicable.

Ethics approval and consent to participate

Not applicable.

CRediT authorship contribution statement

Christy L Davidson (ORCID ID 0000-0002-3638-6932): Writing – original draft, Conceptualization, Review and Editing. Chané Smit (ORCID ID 0000-0003-4047-6356): Writing – Review & Editing, Conceptualization, data curation. Sulette Nel (ORCID ID 0000-0002-0802-079X): Writing – Review & Editing, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

- Hovorakova M, Lesot H, Peterka M, Peterkova R. Early development of the human dentition revisited. *J Anat.* 2018;233(2):135–145. https://doi.org/10.1111/ ion.12825
- Schour I, Massler M. The development of the human dentition. JADA. 1941;20: 270, 427
- 3. Uys A, Bernitz H, Pretorius S, Steyn M. Estimating age and the probability of being at least 18 years of age using third molars: a comparison between Black and White individuals living in South Africa. *Int J Legal Med.* 2018;132(5):1437–1446. https://doi.org/10.1007/s00414-018-1877-6.
- Lan Y, Jia S, Jiang R. Molecular patterning of the mammalian dentition. Semin Cell Dev Biol. 2014;25–26:61–70. https://doi.org/10.1016/j.semcdb.2013.12.003.
- Jernvall J, Thesleff I. Reiterative signaling and patterning during mammalian tooth morphogenesis. *Mech Dev.* 2000;92(1):19–29. https://doi.org/10.1016/s0925-4773(99)00322-6
- Pispa J, Thesleff I. Mechanisms of ectodermal organogenesis. Dev Biol. 2003;262 (2):195–205. https://doi.org/10.1016/s0012-1606(03)00325-7.
- Bei M. Molecular genetics of tooth development. *Curr Opin Genet Dev.* 2009;19(5): 504–510. https://doi.org/10.1016/j.gde.2009.09.002.
 Parner ET, Heidmann JM, Vaeth M, Poulsen S. A longitudinal study of time trends
- Parner ET, Heidmann JM, Vaeth M, Poulsen S. A longitudinal study of time trends in the eruption of permanent teeth in Danish children. *Arch Oral Biol.* 2001;46(5): 425–431. https://doi.org/10.1016/s0003-9969(01)00002-4.
- Dashash M, Al-Jazar N. Timing and sequence of emergence of permanent teeth in Syrian schoolchildren. *J Investig Clin Dent.* 2018;9(2), e12311. https://doi.org/ 10.1111/jicd.12311.
- Ogodescu E, Popa M, Isac C, et al. Eruption timing and sequence of primary teeth in a sample of Romanian children. *Diagnostics*. 2022;12(3). https://doi.org/ 10.3390/diagnostics12030606.
- Nizam A, Naing L, Mokhtar N. Age and sequence of eruption of permanent teeth in Kelantan, north-eastern Malaysia. *Clin Oral Investig*. 2003;7(4):222–225. https://doi.org/10.1007/s00784-003-0228-1.
- Moslemi M. An epidemiological survey of the time and sequence of eruption of permanent teeth in 4-15-year-olds in Tehran, Iran. Int J Paediatr Dent. 2004;14(6): 432-438. https://doi.org/10.1111/j.1365-263X.2004.00586.x.
- Diamanti J, Townsend GC. New standards for permanent tooth emergence in Australian children. Aust Dent J. 2003;48(1):39–42. https://doi.org/10.1111/ j.1834-7819.2003.tb00007.x. quiz 69.
- Folayan M, Owotade F, Adejuyigbe E, Sen S, Lawal B, Ndukwe K. The timing of eruption of the primary dentition in Nigerian children. *Am J Phys Anthropol.* 2007; 134(4):443–448. https://doi.org/10.1002/ajpa.20635.
- Lakshmappa A, Guledgud MV, Patil K. Eruption times and patterns of permanent teeth in school children of India. *Indian J Dent Res.* 2011;22(6):755–763. https://doi.org/10.4103/0970-9290.94568.
- Cieślińska K, Zaborowicz K, Buchwald Z, Biedziak B. Eruption pattern of permanent canines and premolars in polish children. Int J Environ Res Public Health. 2022;19(14). https://doi.org/10.3390/ijerph19148464.
- Esan TA, Mothupi KA, Schepartz LA. Permanent tooth emergence: timing and sequence in a sample of Black Southern African children. Am J Phys Anthropol. 2018;167(4):827–839. https://doi.org/10.1002/ajpa.23714.
- Khan AS, Nagar P, Singh P, Bharti M. Changes in the sequence of eruption of permanent teeth; Correlation between chronological and dental age and effects of body mass index of 5-15-year-old schoolchildren. *Int J Clin Pediatr Dent.* 2020;13 (4):368–380. https://doi.org/10.5005/jp-journals-10005-1797.
- Harris EF, McKee JH. Tooth mineralization standards for blacks and whites from the middle southern United States. J Forensic Sci. 1990;35(4):859–872.
- Uys A, Fabris-Rotelli I, Bernitz H. Estimating age in black South African children. SADJ. 2014;69(2):54–58, 60-58.
- Tompkins RL. Human population variability in relative dental development. Am J Phys Anthropol. 1996;99(1):79–102. https://doi.org/10.1002/(SICI)1096-8644 (199601)99:1<79::AID-AJPA5>3.0.CO;2-V.
- Do Espírito Santo Jácomo DR, Campos V. Prevalence of sequelae in the permanent anterior teeth after trauma in their predecessors: a longitudinal study of 8 years. Dent Traumatol. 2009;25(3):300–304. https://doi.org/10.1111/j.1600-9657 2009 00764 x
- Ash AS. Orthodontic significance of anomalies of tooth eruption. Am J Orthod. 1957;43(8):559–576. https://doi.org/10.1016/0002-9416(57)90160-4.
- Almonaitiene R, Balciuniene I, Tutkuviene J. Factors influencing permanent teeth eruption. Part one–general factors. Stomatologija. 2010;12(3):67–72.
- Boka VMA, Poulopoulos AK. Tooth eruption: topical and systemic factors that influence the process. Balk J Stom. 2009;13(1):11–14.
- Wu H, Chen T, Ma Q, Xu X, Xie K, Chen Y. Associations of maternal, perinatal and postnatal factors with the eruption timing of the first primary tooth. *Sci Rep.* 2019; 9(1):2645. https://doi.org/10.1038/s41598-019-39572-w.
- Klein OD, Oberoi S, Huysseune A, Hovorakova M, Peterka M, Peterkova R. Developmental disorders of the dentition: an update. Am J Med Genet C Semin Med Genet. 2013;163c(4):318–332. https://doi.org/10.1002/ajmg.c.31382.
- Hirst L, Mubeen S, Abou-Ameira G, Chakrapani A. Mucopolysaccharidosis (MPS): review of the literature and case series of five pediatric dental patients. Clin Case Rep. 2021;9(3):1704–1710. https://doi.org/10.1002/ccr3.3885.
- Butler PM. Studies of the mammalian dentition.—differentiation of the post-canine dentition. Proc Zool Soc Lond. 1939;B109(1):1–36. https://doi.org/10.1111/ j.1469-7998.1939.tb00021.x.
- 30. Townsend G, Harris EF, Lesot H, Clauss F, Brook A. Morphogenetic fields within the human dentition: a new, clinically relevant synthesis of an old concept. *Arch*

- Oral Biol. 2009;54:S34–S44. https://doi.org/10.1016/j.archoralbio.2008.06.011. Suppl 1(Suppl 1).
- Osborne JW. Morphogenetic gradients: fields versus clones. In: Butler PM, Joysey KA, eds. Development, Function and Evolution of Teeth. London: Academic Press; 1978:171–201.
- Saarenmaa L. The origin of supernumerary teeth. Acta Odontol Scand. 1951;9(3-4): 293–303. https://doi.org/10.3109/00016355109012791.
- Anthonappa RP, King NM, Rabie AB. Aetiology of supernumerary teeth: a literature review. Eur Arch Paediatr Dent. 2013;14(5):279–288. https://doi.org/ 10.1007/s40368-013-0082-z.
- Brook AH. A unifying aetiological explanation for anomalies of human tooth number and size. Arch Oral Biol. 1984;29(5):373–378. https://doi.org/10.1016/ 0003-9969(84)90163-8.
- Loganathan K, Ahmed VKS, Narayan G, Rajavalli S, Lnu S, Baskara V. A rare case of bilaterally transposed maxillary supernumerary premolars and its management. J Oper Dent Endod. 2018;3:92–96. https://doi.org/10.5005/jp-journals-10047-0063.
- Fleming PS, Xavier GM, DiBiase AT, Cobourne MT. Revisiting the supernumerary: the epidemiological and molecular basis of extra teeth. *Br Dent J.* 2010;208(1): 25–30. https://doi.org/10.1038/sj.bdj.2009.1177.
- Lu X, Yu F, Liu J, et al. The epidemiology of supernumerary teeth and the associated molecular mechanism. *Organogenesis*. 2017;13(3):71–82. https://doi. org/10.1080/15476278.2017.1332554.
- Gallas MM, García A. Retention of permanent incisors by mesiodens: a family affair. Br Dent J. 2000;188(2):63–64. https://doi.org/10.1038/sj.bdj.4800390.
- Rajab LD, Hamdan MA. Supernumerary teeth: review of the literature and a survey of 152 cases. Int J Paediatr Dent. 2002;12(4):244–254. https://doi.org/10.1046/ i.1365-263x.2002.00366.x.
- Mossaz J, Kloukos D, Pandis N, Suter VG, Katsaros C, Bornstein MM. Morphologic characteristics, location, and associated complications of maxillary and mandibular supernumerary teeth as evaluated using cone beam computed tomography. Eur J Orthod. 2014;36(6):708–718. https://doi.org/10.1093/ejo/ cit[0].
- Nayak G, Shetty S, Singh I, Pitalia D. Paramolar a supernumerary molar: a case report and an overview. *Dent Res J.* 2012;9(6):797–803. https://doi.org/10.4103/ 1735-3327 107591
- de La Dure-Molla M, Fournier BP, Manzanares MC, et al. Elements of morphology: standard terminology for the teeth and classifying genetic dental disorders. Am J Med Genet. 2019;179(10):1913–1981. https://doi.org/10.1002/ajmg.a.61316.
- Prasad P, Ahirwal S, Kumar V, Chauhan M, Rathor P. Paramolar with a parapremolar: a rare occurrence. J Clin Diagn Res. 2017;11:ZD01–ZD2. https://doi. org/10.7860/JCDR/2017/30827.10784.
- Bahadure RN, Thosar N, Jain ES, Kharabe V, Gaikwad R. Supernumerary teeth in primary dentition and early intervention: a series of case reports. *Case Rep Dent.*. 2012, 614652 https://doi.org/10.1155/2012/614652, 2012.
- Irish JD. Hyperdontia across sub-Saharan Africa: prevalence, patterning, and implications. Arch Oral Biol. 2022;140, 105463. https://doi.org/10.1016/j. archoralbio. 2022.105463
- Cammarata-Scalisi F, Avendaño A, Callea M. Main genetic entities associated with supernumerary teeth. Arch Argent Pediatr. 2018;116(6):437–444. https://doi.org/ 10.5546/aap.2018.eng.437.
- Subasioglu A, Savas S, Kucukyilmaz E, Kesim S, Yagci A, Dundar M. Genetic background of supernumerary teeth. Eur J Dent. 2015;9(1):153–158. https://doi. org/10.4103/1305-7456.149670.
- Mahabob MN, Anbuselvan GJ, Kumar BS, Raja S, Kothari S. Prevalence rate of supernumerary teeth among non-syndromic South Indian population: an analysis. J Pharm BioAllied Sci. 2012;4(Suppl 2):S373–S375. https://doi.org/10.4103/0975-7406.100279.
- Davis PJ. Hypodontia and hyperdontia of permanent teeth in Hong Kong school children. *Community Dent Oral Epidemiol*. 1987;15(4):218–220. https://doi.org/ 10.1111/j.1600-0528.1987.tb00524.x.
- Brook AH. Dental anomalies of number, form and size: their prevalence in British schoolchildren. J Int Assoc Dent Child. 1974;5(2):37–53.
- Jain A, Saxena A, Jain S, Parihar APS, Rawat A. Prevalence of developmental dental anomalies of number and size in Indian population according to age and gender. Int J Clin Pediatr Dent. 2021;14(4):531–536. https://doi.org/10.5005/jpjournals-10005-1980.
- Van der Merwe AE, Steyn M. A report on the high incidence of supernumerary teeth in skeletal remains from a 19th century mining community from Kimberley, South Africa. SADJ. 2009;64(4):4–6, 162.
- Thomas E, Oettlé A, Becker P. Supernumerary teeth in a sample of South African dental patients. SADJ. 2023;78:74–81.
- Ata-Ali F, Ata-Ali J, Peñarrocha-Oltra D, Peñarrocha-Diago M. Prevalence, etiology, diagnosis, treatment and complications of supernumerary teeth. *J Clin Exp Dent.* 2014;6(4):e414–e418. https://doi.org/10.4317/jced.51499.
- Eshgian N, Al-Talib T, Nelson S, Abubakr NH. Prevalence of hyperdontia, hypodontia, and concomitant hypo-hyperdontia. *J Dent Sci.* 2021;16(2):713–717. https://doi.org/10.1016/j.jds.2020.09.005.
- Henninger E, Friedli L, Makrygiannakis MA, et al. Supernumerary tooth patterns in non-syndromic white European subjects. *Dent J.* 2023;11(10):230. https://doi.org/ 10.3300/dil1100230
- Hajmohammadi E, Najirad S, Mikaeili H, Kamran A. Epidemiology of supernumerary teeth in 5000 radiography films: investigation of patients referring to the clinics of ardabil in 2015–2020. *Int J Dent.* 2021;2021(1), 6669436. https://doi.org/10.1155/2021/6669436.

- Sawai MA, Faisal M, Mansoob S. Multiple supernumerary teeth in a nonsyndromic association: rare presentation in three siblings. *J Oral Maxillofac Pathol*. 2019;23 (1):163. https://doi.org/10.4103/jomfp.JOMFP_99_17.
- Qin B, Jiang W, Jing Z, Zhao L. Non-syndrome multiple impacted teeth and supernumerary teeth in a family: a report of 2 cases. *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology*. 2016;28(2):185–188. https://doi. org/10.1016/j.ajoms.2015.07.007.
- Moradinejad M, Hashemi Ashtiani A, Rakhshan V. Multiple nonsyndromic unerupted supernumerary teeth: a report of a rare case. Case Rep Dent. 2022;2022, 4063856. https://doi.org/10.1155/2022/4063856.
- Lubinsky M, Kantaputra PN. Syndromes with supernumerary teeth. Am J Med Genet. 2016;170(10):2611–2616. https://doi.org/10.1002/ajmg.a.37763.
- Alvira-González J, Gay-Escoda C. Non-syndromic multiple supernumerary teeth: meta-analysis. J Oral Pathol Med. 2012;41(5):361–366. https://doi.org/10.1111/j.1600-0714.2011.01111.x
- Belmehdi A, Bahbah S, El Harti K, El Wady W. Non syndromic supernumerary teeth: management of two clinical cases. *Pan Afr Med J.* 2018;29:163. https://doi. org/10.11604/pamj.2018.29.163.14427.
- Chou S-T, Chang H-P, Yang Y-H, et al. Characteristics of supernumerary teeth among nonsyndromic dental patients. *Journal of Dental Sciences*. 2015;10(2): 133–138. https://doi.org/10.1016/j.jds.2013.12.004.
- Van Buggenhout G, Bailleul-Forestier I. Mesiodens. Eur J Med Genet. 2008;51(2): 178–181. https://doi.org/10.1016/j.ejmg.2007.12.006.
- Alqahtani HA, Talaat WM. Supernumerary maxillary canine in non-syndromic patient: a rare case report. Hamdan Medical Journal. 2020;13(3):172–175. https://doi.org/10.4103/hmj.Hmj 17 20.
- Abouei Mehrizi E, Semyari H, Eslami Amirabadi G. Bilateral mandibular supernumerary canines: a case report. *J Dent Res Dent Clin Dent Prospects*. 2010;4 (4):140. https://doi.org/10.5681/joddd.2010.034.
- Fujita K, Nakano K, Okawa R, et al. A case of supernumerary primary and permanent canines. *Pediatr Dent J.* 2007;17(2):167–172. https://doi.org/10.1016/ S0917-2394(07)70111-8.
- Hume WJ. Supplemental canines A case report. J Dent. 1973;1(6):261–262. https://doi.org/10.1016/0300-5712(73)90101-2.
- Andrei OC, Mărgărit R, Tănăsescu LA, et al. A rare case of mandibulary parapremolars in siblings: case report and literature review. Rom J Morphol Embryol. 2017;58(4):1485–1490.
- Cortés-Bretón-Brinkmann J, Martínez-Rodríguez N, Barona-Dorado C, et al. Clinical repercussions and epidemiological considerations of supernumerary canines: a 26 case series. *Med Oral Patol Oral Cir Bucal*. 2019;24(5):e615–e620. https://doi.org/10.4317/medoral.23035.
- Khalaf K, Al Shehadat S, Murray CA. A review of supernumerary teeth in the premolar region. *Int J Dent.* 2018;2018, 6289047. https://doi.org/10.1155/2018/ 6289047.
- O'Dowling I. Supernumerary pre-molar teeth in the mandible. J Ir Dent Assoc. 2009;55(6):293–295.
- 74. Gardiner JH. Supernumerary teeth. Dent Pract Dent Rec. 1961;12:63-73.
- Duman S, Vural H, Duman SB. Supernumerary teeth and dental development. *J Craniofac Surg.* 2021;32(5):1826–1829. https://doi.org/10.1097/ scs.000000000007516.
- Lam EWN. Chapter 31 dental anomalies. In: White SC, Pharoah MJ, eds. Oral Radiology. seventh ed. St. Louis (MO): Mosby; 2014:582–611.
- Schwartz JH. Supernumerary teeth in anthropoid primates and models of tooth development. Arch Oral Biol. 1984;29(10):833–842. https://doi.org/10.1016/ 0003-9969(84)90014-1
- Cassetta M, Altieri F, Giansanti M, Di-Giorgio R, Calasso S. Morphological and topographical characteristics of posterior supernumerary molar teeth: an epidemiological study on 25,186 subjects. *Med Oral Patol Oral Cir Bucal*. 2014;19 (6):e545–e549. https://doi.org/10.4317/medoral.19775.
- Garvey MT, Barry HJ, Blake M. Supernumerary teeth–an overview of classification, diagnosis and management. J Can Dent Assoc. 1999;65(11):612–616.
- Zhang H, Gong X, Xu X, Wang X, Sun Y. Tooth number abnormality: from bench to bedside. Int J Oral Sci. 2023;15(1):5. https://doi.org/10.1038/s41368-022-00208-x.
- 81. Pippi R. Odontomas and supernumerary teeth: is there a common origin? *Int J Med Sci.* 2014;11(12):1282–1297. https://doi.org/10.7150/ijms.10501.
- Nagpal DB, S A, Ghosh A, Nagpal A, Nagpal A. Mechanism of patterning of dentition: a review. Heal Talk - A J Clin Dent. 2016;9:38–40.
- Dahlberg AA. The changing dentition of man. J Am Dent Assoc. 1945;32(11): 676–690. https://doi.org/10.14219/jada.archive.1945.0112.
- Butler PM. Comparison of the development of the second deciduous molar and first permanent molar in man. Arch Oral Biol. 1967;12(11):1245–1260. https://doi.org/ 10.1016/0003-9969(67)90126-4.
- Greenfield LO. A tooth at the border of two morphogenetic fields. Hum Evol. 1993; 8(3):187. https://doi.org/10.1007/BF02436714.
- Eigbobo JO, Osagbemiro BB. Bilateral tuberculate supernumerary teeth. Clin Pract. 2011;1(2):e30–e. https://doi.org/10.4081/cp.2011.e30.
- Dave B, Patel J, Swadas M, Mallikarjuna R. Multilobed mesiodens: a supernumerary tooth with unusual morphology. *BMJ Case Rep.* 2013;2013. https://doi.org/10.1136/bcr-2012-008088.
- Mangalekar SB, Ahmed T, Zakirulla M, Shivappa HS, Bheemappa FB, Yavagal C. Molariform mesiodens in primary dentition. *Case Rep Dent.* 2013;2013, 750107. https://doi.org/10.1155/2013/750107.
- Kavitha LNG, Rajavalli SK, Ahmed VKS, Baskara VA. A rare case of bilaterally transposed maxillary supernumerary premolars and its management. J Oper Dent Endod. 2018;2:92–96. https://doi.org/10.5005/jp-journals-10047-0063.

- Demiriz L, Durmuşlar MC, Mısır AF. Prevalence and characteristics of supernumerary teeth: a survey on 7348 people. *J Int Soc Prev Community Dent*. 2015;5(Suppl 1):S39–S43. https://doi.org/10.4103/2231-0762.156151.
- Bartolo A, Calleja N, McDonald F, Camilleri S. Dental anomalies in first-degree relatives of transposed canine probands. *Int J Oral Sci.* 2015;7(3):169–173. https://doi.org/10.1038/ijos.2014.72.
- Ely NJ, Sherriff M, Cobourne MT. Dental transposition as a disorder of genetic origin. Eur J Orthod. 2006;28(2):145–151. https://doi.org/10.1093/ejo/cji092.
- Peck S, Peck L. Classification of maxillary tooth transpositions. Am J Orthod Dentofacial Orthop. 1995;107(5):505–517. https://doi.org/10.1016/s0889-5406 (95)70118-4
- Peck L, Peck S, Attia Y. Maxillary canine-first premolar transposition, associated dental anomalies and genetic basis. *Angle Orthod.* 1993;63(2):99–109. https://doi. org/10.1043/0003-3219(1993)063<0099:Mcfpta>2.0.Co;2.; discussion 10.
- Peterková R, Lesot H, Vonesch JL, Peterka M, Ruch JV. Mouse molar morphogenesis revisited by three dimensional reconstruction. I. Analysis of initial stages of the first upper molar development revealed two transient buds. *Int J Dev Biol*. 1996;40(5):1009–1016.
- Jheon AH, Seidel K, Biehs B, Klein OD. From molecules to mastication: the development and evolution of teeth. Wiley Interdiscip Rev Dev Biol. 2013;2(2): 165–182. https://doi.org/10.1002/wdev.63.
- Line SR. Variation of tooth number in mammalian dentition: connecting genetics, development, and evolution. Evol Dev. 2003;5(3):295–304. https://doi.org/ 10.1046/i.1525-142x.2003.03036.x.
- Peterková R, Peterka M, Viriot L, Lesot H. Development of the vestigial tooth primordia as part of mouse odontogenesis. *Connect Tissue Res.* 2002;43(2-3): 120–128. https://doi.org/10.1080/03008200290000745.
- Viriot L, Lesot H, Vonesch JL, Ruch JV, Peterka M, Peterková R. The presence of rudimentary odontogenic structures in the mouse embryonic mandible requires reinterpretation of developmental control of first lower molar histomorphogenesis. *Int J Dev Biol.* 2000;44(2):233–240.
- Nakamura T, de Vega S, Fukumoto S, Jimenez L, Unda F, Yamada Y. Transcription factor epiprofin is essential for tooth morphogenesis by regulating epithelial cell fate and tooth number. *J Biol Chem.* 2008;283(8):4825–4833. https://doi.org/ 10.1074/jbc.M708388200.
- Järvinen E, Tummers M, Thesleff I. The role of the dental lamina in mammalian tooth replacement. J Exp Zool B Mol Dev Evol. 2009;312b(4):281–291. https://doi. org/10.1002/jez.b.21275.
- Chen Y, Wang Z, Lin C, Chen Y, Hu X, Zhang Y. Activated epithelial FGF8 signaling induces fused supernumerary incisors. J Dent Res. 2022;101(4):458–464. https://doi.org/10.1177/00220345211046590.
- Ahn Y, Sanderson BW, Klein OD, Krumlauf R. Inhibition of Wnt signaling by Wise (Sostdc1) and negative feedback from Shh controls tooth number and patterning. *Development*. 2010;137(19):3221–3231. https://doi.org/10.1242/dev.054668.
- 104. Sofaer JA. Aspects of the tabby-crinkled-downless syndrome. I. The development of tabby teeth. J Embryol Exp Morphol. 1969;22(2):181–205.
- Ohazama A, Modino SA, Miletich I, Sharpe PT. Stem-cell-based tissue engineering of murine teeth. J Dent Res. 2004;83(7):518–522. https://doi.org/10.1177/ 154405010408307702
- Nakao K, Morita R, Saji Y, et al. The development of a bioengineered organ germ method. Nat Methods. 2007;4(3):227–230. https://doi.org/10.1038/nmeth1012.
- Takahashi K, Kiso H, Murashima-Suginami A, et al. Development of tooth regenerative medicine strategies by controlling the number of teeth using targeted molecular therapy. *Inflamm Regen.* 2020;40(1):21. https://doi.org/10.1186/ s41232-020-00130-x
- Langowska-Adamczyk H, Karmańska B. Similar locations of impacted and supernumerary teeth in monozygotic twins: a report of 2 cases. Am J Orthod Dentofacial Orthop. 2001;119(1):67–70. https://doi.org/10.1067/ mod.2001.111225.
- Orhan AI, Ozer L, Orhan K. Familial occurrence of nonsyndromal multiple supernumerary teeth. A rare condition. *Angle Orthod.* 2006;76(5):891–897. https://doi.org/10.1043/0003-3219(2006)076[0891:Foonms]2.0.Co;2.
- Wang X-P, Fan J. Molecular genetics of supernumerary tooth formation. *Genesis*. 2011;49(4):261–277. https://doi.org/10.1002/dvg.20715.
- Balic A, Thesleff I. Tissue interactions regulating tooth development and renewal. *Curr Top Dev Biol.* 2015;115:157–186. https://doi.org/10.1016/bs. ctdb.2015.07.006.

- Liu F, Chu EY, Watt B, et al. Wnt/beta-catenin signaling directs multiple stages of tooth morphogenesis. *Dev Biol.* 2008;313(1):210–224. https://doi.org/10.1016/j. vdbio.2007.10.016.
- Cobourne MT, Sharpe PT. Making up the numbers: the molecular control of mammalian dental formula. Semin Cell Dev Biol. 2010;21(3):314–324. https://doi. org/10.1016/j.semcdb.2010.01.007.
- 114. Järvinen E, Salazar-Ciudad I, Birchmeier W, Taketo MM, Jernvall J, Thesleff I. Continuous tooth generation in mouse is induced by activated epithelial Wnt/β-catenin signaling. Proc Natl Acad Sci USA. 2006;103(49):18627–18632, 10.1073/pnas.0607289103.
- Jia S, Zhou J, Gao Y, et al. Roles of Bmp4 during tooth morphogenesis and sequential tooth formation. *Development*. 2013;140(2):423–432. https://doi.org/ 10.1242/dev.081927.
- 116. The APC of toothiness. Development. 2009;136(11):e1106-e.
- Kuraguchi M, Wang XP, Bronson RT, et al. Adenomatous polyposis coli (APC) is required for normal development of skin and thymus. *PLoS Genet*. 2006;2(9):e146. https://doi.org/10.1371/journal.pgen.0020146.
- Wang XP, O'Connell DJ, Lund JJ, et al. Apc inhibition of Wnt signaling regulates supernumerary tooth formation during embryogenesis and throughout adulthood. *Development.* 2009;136(11):1939–1949. https://doi.org/10.1242/dev.033803.
- Basaran G, Erkan M. One of the rarest syndromes in dentistry: gardner syndrome. Eur J Dent. 2008;2(3):208–212. https://doi.org/10.1055/s-0039-1697380.
- Roberts T, Stephen L, Beighton P. Cleidocranial dysplasia: a review of the dental, historical, and practical implications with an overview of the South African experience. Oral Surg Oral Med Oral Pathol Oral Radiol. 2013;115(1):46–55. https://doi.org/10.1016/j.oooo.2012.07.435.
- Åberg T, Cavender A, Gaikwad JS, et al. Phenotypic changes in dentition of Runx2 homozygote-null mutant mice. *J Histochem Cytochem*. 2004;52(1):131–139. https://doi.org/10.1177/002215540405200113.
- Callea M, Fattori F, Yavuz I, Bertini E. A new phenotypic variant in cleidocranial dysplasia (CCD) associated with mutation c.391C>T of the RUNX2 gene. BMJ Case Rep. 2012;2012. https://doi.org/10.1136/bcr-12-2011-5422.
- 123. Saito K, Takahashi K, Huang B, et al. Loss of stemness, EMT, and supernumerary tooth formation in Cebpb(-/-)Runx2(+/-) murine incisors. Sci Rep. 2018;8(1):5169. https://doi.org/10.1038/s41598-018-23515-y.
- Huang B, Takahashi K, Sakata-Goto T, et al. Phenotypes of CCAAT/enhancer-binding protein beta deficiency: hyperdontia and elongated coronoid process. *Oral Dis*. 2013;19(2):144–150. https://doi.org/10.1111/j.1601-0825.2012.01963.x.
- Togo Y, Takahashi K, Saito K, et al. Antagonistic functions of USAG-1 and RUNX2 during tooth development. PLoS One. 2016;11(8), e0161067. https://doi.org/ 10.1371/journal.pone.0161067.
- Yanagita M, Okuda T, Endo S, et al. Uterine sensitization-associated gene-1 (USAG-1), a novel BMP antagonist expressed in the kidney, accelerates tubular injury.
 J Clin Investig. 2006;116(1):70–79. https://doi.org/10.1172/jci25445.
- 127. Mishima S, Takahashi K, Kiso H, et al. Local application of Usag-1 siRNA can promote tooth regeneration in Rumx2-deficient mice. *Sci Rep.* 2021;11(1), 13674. https://doi.org/10.1038/s41598-021-93256-v.
- Kiso H, Takahashi K, Mishima S, et al. Third dentition is the main cause of premolar supernumerary tooth formation. *J Dent Res.* 2019;98(9):968–974. https://doi.org/10.1177/0022034519858282.
- Hua W, Gan Z, Wu Y, Zhao L. Identification of a novel missense mutation in nonsyndromic familial multiple supernumerary teeth. *Arch Oral Biol.* 2022;143, 105542, https://doi.org/10.1016/j.grcboralbio.2022.105542
- 105542. https://doi.org/10.1016/j.archoralbio.2022.105542.
 Suzuki A, Nakano M, Yoshizaki K, Yasunaga A, Haruyama N, Takahashi I. A longitudinal study of the presence of dental anomalies in the primary and permanent dentitions of cleft lip and/or palate patients. *Cleft Palate Craniofac J*. 2017;54(3):309–320. https://doi.org/10.1597/15-186.
- 131. Consolaro A, Medeiros MCM, Miranda DAO, Oliveira IA. Supernumerary teeth in patients with cleft lip and palate: the tooth germs do not separate. *Dental Press J Orthod.* 2021;26(4):e21ins4. https://doi.org/10.1590/2177-6709.26.4.e21ins4.
- 132. Haque S, Alam MK. Common dental anomalies in cleft lip and palate patients. *Malays J Med Sci.* 2015;22(2):55–60.
- Ezzeldin M, Gee S, Curtis J, Clark VJ, Smallridge J, Collard M. Dental anomalies in cleft lip and/or palate children at age 10 - a retrospective review across three cleft centres: Part 1. Br Dent J. 2023;234(12):926–930. https://doi.org/10.1038/ s41415-023-5976-5.
- 134. Jain P, Kaul R, Saha S. Rare molariform supernumerary teeth: why are they bilateral? *Indian J Dent Res.* 2017;28(6):702–705. https://doi.org/10.4103/ijdr. IJDR 242_17.