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Commentary: Supernumerary teeth

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The case report by Gyongyi Szabó and colleagues (*Dental Anthropology* 2009;22(1):18-21) raises several interesting issues. A challenging aspect of examining teeth—which are the end-products of foregone cascades of developmental events—is that interpretations of the formative processes that produced the final form are conjectural, and there is no way to test assumptions. Experience and encountering repeated occurrences of a dental condition are helpful, but they are hardly infallible.

Terminology

A fundamental consideration raised by this case report is terminology. Specifically, what constitutes a supernumerary tooth? Or, for that matter, what is a tooth? I looked through a number of recent papers on hypo- and hyperdontia, and there is a striking absence of an operational definition of what a "tooth" is. Recognition of a tooth evidently is considered so obvious (or so difficult) that it doesn't warrant a definition. It seems that mineralized tissues (dentin, enamel) are an important criterion, but this is simply because most studies nowadays are radiographic surveys, so premineralized tissues are undetectable. However, dental histologists are quite comfortable that the premineralized structures seen in the bud, cap, and bell stages constitute a "tooth," so mineralization cannot be an essential feature.

Popular textbooks on dental anatomy (*e.g.*, Zeisz and Nuckolls, 1949; Kraus *et al*., 1969; Ash, 1993) launch right into descriptions of the morphology of each tooth type, apparently supposing that a definition would be superfluous. The normally-occurring teeth (20 primary, 32 permanent) are all characterized by a crown (enamel, dentin, pulp) and one or more roots (cementum, dentin, pulp), but it is not clear whether a dental element must have all of these features to achieve "toothness." Also, sizes of the crown and root do not seem to be important criteria. One might claim that teeth obviously are found in the two dental arches, but locality is not definitive given the extraordinary

Fig. 4. A supernumerary tooth in the enlarged incisive foramen of a prehistoric American Indian. Ectopic teeth tend to be in the vicinity of the dental arches, but they may form or migrate elsewhere.

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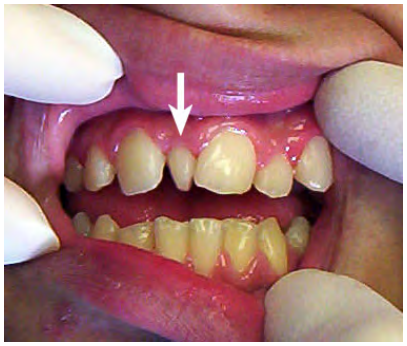

Fig. 5. A mesiodens—a supernumerary tooth located between the maxillary central incisors—is common. Note how this erupted mesiodens displaces the incisors. There is chipping of the occlusal border of the mandibular right central incisor because of the edge-to-edge malocclusion. Supernumerary incisors typically are single-cusped and conical with a single root.

places a "tooth" can occur. Fig. 4‡ is an example where a supernumerary incisor (probably a mesiodens) is hidden in the subject's incisive foramen. The literature describes ectopic teeth located in various midface regions, such as the nasolacrimal duct (Alexandrakis *et al*., 2000), the bony orbit (Savundranayagam, 1972), and the eyelid (Subramaniam *et al*., 1966). Many of us were taught in an embryology class or elsewhere about dermoid cysts (*e.g*., Shafer *et al*., 1983), which contain well-differentiated skin and other identifiable tissues (*e.g*., hair, sweat glands, bone, cartilage, *etc*.), including teeth. These "teeth" commonly are of identifiable types, often incisors and premolars, which shows that the same complex of biochemical signals that produce a tooth in a dental arcade can perform just as well elsewhere in the body (*e.g*., Jernvall and Thesleff, 2000). This is not surprising given the landmark embryological studies

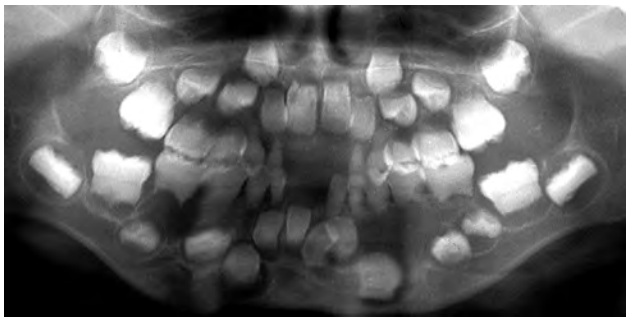

Fig. 6. A cropped view of a panoramic radiograph of a subject with dentin dysplasia I, where root formation is severely restricted, so several of the teeth appear to be 'root-less' though they generally erupt normally. Note the apical radiolucencies around several of the teeth, which is characteristic of this condition. Also, the pulp chambers are obliterated and filled with dysplastic dentin.

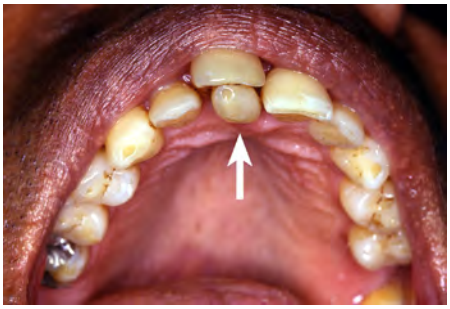

Fig. 7. An exceptionally large tuberculum dentale is located on the subject's right maxillary central incisor (arrow). Large examples such as this with a free cusp often are labeled *talon cusps* because the appearance of an incisor with a labial and lingual cusp is reminiscent of a raptor's claw (*e.g*., Harris and Owsley, 1991). Based on size, this tubercle (with a free apex, a pulp horn, and an independent root) would qualify as a "tooth," but it is not counted as such because (A) it developed from the cingulum of the parent tooth and (B) it is a fused feature of the incisor, sharing dentin and pulp.

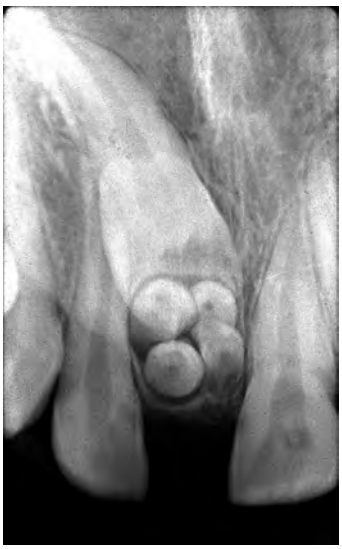

Fig 8. Radiograph of a compound odontoma in the maxillary midline. There are four 'toothlets' visible here, but it is unclear whether they should be labeled as four supernumerary teeth because of their petite size and absence of any crown-root morphology. Even on X-ray, it is evident that these dental elements consist of enamel, dentine, and a pulp chamber. Note how this tumor is preventing the subject's right maxillary central incisor from erupting and how it maintains a several-millimeter gap between the left central and right lateral incisor. Radiograph courtesy of James E. Turner.

‡Figures 1-3 are those in published in the prior article by Szabó *et al*. (2009).

of growing implanted tooth buds in the globes of eyes of laboratory animals (*e.g.*, Yoshikawa and Kollar, 1981). Dermoid cysts occasionally occur in ovaries (*e.g.*, McGinnis and Parham, 1978; Dick and Honoré, 1985; Liberis *et al*. 2008), which means they should be recoverable archeologically, though I'm unaware of any reference to them.

A tooth does not have to be normal size or shape to be counted. Diminutive elements, such as pegged and microdont teeth, are routinely counted. Many authors include mineralized elements of any morphology, including "dental masses" of amorphic mineralized objects as found in odontogenic tumors, notably compound odontomas (*e.g.*, Shafer *et al*., 1983; Owens *et al*., 1997). A supernumerary tooth in the maxillary incisor region is probably the most common sort of supernumerary tooth, and these are characteristically petite single-cusped, often conical teeth with a single root (Fig. 5).

Once mineralized, a "tooth" normally has a crown and root, but there are exceptions: A primary tooth in which the root has been completely lysed as part of the exfoliation process is still considered a tooth. So-called root-less teeth (as in dentin dysplasia I; OMIM #125400) also are considered teeth, though roots can be quite abbreviated if present (Fig. 6). Size alone does not define a tooth. The lingual tubercle (talon cusp) in Figure 7 is virtually as large as the incisor crown proper, but it would not be counted as a tooth because (1) it is developmentally a component of that incisor and (2) it has always been united with the incisor. At the other extreme, Figure 8 shows a compound odontoma (de Oliveira *et al*., 2001), where four distinct tooth-like 'denticles' are evident (with the normal but impacted central incisor apical to them). Do these 'toothlets' qualify as teeth? They have fully-differentiated enamel and dentin, but no crown-and-root morphology.

Does a "tooth" need to be physically separate from others to be counted? This seems to be an important distinction implied in most studies (Patterson, 1956; Hershkovitz, 1967). For example, cusp-like cingular elements are not counted as teeth. Tubercles, accessory cusps, and styles are considered parts of the main tooth. Cingular elements can be fairly large, but they are almost invariably coalesced with the permanent tooth so there should be no misidentification. These include talon cusps on the incisors, tuberculum dentale on canines, Carabelli's cusps on the lingual of upper molars, and paramolar tubercles on the buccal aspect of upper and lower molars (Scott and Turner, 1997). All of these cingular elements normally are single-cusped, and they all have at most a single root (*e.g.*, Bolk, 1916). Ambiguity arises when, apparently in rare instances, a dental feature becomes physically separated from the main tooth (Dubuk *et al*., 1996). Paramolar tubercles do occasionally achieve physical independence when large, and these meet criteria for a "tooth," namely possession a crown (enamel), root (dentin), and a tooth-like morphology (though simplified).

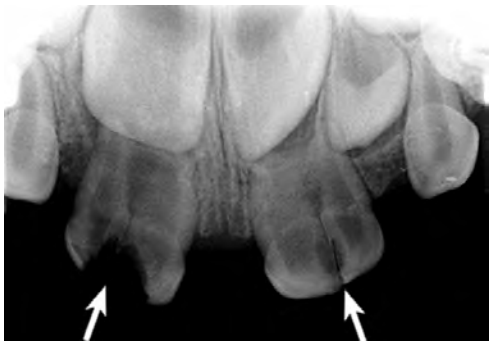

Fig. 9. A rare instance of bilateral fusion of the primary maxillary incisors (arrows). (Most cases are unilateral.) Fusion is confirmed by (A) the appearance of confluent tooth forms in each quadrant and (B) the 'absence' of independent lateral incisor teeth. Both compound teeth are carious, but their shared enamel, pulp chambers, and root dentin are evident. Radiograph courtesy of Ann S. Smith.

Overlooking the details of what constitutes a tooth, there are countless anthropological and clinical dental studies of abnormal tooth numbers—either the congenital absence of one or more teeth (hypodontia) or hyperdontia, an excess number of teeth (Table 1). Studies rarely press the definition of a tooth too closely; instead, wording is used such as: hypodontia is a deficit in the normal dental formula or hyperdontia is teeth in excess of the normal dental complement.

TABLE 1. Operational definitions[1]

Condition	Definition
Hypodontia	Congenital absence of one to five permanent teeth, generally excluding third molars.
Oligodontia	Absence of more than five teeth. The study may or may not exclude third molars.
Anodontia	The complete absence of all primary and/or permanent teeth. The phrase "partial anodontia" (actually denoting hypodontia or oligodontia) is an oxymoron.
Hyperdontia	Presence of one or more teeth in excess of the species' normal dental formula.

[1]Partly from Schalk van der Weide (1992), reproduced in Koch and Thesleff (2001, p 261).

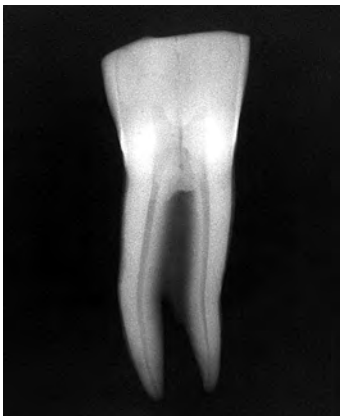

Fig. 10. Radiograph showing fusion between a lower right central and lateral incisor (labial view). The lateral incisor is to the left of the figure. Note the confluence of enamel and dentin between the crowns, though the pulp chambers and roots are separate.

Ontogeny

The structure imaged in Szabó's figures clearly emanates from the premolar's buccal cingulum, and it shows developmental features in common with the tooth proper. As Szabó *et al*. point out, there is a common pulp chamber, and the dentin is confluent between the tooth crown proper and the tubercle even though the tubercle has a well-developed root and pulp chamber (Ohishi *et al*., 1999). It is most probable that this cingular feature was initiated by an enamel knot that, in the presumptive tooth, was located at the cusp apex, which has now (Fig. 2) been abraded or is hidden by subsequent enamel deposition. A primary enamel knot is essential for a tooth's formation, and later-forming secondary knots define each of a tooth's cusps (*e.g*., Jernvall *et al*., 1994; Thesleff and Jernvall, 1997;

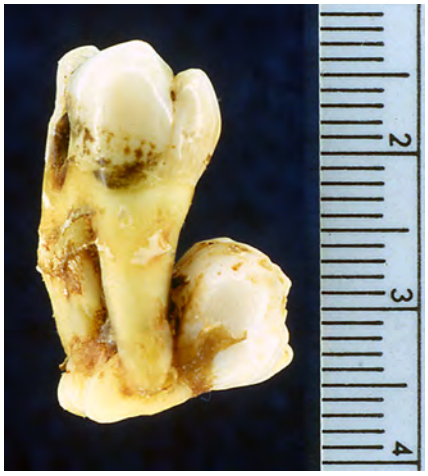

Fig. 11. Example of acquired concrescence between a second and third molar. Roots of the two teeth are only united by cementum; there is no confluence of the underlying dentin.

Fig. 12. A paramolar tubercle on a maxillary left second molar. This tubercle (arrow) clearly is associated with the metacone rather than the molar's paracone. Bolk (1916) was very keen that paramolar tubercles were only derived from the paracone, though Kustaloglu (1962) showed that this is untrue.

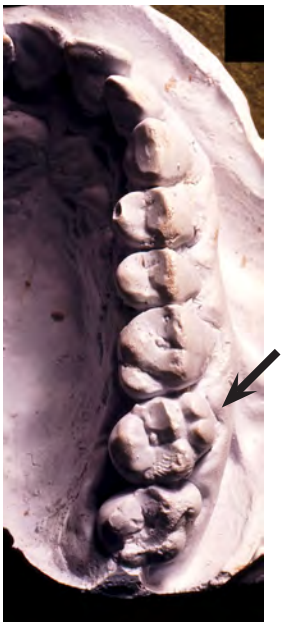

Fig. 13. A rare instance of two paramolar tubercles on a maxillary left second molar (arrow). (No cingular feature could be seen on the contralateral molar.) It appears that both tubercles are attached to the paracone (mesiobuccal cusp), though part of the distal tubercle crosses onto the metacone. Note too a large, single paramolar tubercle on the paracone of the third molar. (Paramolar tubercles rarely occur on permanent first molars.)

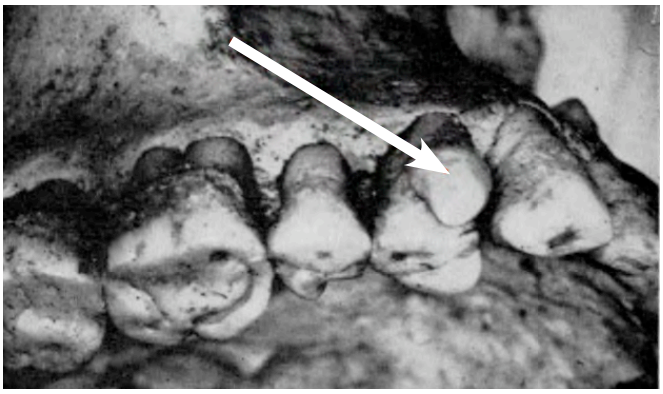

Fig. 14. A large parastyle on the maxillary right first premolar (line). A parastyle is a tubercle derived from the buccal cingulum of, in this case, the premolar's paracone. (From Kustaloglu, 1962.)

Thesleff *et al*., 2001; Obara and Lesot 2007). I think it is notable that this cingular feature has a free apex that is occlusal to the developmental groove that distinguishes this tubercle from the tooth proper; this shows that the tubercle was developed as part of the differentiating morphology of the inner enamel epithelium because mineralization of dentin and enamel only proceeds in the occlusal-to-apical direction.

These morphological components that are developmental parts of a tooth are not considered as separate teeth in tooth counts. Ambiguous cases occur when a feature that is supposed to arise from an adjacent tooth's cingulum is a physically separate dental element. Bolk (1916) describes such cases in his classic paper on paramolar tubercles. Either of two events may cause this, though the end products seem identical. One, the secondary enamel knot may have formed far enough away from the rest of the crown that the tubercle fissions off from the main tooth. This process of gemination (the word is derived from Gemini, the star constellation of twins in Greek mythology) is commonly described in dental texts on dental anomalies (*e.g*., Pindborg, 1970; Shafer *et al*., 1983), though actual examples of twinning are rare (*e.g*., Gündüz and Açikgõz, 2006; Sivolella *et al*., 2008). Twinning needs to occur during the cap or bell stage prior to crown mineralization, but the actual process is not understood. A critical feature defining geminated teeth is the presence of all of the other teeth in the morphogenetic field, so the twinned teeth clearly are not fused teeth (Fig. 9). Twinning requires duplication of the biochemical signals for tooth development within the dental sac. How this occurs seems to be a complete mystery at present. A traditional view is that two tooth-forming sites are stimulated to form close together in the dental lamina, which develops well before differentiation of the dental sac. It is supposed (Pispa and Thesleff, 2003) that, in normal dental development, a reaction-diffusion gradient develops around a formative teeth, where activators induce placode formation while negative regulators are intensified in interplacodal regions, which inhibit tooth formation and, thus, account for the orderly spacing of teeth. Gemination might, then, be viewed as an exception where two sets of signals are preserved (or initiated) within the same dental sac that, then, gives rise to 'twinned' but fused teeth. Geminated teeth (more common in the primary dentition) usually have a shared root and shared pulp cavity.

The second process involves fusion, where two tooth buds begin to form independently, but, again, for reasons unknown, the formative teeth grow together. Fusion typically starts at the cap or bell stage, so that the united teeth are combined along the lengths of their crowns and roots (Fig. 10). Fusion must involve the dentin, so the twinning is initiated during formation of the outer enamel epithelium (Avery, 1994). The key feature for identification is that, counting the fused pair of elements as one, there needs to be a 'missing' tooth elsewhere in that morphogenetic field. This method of defining fusion is not thorough-going, because it supposes that development was disruptive enough to meld two tooth buds, but the same disruption did not cause agenesis of the "missing" tooth. Reliance on the fused tooth morphology can be a help here, but convincing discrimination between fission and fusion may be impossible from inspection of the end product alone.

A rare but classic case of tooth fusion is in people (and laboratory animals) with developmental midline problems, notably holoprosencephaly (HPE). HPE is the embryological failure of divisions of the head to form along the left-right, transverse, and/or craniocaudal axes (Cohen, 2001). A remarkable dental consequence of this heterogenous group of anomalies can be a solitary median maxillary central incisor (SMMCI). Nanni *et al*. (2001) provide a current review of this condition. Experimental work shows that sonic hedgehog (shh), a signaling protein, is critical for the initiation of a tooth germ, probably by directing epithelial cell proliferation. In mice, the absence of shh can either prevent maxillary incisor formation (congenital absence) or cause these incisors to fuse. The maxillary central incisors begin formation close together and these tooth germs coalesce into a single symmetric central incisor (Hardcastle *et a*l., 1998). Of note, the molar teeth are unaffected. Alterations in the structure-function of shh provide the common etiology between the head (central nervous system) and tooth anomalies (Cohen, 2004).

Aside from fusion and fission (gemination), yet a third situation occasionally occurs, namely concresence. Pindborg (1970) valuably distinguishes between true concrescence and acquired concrescence. Acquired concrescence occurs when two fully formed teeth are only united by the fluorescence of cementum (Fig. 11). Colby *et al*. (1961:42) note that two factors are required here, (1) the teeth, specifically the roots, of adjacent teeth

need to be in close proximity and (2) hypercementosis—excessive cementum deposition—unites the proximate roots. Acquired concrescence is only distantly related to the fission and fusion of teeth because it occurs after tooth formation in contrast to being the consequence of some developmental aberration. In contrast, true concrescence involves confluence of the roots (dentin) of adjacent teeth, so it is a sort of fusion.

Paramolar tubercles

Numerous researchers have described "paramolar tubercles," a term coined by Bolk (1916:110). Bolk surveyed some 30,000 skulls, so he is still a contender for the record number of identified tubercles. Bolk argued that these tubercles on maxillary molars always develop from the mesial cusp. In fact, they can arise from the cingulum of either buccal cusp, and Kustaloglu (1962) notes that they therefore should be labeled parastyles (mesiobuccal) or metastyles (distobuccal) depending on the cusp of origin. Figure 12 shows a characteristic expression, where the tubercle developed buccal to the metacone, well distal of the lingual developmental groove that demarcates the union of the paracone and metacone. Figure 13 shows a second molar with two equal-size paramolar tubercles, and it appears that both developed from the tooth's paracone.

Such buccal tubercles are less common in the mandible, where, occasionally, they develop from the mesiobuccal cusp, thus making them protostylids (*e.g.*, Dahlberg, 1950). Protostylids occur frequently enough that there is an ASU dental plaque to score their size (Turner *et al.*, 1991; also see Hlusko, 2007; Skinner *et al.*, 2008). Paramolar features also can occur on the premolars. Figure 14 is reproduced from Kustaloglu's article, showing a large tubercle on the facial aspect of the paracone (buccal cusp) of a maxillary premolar; this example is not dissimilar from the example described by Szabó and coworkers (Fig. 1).

Hyperdontia

Various ideas have been put forth over the years to explain why a supernumerary tooth might occur. Some of these are noted in the reviews by Rajab and Hamdan (2002), Botra *et al.* (2005), and elsewhere. These conjectures are of historical interest, but they comport poorly with current knowledge of the molecular control of tooth formation (*e.g.*, Mitsiadis and Smith, 2006). A popular idea was atavisim, which is the idea that some phylogenetic ancestral condition (where more teeth were the norm) is being re-expressed. Recall, for instance, that the baseline mammalian condition was at least 44 teeth (Gregory, 1922; Ji *et al.*, 2002), and the human dental formula involves reductions of all tooth types except the canines (see review by Peterkova *et al.*, 2006). Another conjecture was that one or more of the normally-occurring teeth splits (the dichotomy theory) to produce additional teeth (Foley and Del Rió, 1970; Taylor, 1972). Another idea with some persistent credibility involves an extension of dental lamina at the end of the tooth row that is induced to form an additional tooth (Saarenmaa, 1951), but this idea must include the reciprocal epithelial-mesenchymal inductions that promote tooth formation, "extra" dental lamina in itself does not cause teeth to form. Such historical conjectures suppose that extra teeth are due to additional developmental activity, with the term "hyperactivity" often used in some vague sense to explain the over-production of teeth.

Recent evidence suggests that the opposite is true—that biochemical signaling is responsible for *stopping* the enumeration of teeth and is necessary for holding a species' dental formula in check. A prime example is now known in some detail for humans: Runx2 is a transcription factor that is key for osteogenic cell differentiation (Ziros *et al.*, 2008). Mutations of Runx2, which also is known as Cbfa1, can cause cleidocranial dysostosis (CCD; OMIM #119600), the condition that is, perhaps, archetypical of hyperdontia in man (Jensen and Kreiborg, 1990; Whittington and Durward, 1996). People with CCD are likely to exhibit hyperdontia, especially in the premolar region (along with systemic problems of non-eruption due to a failure of bone resorption ahead of the erupting tooth). CCD shows the important role that Runx2 normally plays in *preventing* excess budding of the dental lamina. However, hyperdontia in people with this autosomal dominant allele show variable expressivity, ranging from no extra teeth to cases with numerous extra teeth. The percentage of cases of CCD with hyperondia is around 1/5, showing that even in this archetypical condition, the formation of extra teeth is uncertain—presumably due to differences in allelic conditions and differences in genetic backgrounds.

Comparably, Kantaputra and coworkers (2008) describe a single subject with unerupted teeth in the premolar-molar region evidently due to an inherited defect in Trps1 causing gain of function. These authors suggest that this mutation mimics the dental phenotype of persons with Runx2.

Murashima-Suginami *et al.* (2007, 2008) show that up-regulated bone morphogenetic protein (BMP) signaling causes supernumerary tooth formation in mice, notably in the incisor region (also see Kassai *et al.* 2005). They interpret their experimental results as showing that odontogenic mesenchymal cells normally are killed off at the end of tooth rows because antagonists to BMP play a crucial role in controlling the enumeration of tooth buds. When an antagonist (termed ectodin or, synonymously, "uterine sensitization associated gene-1" or USAG-1) is absent, BMP function is left uncontrolled, and the result is supernumerary tooth formation. That is, ectodin normally binds to BMP

and inhibits its function; without inhibition, BMP can promote additional tooth sites.

These studies show that extra teeth result from inadequate suppression of tooth-forming capacity, not the over-activity of tooth-promoting events.

At this point in our understanding of tooth-promoting conditions, it is unknown (A) how many genes (alleles, proteins) are responsible along the involved pathway of tooth development either to form an extra tooth or curtail formation of a normal tooth, (B) whether extra teeth at the end of the dental lamina (*e.g.*, mesiodens, fourth molars) are due to the same causes as those within the tooth rows (such as the common extra premolars). Other issues of interest involve (A) how and why human population differences in hypo- and hyperdontia have developed, (B) what causes the persistent sex differences (hypodontia is more common in females; hyperdontia is more common in males) seen among humans, and (C) why the locations of missing and extra teeth differ among human groups. It also is effectively unknown how the environment affects any or all of these differences. It seems unlikely that there are simple or single, all-inclusive reasons for any of these issues. It is noteworthy that most supernumerary teeth are few in number within and among subjects, undersize and morphologically simplified. Overall, it seems to be a major genotypic effort to increase tooth number, perhaps because of the large number of necessary steps needed to form a tooth.

Studies of supernumerary teeth in laboratory animals have certainly been informative (D'Souza and Klein, 2007). Several studies show that perturbations of signalling molecules—either genetic knockouts or the overproduction of certain molecules—can cause the formation of extra teeth. For example, mice that over-express ectodysplasin (Pispa *et al.*, 2004) or under-express antagonists to FGF (fibroblast growth factor; Klein *et al.*, 2006) can produce supernumerary teeth. But, it is important to question the relevance of these findings to humans. Mice—the favored animal for studying tooth development—have a diastema in each quadrant where formation of lateral incisors, canines, and premolars is suppressed. However, several of these teeth initiate formation but are arrested and resorbed in the bud stage (Peterkova *et al.* 2002, 2006) so the "rescue" of these tooth buds to permit them to develop into "supernumerary diastema teeth" is of considerable interest, but it is fundamentally different from the human condition where no primordia normally form.

Laterality

Another question raised by Szabó's case report is why their tubercle occurs unilaterally. Conventional wisdom is that the genotypic information is the same in the left and right hemispheres of the body (Polak 2003), so disparate phenotypes between quadrants are supposed to be the exception rather than the rule. Researchers familiar with dental morphology recognize that, while left-right symmetry may be the norm, even striking exceptions are not hard to find. Alvesalo and coworkers (1975) suggested that, for Carabelli's trait, expression on one tooth is always associated with some expression on the contralateral tooth, but this has not been my own experience. Kustaloglu (1962) examined the osteological collections at the Chicago National History Museum (roughly 500 individuals) and found that paramolar tubercles tend to occur unilaterally more often than bilaterally, with a ratio of 18:4 among the permanent molars, though bilateral occurrences predominated in the primary dentition.

Dental anthropologists have embraced the idea that morphologic dental traits have a quasicontinuous mode of inheritance. Supporting evidence stems primarily from animal studies (*e.g.*, Grüneberg, 1950, 1952) because few anthropological studies have subjects of known biological relationship (*cf.* Saunders and Mayhall, 1982; Sjøvold, 1996). The quasicontinuous (QC) model of inheritance suggests that morphological dental traits are under polygenic control, but with a threshold below which the feature is not expressed (Wright, 1934a,b; Falconer, 1965). The question arises whether unilateral expression (Fig. 1) is indicative of the subject's genotype being close to the threshold. That is, subjects with a genotype for trait expression might be prone to expressing the trait unilaterally due to local environmental vagaries between the jaw's quadrants. Supposition is that genotypes farther above the threshold would be more likely to exhibit bilateral symmetry. This aspect of a QC model does not seem to have been tested for dental traits.

OVERVIEW

In sum, my contention is that the case described by Szabó and coworkers is a paramolar tubercle on the lower left first premolar, and, thus, should be labeled a protostylid. It is possible that this cingular feature developed from local trauma or infection, which would account for its unilateral expression, though that is sheer speculation. This tubercle is unquestionably a developmental feature of the premolar itself, as its union (shared enamel, dentin, and pulp cavity) precludes it being a supernumerary tooth.

These comments are set forth in hopes of stimulating discussion among readers regarding this interesting case.

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