

oral pathology

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Globodontia in the otodental syndrome

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A gross morphologic anomaly of tooth form affecting both primary and secondary posterior teeth has been observed segregating as an autosomal dominant trait in a kindred of Polish extraction. The crowns of the canine, premolar, and molar teeth resemble massive globes; the pulp chambers are large and may be duplicated; and the occlusal surfaces lack definite cusps, often resembling the tied end of a sausage. The relationship of the tooth anomaly to high-frequency hearing loss previously associated with this tooth defect appeared to be variable in this kindred.

The association of gigantic globe-shaped posterior teeth and high-frequency sensorineural hearing loss was first reported by Levin and Jorgenson^{1,2}; a second family was reported by Gundlach and associates.³ Levin, Jorgenson, and Cook⁴ followed up their initial report with a detailed investigation of 189 members of a kindred of Italian extraction in which thirty-four persons were considered to be affected. This study showed that twenty-eight kindred members had both massive globe-shaped posterior teeth and a high-frequency hearing loss characterized by hearing thresholds at 6,000 to 8,000 cycles per second of greater than 50 decibels. Two patients had anomalous teeth without loss of hearing, and four patients had loss of hearing without abnormal molars but had offspring with the dental defect. The two traits thus showed a high but somewhat variable association in this kindred and segregated as an autosomal dominant trait. Congenital absence of one or more premolar teeth occurred in fourteen of the thirty patients with globe-shaped teeth. A frequent finding was the presence of circumscribed yellow-white spots, especially on the labial cervical portion of the

This investigation supported by National Institutes of Health Grant No. DE 03686-02.

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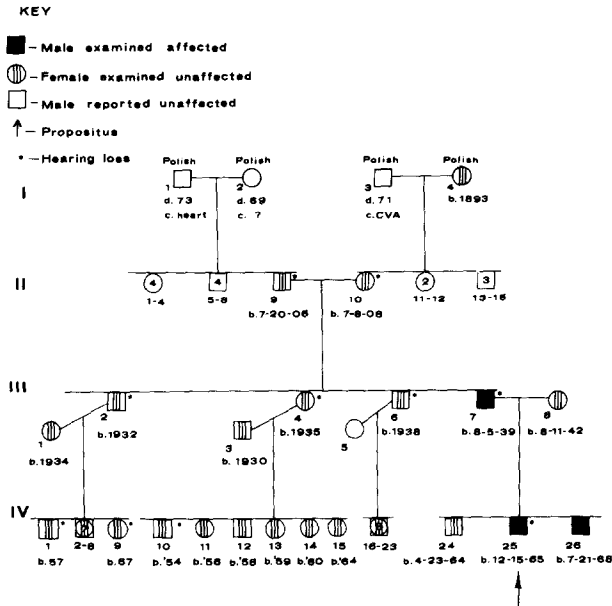


Fig. 1. Kindred of a family with globodontia and loss of hearing at high frequencies compatible with an autosomal dominant mode of inheritance.

enamel of cuspid teeth. The present report describes the features of this syndrome in a family of Polish extraction (Fig. 1).

FAMILY HISTORY

The four grandparents of the propositus, IV-25, were of Polish extraction. No known consanguinity was present within two generations prior to the marriage of II-9 and II-10 or between III-7 and III-8. The first known person in the kindred to have abnormally large teeth was the father of the propositus, III-7, and examination revealed that his parents and one living grandmother did not have abnormal dentitions. The initial history and subsequent audiogram of the paternal grandfather, II-9, and the paternal grandmother, II-10, showed that they had a severe loss of hearing which included the middle frequency range in addition to a high-frequency loss.

CASE REPORTS

PROPOSITUS IV-25

The propositus was a 7-year-old boy who came to attention when he was referred for orthodontic treatment (W. J. S.). He was a full-term infant, the product of an uncomplicated pregnancy. His past history was not unusual, with the exception of infectious childhood illnesses and a chronic otitis media that affected the right ear. One year prior to this examination, he had been treated for a persistent purulent infection of the right ear, which had resulted in perforation of the ear drum. Psychosocial and physical developmental milestones were reached at the expected times. The primary incisor teeth erupted at 6 to 9 months, but the posterior teeth were delayed, the first molars appearing when he was 2 years old. On physical examination, he appeared to be a well-developed, well-nourished boy with no

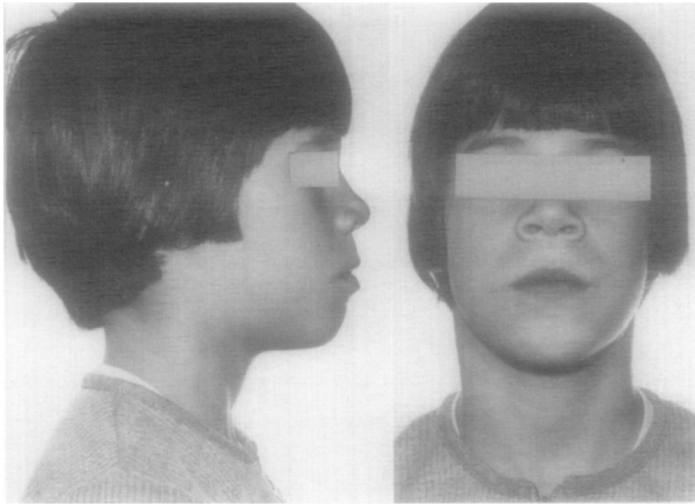


Fig. 2. Propositus IV-25 (see Fig. 1). Patient has a "full-mouth" appearance, slightly antverted nostrils, and a long philtrum.



Fig. 3. Dental cast of the dentition of the propositus, IV-25 (see Fig. 1), shows the dentition at the time of initial examination. The maxillary cast (*left*) illustrates that the primary central incisors are exfoliated, the primary lateral incisors are of normal size, and the canine and molar teeth are large, globe-shaped structures with numerous accessory grooves and fissures. The mandibular cast (*right*) shows four erupted secondary incisors, globe-shaped primary canines, and molars. There are only two primary molar teeth in each quadrant. The secondary first molars are unerupted. Note particularly the towering mesial or mesiobuccal cusps of the first primary molars.

abnormalities other than those attributable to his oral problem and a retracted scarred right ear drum. His facial appearance was unusual (Fig. 2). He had a long-appearing face, antverted nostrils, a long philtrum, and a full-cheek appearance. Submandibular lymph nodes were enlarged and firm to palpation. The palatine tonsils were enlarged bilaterally and nearly met in the midline. The patient had a mixed dentition (Fig. 3). When seen initially, all lower permanent incisors were erupted and had a normal anatomic configuration. The primary maxillary incisors had exfoliated, and the maxillary primary lateral incisors had a normal appearance (Fig. 3). The primary canines and molars were larger than normal, with



Fig. 4. The dental condition of the propositus, IV-25 (see Fig. 1), after the removal of the mandibular primary canines. Note the towering mesial or mesiobuccal cusp of the primary first mandibular molars which also have an extra buccal or mesial facial bulge. Also note the mottled spots on the enamel of these teeth.

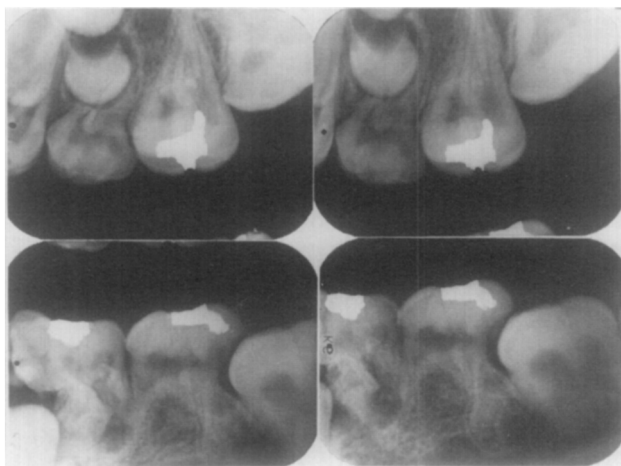


Fig. 5. Radiographs of the left quadrant of the propositus, IV-25 (see Fig. 1), show massive, globe-shaped crowns with numerous accessory radiolucent lines marking the accessory grooves and fissures in the crown. Note the apparent duplication of pulp chambers in the molar teeth. Whereas the crowns, pulp chambers, and root canals appear to be duplicated, there is the suggestion that the roots are normal in number or even fused.

globe-shaped crowns, anomalous grooves extending from the labial and lingual aspects of the crown onto the incisal or occlusal surfaces. The occlusal surfaces of the molar teeth resembled the tied end of a sausage (Fig. 3).

Individual primary canines and molar crowns had various patterns which appeared to be composed of fused cusp growth centers (Fig. 3). The maxillary canines had two labial and one lingual cusplike protrusions separated by shallow grooves extending cervically over the crown. The mandibular canines appeared to have one large labial cusp with three subdivisions, two lingual cusps and a smaller cusp in the position of a lingual cingulum. The molar teeth resembled pumpkins. The maxillary first molars had six major cusplike projections—mesial, buccal, distobuccal, distolingual, mesiolingual, and central occlusal. In addition, there were minor projections in the major buccal and lingual facial grooves. The second maxillary molars had four major cusps each, but eight or nine minor cusps delineated by shallow grooves were present also. The most grossly distorted teeth were the mandibular first molars. A

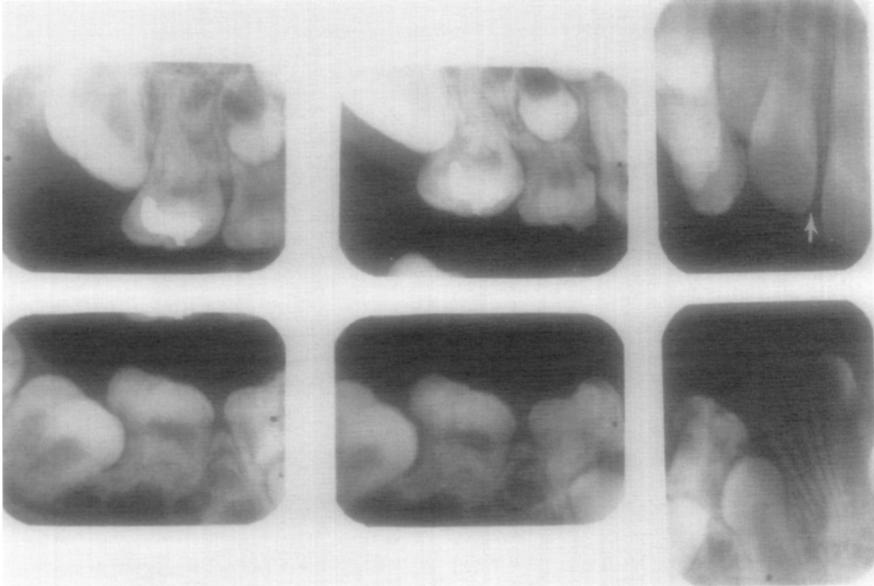


Fig. 6. Radiographs of the right quadrant and anterior segment of the propositus, IV-25 (see Fig. 1), shows thin enamel on the anterior teeth (*arrow*) as well as the posterior teeth. Note the excessively high mesial cusps on the primary first molars, the numerous grooves on the crowns, and the appearance of duplication of coronal and pulpal features of the molar teeth.

towering mesial or mesiobuccal cusp extended above the occlusal surface and was folded distally, overhanging the occlusal surface. These teeth, although grossly distorted, had what appeared to be five major cusps and four or five projections that appeared to be attempts at cusp formation. The mandibular second molars had eight cusps. In addition, affected teeth had anomalous projections on the buccal and lingual surfaces. Fig. 4 shows the dentition of the patient after removal of the mandibular primary canines. Note the buccal bulges on the primary first molars. Yellow-white spots were present on local areas of the enamel, particularly on the labial faces of primary canines. The occlusion was basically a Class I type, but with crowded arches because of the gigantic size of the teeth, which contributed to the patient's full-cheek appearance (Fig. 2).

The radiographic appearance of the teeth was most striking (Fig. 5). Primordia for developing premolar teeth could not be identified for the maxillary right second premolar, the mandibular right first and second premolars, and the mandibular left second premolar. The enamel layer on all teeth, the morphologically normal-appearing anterior teeth, as well as the abnormally shaped posterior teeth, was approximately half the thickness normally found (Fig. 6). The posterior teeth tended to have a taurodontic configuration with a bifurcation or trifurcation apically placed; however, in contrast to true taurodontism, the root length was short compared with crown height. Part of this taurodontic appearance was ascribable to the massive size of the crowns and the large appearance of the pulp chambers rather than to an over-all elongation of the tooth and pulp chamber as is seen in true taurodontism. In many of the posterior teeth, the pulp chambers appeared to be duplicated. When the apparent duplication of pulp chambers was observed in relationship to the radiographic appearance of the overlying cuspal anomalies, the impression was that each posterior tooth crown had been duplicated and fused into one twinned crown (Fig. 5). The first permanent molar crowns were impacted against the overlying distal projection

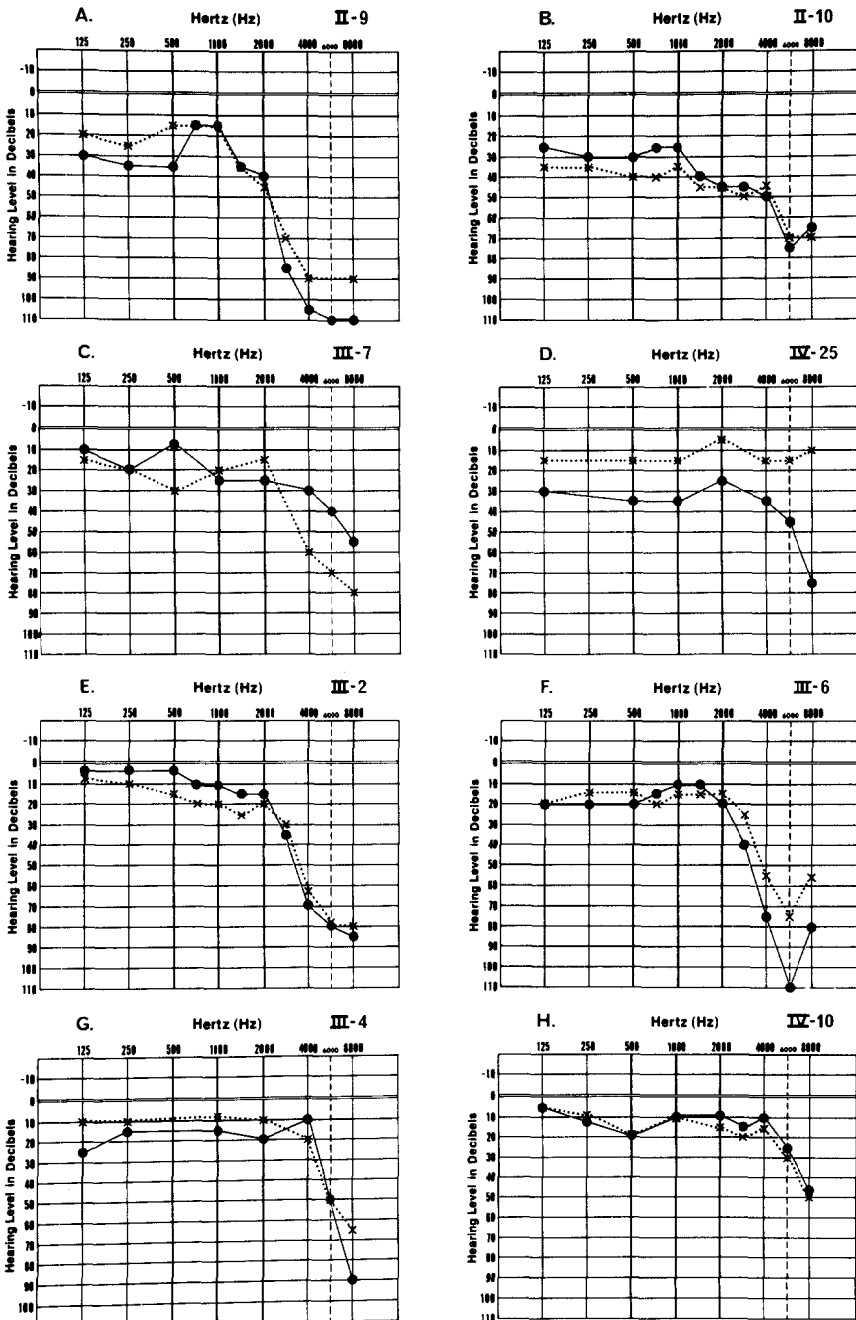


Fig. 7. Audiograms of kindred members show a loss of acuity at the frequencies above 4,000 Hz as the most consistent finding. *A*, Grandfather II-9; *B*, Grandmother II-10; *C*, Father III-7; *D*, Propositus IV-25; *E*, Paternal uncle III-2; *F*, Paternal uncle III-6; *G*, Paternal aunt III-4; *H*, Paternal first cousin IV-10. ×-----× left; ●-----● right.



Fig. 8. Affected brother of the propositus, Patient IV-26, at age 6 years shows the full-cheeked appearance and long philtrum that were also present in his sibling.

of the primary second molar. Fig. 5 gives the impression that a portion of the distal aspect of the second primary molar had been resorbed by the developing first permanent molar, but additional films suggest that this was an artificial effect of image superimposition. The developing second molars were also gigantiform, with the mandibular teeth set high in the ramus and the right mandibular second molar transversely oriented.

Audiometric examination (air conduction) showed no gross abnormality in the left ear. The right ear showed hearing levels of 25 to 35 decibels across most frequencies up to 4,000 Hz, with a decrease to 45 decibels at 6,000 Hz, and to 75 decibels at 8,000 Hz (Fig. 7, D).

PATIENT IV-26 (Fig. 1)

This subject was the 5-year-old brother of the propositus. His gestation, birth, and past medical history were not unusual, except that his posterior teeth had been slow in erupting. On examination, he was found to be a well-developed, intelligent boy in good physical condition. No abnormalities were found in any system other than those attributable to his oral problem. His face was long, with a long upper lip and philtrum. His cheeks bulged (Fig. 8), giving him a "full-mouth" appearance. The submandibular lymph nodes were palpable bilaterally. His tonsils were not unusual.

He had a full primary dentition, with normally shaped incisors but with gigantic, globe-shaped canine and molar teeth (Fig. 9). The teeth also showed yellow-white spotting of the enamel on the labial cervical crown, most prominent in the canines. His occlusion was Class I, but with crowded arches because of the size of the teeth. The morphologic changes in the canine and posterior teeth were similar to those of his brother.

Radiographically, primordia for the maxillary right second premolars, the mandibular right and left first and second premolars, and the maxillary left second premolars could not be identified. The radiographic changes were similar to those of his brother, with the exception that the primary maxillary canines contained radiodense areas resembling pulp stones (Fig. 10). His audiogram was not unusual. There was a slight decrease in the hearing level to 20 decibels at 8,000 Hz, which, by itself, would not ordinarily be interpreted as unusual but may presage a continuing loss of hearing when interpreted in the light of the history of this syndrome.

PATIENT III-7 (Fig. 1)

This subject was the 34-year-old father of the affected boys; he had worked as a tool and die maker in a forge and foundry company for the previous 10 years. His gestation,

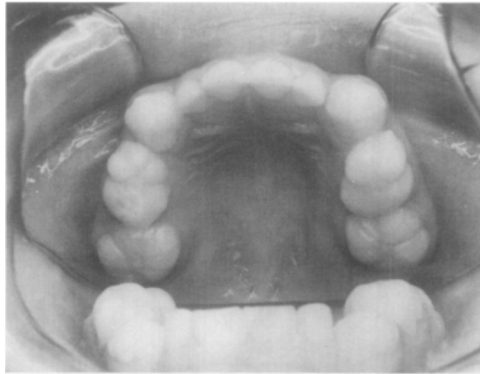


Fig. 9. The maxillary dentition of Patient IV-26 at 6 years of age shows normal primary incisors and abnormal primary canines and molars.

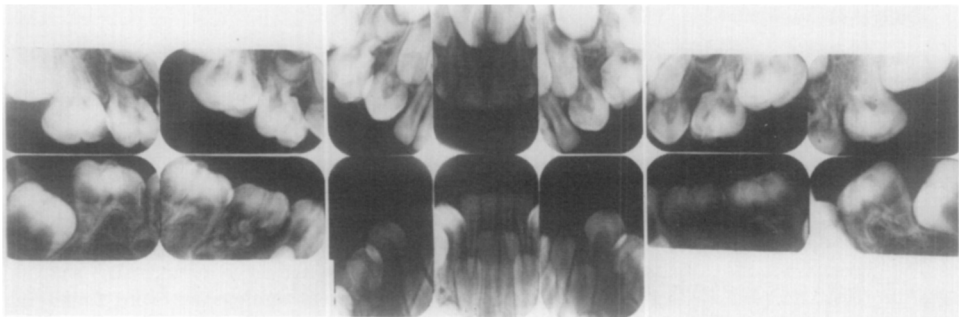


Fig. 10. Radiographs of Patient IV-26 show the appearance of duplication of coronal and pulpal structures and the presence of pulpal calcifications in the maxillary canines.

birth, and childhood history were not unusual, except for delayed eruption of primary and secondary teeth. When he was 9 years old, four unspecified primary teeth had been removed "to make room for the permanent teeth," and what was thought to be a lower right permanent first molar was extracted for orthodontic purposes. (Note that Fig. 11 shows the first permanent molar present.) At this time, a diagnosis of mandibular prognathism was made and the condition was treated orthodontically and surgically, but the exact nature of the operation was unknown by the patient. At 24 years of age, the patient passed two kidney stones; at 26 years of age, he underwent repair of a bilateral inguinal hernia; and at 30 years of age, he had a basal-cell carcinoma removed from the left cheek. Physical examination revealed no abnormalities other than healed bilateral hernia scars, anomalies of the teeth, an abnormal audiogram.

The right first mandibular premolar was missing and appeared radiographically to have been extracted. The right second premolar was impacted, as were three third molars (Fig. 11). In contrast to his sons' dentitions, the crowns of the canines and premolars were constricted coronally, with a tendency toward peg-shaped teeth. The molar teeth showed the same globe form as seen in the sons. Some of these teeth had partially obliterated pulp chambers, apparently from pulpal calcifications.

The audiogram (Fig. 7, C) showed a hearing level in the right ear of 30 decibels at 4,000 Hz, with a decrease in acuity to 40 decibels at 6,000 Hz and to 55 decibels at 8,000



Fig. 11. Radiographs of the affected father (Patient III-7) show that the molar teeth have an anatomic configuration similar to that seen in his sons. The left mandibular premolars had a pegged shape similar to that of the impacted right maxillary second premolar illustrated, seen in families in which these same teeth are missing in other kindred members.

Hz. The defect in the left ear was more severe, with a sharp drop to 60 decibels at 4,000 Hz and to 80 decibels at 8,000 Hz.

The parents of the affected father, II-9 and II-10, did not have abnormally shaped posterior teeth, nor did any of his collateral relatives. Abnormal audiograms were found in the paternal grandfather of the propositus, II-9 (Fig. 7, *A*), the paternal grandmother, II-10 (Fig. 7, *B*), two paternal uncles, III-2 and III-6 (Fig. 7, *E* and *F*), the paternal aunt, III-4 (Fig. 7, *G*), and her eldest child, IV-10 (Fig. 7, *H*). Two of the children of the uncle III-2 (IV-1 and IV-9) also had loss of hearing above 50 decibels at frequencies above 4,000 Hz (not illustrated).

HISTOLOGIC FINDINGS

Two primary canine teeth from Patient IV-25 were subjected to histologic examination. Grossly, the teeth had large bulbous crowns with superficial grooves extending from the cemento-enamel junction onto the "occlusal" surface of the teeth. There were no definite incisal line angles on these teeth. Both teeth had ovoid, yellow-white spots on the enamel of the labial surface. One tooth was slightly larger than the other and measured 1.7 cm. in length, 7 mm. mesiodistally, and 8 mm. buccolingually. The labial "cusp" portion of the crown consisted of three distinct projections. On the lingual portion of the crown were a mesiolingual and a distolingual projection separated by a smaller projection in the position of the cingulum. All of these projections were separated by shallow grooves extending onto the "occlusal" surface. Thus, it appeared as if the tooth consisted of three hyperplastic mamelons, two marginal ridges and the cingulum all approaching cusp size.

Ground sections through the apical third of one tooth showed three distinct root canals which connected to a single large pulp chamber coronally. Sagittal sections showed no structural abnormality in any tooth element, except for a slightly reduced enamel thickness and alterations in the enamel in the area of the yellow-white labial spots. In this area, the enamel rods were prominent, the incremental lines were irregular, and the rod sheath area contained voids similar to those in hypomaturation defects of enamel. The dentinoenamel

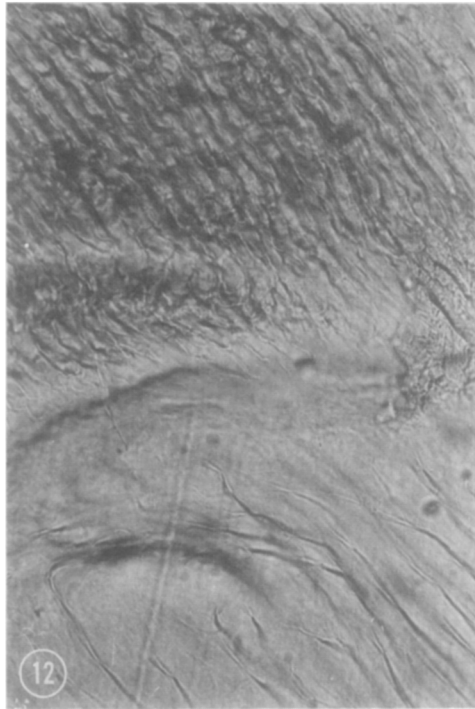


Fig. 12. Ground section of an extracted primary cuspid from Patient IV-25 through the area clinically demonstrating a yellow-white spot. Note the prominent inter-rod areas and distorted rods. The dentinoenamel junction is bulged into the enamel area, and the underlying dentin is amorphous with few tubules.



Fig. 13. Ground section through the labial face of the primary right mandibular canine shows a small projection at the cementsoenamel junction. Proceeding from the surface of the projection, the layers encountered are: *c*, cementum; *d*, dentin; *s*, space; *d*, dentin; *e*, enamel; *s*, space; *e*, enamel; and *d*, dentin of the main body of the tooth. This structure appears to be an attempt to form a cusp. (Magnification, $\times 30$.)

junction adjacent to those areas in the enamel was displaced toward the surface of the tooth, and the subjacent dentin had scanty irregular tubules (Fig. 12). Except for these minor irregularities, the over-all structure of enamel, dentin, and cementum appeared to be normal. Section through the buccal face of the tooth revealed what was interpreted as an attempt to form an accessory cusp (Fig. 13).

DISCUSSION

The association of high-frequency sensorineural hearing loss and globe-shaped teeth was not striking nor thought to be causally associated on the evidence presented upon initial examination of this kindred. There was at least presumptive evidence that the loss of hearing could have been ascribable to causes other than a genetic one. The propositus, IV-25, had a history of severe otitis media and visual evidence of a scarred right ear drum. The audiogram of his right ear showed a decrease in acuity over all frequencies tested, with severe loss at those over 6,000 Hz. His left ear did not show a loss. The father, III-7, had a history of working in a high-noise-intensity environment that had only recently been the object of a program by industrial health authorities to reduce the noise. The pattern of high-frequency hearing loss in his audiogram was thought to be compatible with that expected from environmental noise damage. Similarly, the hearing threshold of 40 to 60 decibels at 6,000 to 8,000 Hz seen in Patient IV-10 was attributed to a similar cause, since he had raced and repaired motorcycles; and the uncles worked with heavy machinery. The grandparents, II-9 and II-10, had an over-all hearing loss which could have been attributed to presbycusis. The possible association of loss of hearing with the tooth defect was not recognized until we received the report of this association in the extensive kindred of Levin and Jorgenson.^{1, 2} An additional unreported family seen in South Carolina by Jorgenson⁵ had losses over all frequencies, and their audiograms did not show losses confined to the higher frequencies. The question remains whether the paternal siblings should be considered to be affected with the syndrome on the basis of the audiometric findings alone and a hearing loss in their children. In the event that the children, IV-1, IV-9, IV-10, had children with the tooth defect, then III-2 and III-4 would have to be considered to be affected. Possibly one of the grandparents is also affected on the basis of a hearing loss alone and with the further evidence of the two defects in the son, III-7.

The problem illustrated by this family and this syndrome is that the investigator is unable to determine definitely who is affected when only one feature of a syndrome is present, especially when that feature may be caused by factors other than the gene that determines the syndrome. In this case, high-frequency sensorineural deafness may be due to a variety of other genetic and environmental causes. It is only after the appearance of offspring who show all features of the syndrome that, retrospectively, the status of the parent can be determined. Osteogenesis imperfecta is another disorder whose variable expressivity plagues the genetic counselor.

The process leading to the gigantic, globe-shaped teeth is somewhat difficult to interpret. The primary canine crown form could arise from hyperplasia of three mamelons, the two marginal ridges and the cingulum. The posterior teeth

appear to result from at least a partial duplication of the individual growth centers, which also involves the pulp chamber but tends to spare the root portion of the tooth. As in dentin dysplasia Type I (radicular dentin dysplasia) and in taurodontism, the development of the crown in this defect is somewhat independent of root development, since the gross abnormality of the crowns in this condition is not associated with an equally severe anomalous root formation.

Two other features of the dentition in this family are remarkably similar to the findings in the previously reported kindreds. In the three known kindreds,¹⁻⁵ many affected patients have premolars missing and yellow-white areas of enamel hypomaturations, particularly on the labial surfaces of canine teeth.

SUMMARY

A family of Polish extraction was studied in which massive, globe-shaped posterior teeth were found in a father and two of his sons, similar to those described in a previous family in which persons with this type of teeth also had a high-frequency sensorineural deafness. The audiograms in this family showed high-frequency air-conduction thresholds in the father and one son with globodontia and in other relatives without the tooth defect. The other son with abnormal teeth had a normal-appearing audiogram. Absence of premolar teeth and yellow-white spots of local hypomaturations of enamel on canine teeth were also findings in this kindred, as reported or observed in other kindreds. The disorder illustrates the problem of variable expressivity of a trait, which makes it difficult to predict the risk of having an affected child when only one feature of a syndrome is present in a relative of a fully affected patient.

REFERENCES

1. Levin, L. S., and Jorgenson, R. J.: Familial Otodontodysplasia: A "New" Syndrome, American Society of Human Genetics Annual Meeting, October 11-14, 1972, Philadelphia, Pa., Abstract 61a.
2. Levin, L. S., and Jorgenson, R. J.: Otodontal Dysplasia: A Previously Undescribed Syndrome, *In* Bergsma, D., editor: *Clinical Delineation of Birth Defects. XVI. Urinary System and Others*, Baltimore, 1974, Williams & Wilkins Company, pp. 310-312.
3. Gundlach, K. K. H., Witkop, C. J., Jr., Streed, W. J., and Sauk, J. J., Jr.: Globodontia: A New Inherited Anomaly of Tooth Form, American Academy of Oral Pathology Annual Meeting, April 29-May 3, 1974, New Orleans, La., Abstract 9.
4. Levin, L. S., Jorgenson, R. J., and Cook, R.: Otodontal Dysplasia: A New Ectodermal Dysplasia, *Clin. Genet.* 8: 136-144, 1975.
5. Jorgenson, R. J.: Personal communication. School of Dentistry, Medical University of South Carolina, Charleston, S. C., 1975.

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