DENTAL MANIFESTATIONS OF PSEUDOHYPOPARATHYROIDISM

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Pseudohypoparathyroidism is a metabolic disease caused by a disturbance in the peripheral action of parathormone. Clinically the disease is similar to idiopathic hypoparathyroidism.

Characteristically the patients are dwarfish in stature, thick set, and obese, having round faces and greasy skin. There is considerable reduction in the length of the 3rd and 4th fingers and toes and dimpling of the corresponding knuckles when the fist is clenched. Mentally these patients are slightly retarded.

Radiographs show that the 3rd and 4th metacarpals and metatarsals are short. Epiphysial closure is in advance of age, and there are patches of soft tissue calcification and ectopic ossification, usually in the thighs. Radiating striae of calcification of the basal ganglia are also described as a frequent finding.

Investigation of the clinical pathology shows that the calcium level is low, resulting in tetany in the untreated case, and the inorganic phosphorus level is raised.

Biopsies have shown that the parathyroid glands are normal or even slightly hyperplastic, and no phosphate diuresis follows administration of the hormone.

Case Reports

Four cases of this disease have been studied and the dental findings are presented. In two the family history is of considerable interest.

Case 1. This was a stockily built little boy of 10 years, with broad jaws and chin, depressed root of nose, and eyes set widely apart. The skull exhibited bossing and the fingers and toes were short and stubby. Gait was slow and rolling, and he was unable to run. Mental development was slightly retarded but he was a placid and amiable child.

Radiographically the metacarpals and metatarsals were short and there were scattered areas of soft tissue calcification but no calcification of the basal ganglia.

The following blood levels were present: serum calcium 8.3 mg./100 ml., serum phosphorus 8.2 mg./100 ml., and alkaline phosphatase 10 King Armstrong units/100 ml.

Family History. There was no family history of mental defect, epilepsy, or abnormal physical features. Normal pregnancy was terminated at 39 weeks by caesarean section, but at 10 weeks it was noted that the child was 'odd' looking and had a marked micrognathia. He had two older brothers both of whom were normal.

At 10 years the following teeth were present in the mouth: C B 1 1 3 . The deciduous teeth had been lost early due to caries. The incisors were a dull dark yellow colour and were grossly hypoplastic. Both upper lateral incisors were missing, or the right one may have been present as a very reduced tooth. The first molars on the right side were just beginning to erupt. The pulps of all the teeth were large, and there was considerable calcification present especially in the lower incisors.

Radiographically the enamel layer was thin and hypoplastic, and both lower first molars had very thin roots. Both upper lateral incisors, upper right second premolar, and lower right first premolar were missing.

Case 2. This was a 16-year-old girl with the typical clinical and radiographic features of the disease; intellectually she was rather slow and fell into the dull average range.

The serum calcium level was 8.5 mg./100 ml., serum phosphorus 4.5 mg./100 ml., and the alkaline phosphatase 7.9 King Armstrong units/100 ml.

Family History. Both parents were alive and well: The mother, who was short in stature and of dull intelligence but otherwise normal, had given birth to six previous children all of whom were girls. Two, in addition to this patient, survived and are well and three died from convulsions on the day of birth.

Dental Investigation. The following teeth were missing at 16 years: 6 | 2 4 6 . The 4 | had never developed and the lower premolars and canines were very hypoplastic.
FIG. 1.—Case 2. Intra-oral radiographs at 18 years show several missing teeth, including 8/8, and the premolars have short stubby roots. The enamel is thin and the pulps large with considerable calcification.

The teeth were dull white in colour and many were carious. Radiographically, 8/8 were missing and the upper premolars had short stubby roots. All the teeth had thin enamel especially the lower incisors. The pulps, which were large, contained considerable amounts of calcified material (Fig. 1).

Case 3. This girl had developed mild symptoms of tetany at 6 years of age following operation for an acute mastoid infection.

At 18 years she presented with all the typical physical and radiographic features of the disease including bowing of the tibia, frontal bossing (Fig. 2), slight mental retardation, and calcification of the basal ganglia on skull radiography.

The serum calcium level varied between 6·0-6·6 mg./100 ml., the serum phosphorus was 4·24-6·8 mg./100 ml., and the alkaline phosphatase 2·7-6·9 King Armstrong units/100 ml.

FIG. 2.—Case 3. Typical facial appearance in pseudohypoparathyroidism, with frontal bossing and short wide jaws.

FIG. 3.—Case 3. Radiographs at 29 years show several unerupted posterior teeth, the crowns and roots of which are small. Here also the enamel is thin and pulps are large and calcified.
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FIG. 4.—Case 4. Radiograph shows reduction in length of all the metacarpals.

In this case there was no significant family history. A dental report at this age noted that the lower first premolars, and all the first and second molars were unerupted. The second molars showed no proper root formation (Fig. 3). The following teeth were present at 29 years. 8 7 5 3 4 3 2 1 | 7 8 7 6 , but only the lower six front teeth were erupted. These teeth were dull white in colour with bands of pitted hypoplasia. The crowns and roots of all these teeth were small and the enamel was thin. The pulps were large and extensively calcified.

Case 4. This girl was diagnosed as having pseudo-hypoparathyroidism when she was 10 years old. She was short in stature, obese, round faced, and the bridge of her nose was flat. The limbs, hands, and fingers were characteristically short and she was mentally retarded. Radiographic examination revealed characteristically short metacarpals and metatarsals (Fig. 4), spur formation of the tibia, and scattered soft tissue calcification of the basal ganglia, though this was apparent 10 years later.

The serum calcium level was 4.5 mg./100 ml., and the serum phosphorus 10 mg./100 ml. at 10 years of age.

Family History. Both parents were alive and well, but there was a history of epilepsy on the father's side of the family, though he was not affected himself. There was a remarkable physical resemblance between mother and daughter. The mother was short in stature with characteristic shortness of the 3rd and 4th metacarpals (Fig. 5) and metatarsals, soft tissue calcification, and spurs on the tibia. She has had four other children all of whom died at birth or were stillborn. One of four children herself she was the only one with the characteristic deformities. She had lost all her own teeth early in life.

Dental Investigation. The teeth present at 24 years were as follows: 7 5 3 | 7 8 7 6 4 3 2 1 . These teeth were well formed but had small clinical crowns, except for the canines. The incisors were lost due to paradontal disease, and these were small teeth also.

Summary of Dental Findings

The clinical findings in these cases of pseudo-hypoparathyroidism are similar to those reported in cases of idiopathic hypoparathyroidism, and may be summarized as follows.

1. Teeth dull white in colour with hypoplastic pit-
Crowning. (2) Crowns are small and the roots are often short with blunt ends. (3) The enamel is thin and the pulp chambers large, often nearly occluded by calcified deposits. (4) In some cases there may be many unerupted teeth. (5) A full complement of teeth is not always developed, premolars being the teeth most usually missing. (6) The teeth are lost early due to caries. (7) The jaws are short and wide in all cases.

**Treatment**

These cases have been treated with vitamin D and A.T.10: this has resulted in an improvement in the general medical condition, and attacks of tetany have been avoided. The tooth substance laid down after the initiation of this treatment appears normal, though no improvement takes place in that already laid down and calcified.

Hypoplastic teeth are prone to caries and regular dental inspection is advisable, with the importance of oral hygiene stressed. The use of topical fluorides and fluoride toothpastes may assist in reducing the incidence of caries.

Orthodontic treatment may be necessary to correct a malocclusion, and a careful radiographic watch should be kept for the possible development of dentigerous cysts where unerupted teeth are present.

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**Dental Histology**

The histology of the dental tissues during the time of the metabolic upset shows certain abnormalities (Figs. 6 and 7). The dentine had an irregularly calcified matrix, indicated by the mottled pattern of dark spheres on a lighter staining background with haematoxylin and eosin staining. There was normal scalloping of the amelodentinal junction, but the tubules exhibited sharp bends near the pulpal and amelodentinal junctions. The cementum was thick, cellular, and cartilage-like, with what appeared to be vascular channels in the deeper layers extending into the dentine. The canalized area appeared to be less well calcified compared with the surrounding tissues. Most pulps were largely occluded by a calcified tissue which exhibited a series of whorl patterns (Fig. 8). The canalization was similar to that reported by Humphreys (1939) and Sunde and Hals (1961). This, however, occurred in the most recently formed dentine nearest the pulp in patients who were suffering from idiopathic hypoparathyroidism. Similar canalization was produced experimentally in parathyroprivic rats by Schour, Chandler, and Tweedy (1937).

**Review of Reported Cases**

Relatively few cases of pseudohypoparathyroidism...
have been reported and most of these contain little or no reference to the state of the dental tissues. Mackler, Fouts, and Birsner (1952) reported two interesting cases of familial disease, and noted that there were many unerupted teeth and those that were erupted were notched. Prentice (1954) reported a case in which the few remaining teeth were hypoplastic, malformed, and misplaced. Peterman and
Garvey's (1949) case had incisors with short roots, and the second premolars were missing. Among the findings in a case reported by Moehlig and Gerisch (1950) were enamel hypoplasia and non-eruption of several teeth, and poorly-formed teeth with lack of proper root formation of the second molars. Non-eruption of the first molars and lower first premolars was reported by de Mowbray, Llewellyn Smith, and Symonds (1954). Trevathan (1961) described the dental manifestations of a case in some detail. The incisors were conical and had thin enamel. The first premolars and deciduous upper canines had short roots and many teeth were unerupted. One of the cases reported by Elrick, Albright, Bartter, Forbes, and Reeves (1950) was totally edentulous at 12 years.

There have been several reviews of cases of idiopathic hypoparathyroidism, notably by Drake, Albright, Bauer, and Castleman (1939), Sutphin, Albright, and McCune (1943), Lovestedt (1950), Steinberg and Waldron (1952), and Hinrichs (1956). Lovestedt reported 16 cases, 8 of which had hypoplastic ridged or malformed teeth; 2 had premolars and molars with short stubby roots; 3 had several unerupted teeth and 1 was totally edentulous at 13 years. In spite of this Lovestedt made the surprising statement that 'clinical dental findings in cases of parathyroid insufficiency were rare'. Emerson, Walsh, and Howard (1941), Mortell (1946), and Miller (1957) each reported a case featuring hypoplastic teeth and unerupted teeth. Barr, McBryde, and Sanders (1938) recorded a case with gross hypoplasia. MacGregor and Whitehead (1954) and McLean (1954) each recorded one case having unerupted teeth and mention early loss of others. One of Drake et al.'s cases had premolars with short stubby roots. Hinrichs (1956) reviewed 5 cases, of which 4 had hypoplastic enamel and large pulps, 2 had premolars with short stubby roots, and 2 had unerupted teeth.

From this brief review, the similarity of dental abnormality in pseudohypoparathyroidism and idiopathic hypoparathyroidism is evident, and the cases reported here agree with this.

**Histological Findings in Cases of Idiopathic Hypoparathyroidism**

The first to note microscopical histological changes in the dental tissues was Humphreys (1939), who drew attention to the similarity with those in parathyropic rats. A second case has been reported at some length by Sunde and Hals (1961).

Humphreys' case was a young woman aged 23 years who had suffered tetanic convulsions for 11 years. Parathormone had improved the clinical picture and had raised the serum calcium level to normal. Ground sections of the teeth showed hypoplasia of the enamel dating from the 6th year and disturbance of the dentine from the ninth year, which worsened after the twelfth year. There were alternating bands of normal dentine and dentine with a coarse granular matrix and interglobular spaces. The dentine nearest the pulp resembled osteodentine and contained vascular inclusions.

The case described by Sunde and Hals was a young woman aged 27 years who had suffered tetanic convulsions since she was 15 months old. She had all the physical, mental, and radiographic features of idiopathic hypoparathyroidism including calcification of the basal ganglia. All the deciduous teeth were believed to have been present and erupted. At 11 years the following teeth were present. E D C | I 2 E: these were mobile and there was gingival hyperplasia. Eruption of the permanent teeth was delayed for about 2 to 23 years. Radiographs showed resorption of the roots of the retained deciduous teeth and that the lower second premolars were absent. Development was incomplete in both erupted and unerupted teeth with premature narrowing of the apical foramina. Ground and decalcified sections showed hypoplasia and hypomineralization of the enamel. The dentine matrix was irregular and granular with interglobular spaces. In the cervical parts of the teeth there were spaces containing vascular tissue. A lamella of bone-like tissue partially occluded the pulp chambers.

The histological findings in these cases are similar to those reported here from cases of pseudohypoparathyroidism, except for the site of the vascular inclusions.

**Discussion**

Gottlieb (1920) reported that parathormone deficiency resulted in delayed eruption, though Schour et al. (1937) found it had no influence on the rate of eruption in rats. Albright and Strock (1933) maintained that eruption might be delayed or fail altogether and that the enamel was often deficient and ridged. Changes might also occur in the dentine. No decalcification of the teeth occurred in adulthood. Hinrichs (1956) stated there was no conclusive evidence that hypoparathyroidism prevented initiation of tooth germ formation, but that there was some evidence that deficiency was associated with delayed eruption and affected both matrix formation and calcification.

The effect of thyroparathyroidectomy in rats was studied by Ziskin, Salmon, and Applebaum (1940) and was found to cause severe retardation of growth and development generally and especially the length
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of the jaws rather than the width. Eruption time, dentine, and root development were retarded also. The size of the molar crowns, however, was not affected.

The effect of parathyroidectomy in rats has been extensively studied by Schour et al. (1937). Classically this results in a calcio-traumatic response in the dental tissues. However, deficiency of parathormone is not the only cause for this response which is characterized by bands of hyper- and hypocalcification in the dentine. In decalcified section the hypercalcified areas stain darkly with haematoxylin and the hypocalcified areas stain strongly with eosin. It has been suggested that the darker areas represent an increase in the amount of cement substance between the fibrils and that this cement substance takes up an increased quantity of calcium salts. If this is so, then presumably there is interference with the metabolism of both odontoblasts in calcification and in the pulp cells in laying down the matrix. Hypocalcification of the pre-dentine may result from changes in the metabolism of the odontoblasts or changes in the local composition of the tissue fluid. Hypercalcified areas on the other hand may result from temporary cessation of matrix production, so that the deposition of calcium salts is concentrated into a smaller area. Tooth studies in rats following parathyroidectomy have shown that no changes take place in the first three weeks following operation but thereafter the enamel is affected. The ameloblasts shorten and this is followed by a break-up of the enamel organ and the formation of epithelial cysts. The calcio-traumatic response was observed in the dentine with irregular areas of defective dentine formation, the layers or increments becoming progressively less well calcified. This was emphasized in animals on a calcium-deficient diet.

Disorganization of the odontoblast layer of the pulp results in folds in the dentine, which contain vascular and pulpal tissue. This tissue becomes trapped in the dentine, giving rise to the vascular inclusions. Except for the site of the vascular inclusions, the dental manifestations in pseudohypoparathyroidism are very similar to those in idiopathic hypoparathyroidism and in parathyroprivic rats.

Parathormone deficiency has an effect on the calcification of the dental tissues and to a lesser extent on matrix production also, but the mechanism is obscure.

In pseudohypoparathyroidism there is presumably a second hormone factor missing or a deficiency of some intermediate substance which is responsible for the manifestations common to the three conditions. Vitamin D has two independent actions, first it increases calcium absorption from the gut, and secondly it increases phosphorus excretion in the urine. A.T.10 has the same action but gives a greater phosphorus excretion relative to the increase in calcium absorption. It is the hypocalcaemia that is responsible for such signs and symptoms as mental retardation, calcification of the basal ganglia, and tetany.

Albright (1938), quoting the work of J. S. L. Brown, stated that parathormone may produce somewhere in the body a lipid substance similar to A.T.10 and differing in the same way that A.T.10 differs from vitamin D.

Conclusions

Pseudohypoparathyroidism is a disease very similar to idiopathic hypoparathyroidism and having almost identical dental manifestations, clinical, radiographic, and histological.

Treatment with vitamin D or A.T.10 improves the medical condition by controlling the hypocalcaemia; dental tissues developed after the initiation of successful treatment are almost normal. No alteration, however, takes place in existing dental abnormalities. Careful correlation of the dental abnormalities in relation to the chronological development of the teeth can indicate the time of onset of the disease. It is possible that a deficiency of an unidentified principle in parathormone secretion, or an intermediate substance, is responsible for these characteristic manifestations.

Summary

Four cases of pseudohypoparathyroidism are described. The dental findings are similar to those reported in cases of idiopathic hypoparathyroidism. The teeth have small crowns with thin hypoplastic enamel, the roots are often short with blunt apices, and the pulp chambers large but nearly occluded by calcified deposits. Some teeth may not be developed and others remain unerupted. Histologically, there are what appear to be vascular canals in the peripheral dentine and cementum of the root.

The published reports are reviewed, noting the references to dental manifestation in cases of idiopathic and pseudohypoparathyroidism, and correlating these with the reported findings in parathyroprivic rats.

The possible action of parathormone in these conditions is discussed briefly.

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