Radicular Invagination (Dens in Dente) and Dentinogenesis Imperfecta in a Rat Incisor.

By

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Introduction.

In 1929 COOLIDGE (1) published a case of heterotopic ossification in the pulp of an upper incisor of a white rat. Cases of a similar nature do not seem to have been published, either before or later. By histological and roentgenological examination of the maxillae of 21 hypophysectomized rats (CHRISTENSEN and PINDBORG, 1950 (2)) the author found a case which bears a striking resemblance to that reported by COOLIDGE and which, furthermore, is interesting in that it presents a radicular invagination (dens in dente) in the upper as well in the lower maxilla. To the author's knowledge cases of such abnormity in rat incisors have not been previously reported.

Material and Methods.

The rat concerned (No. 12) was hypophysectomized at an age of 124 days. After having lived for 46 days after operation during which period the weight declined from 223 gm to 145 gm the animal was killed and decapitated. The cranium was cut sagittally, x-rayed, decalcified in 5 % nitric acid and embedded in celloidin.

The sections were stained by hematoxylin-eosin, Bock's stain, Mallory's connective-tissue stain and Hansen's connective-tissue stain respectively.

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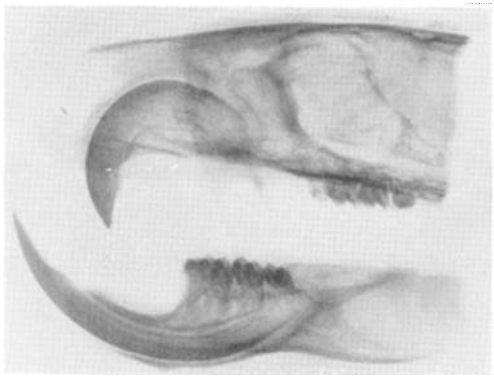


Fig. 1. Shows roentgenogram of upper and lower maxillae of hypophysectomized rat, No. 12. Note a narrow, calciferous border lingual to the basal part of the incisors.

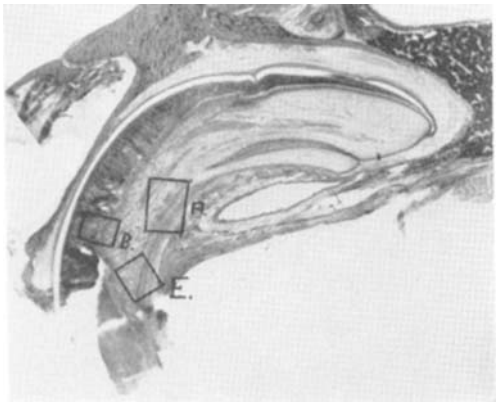
Findings.

X-ray examination shows a labial hypoplastic wedgeshaped defect in the upper maxilla at the transition between the apical and middle thirds. The defect and the other dental symptoms caused by the hypophysectomy will not be described here; interested readers are referred to the paper which will be published by CHRISTENSEN and PINDBORG, 1950. Corresponding to the lingual-apical area a narrow border of hard tissue is seen within the normal contour of dentin, fig. 1. Also in the lower maxilla a similar formation is seen.

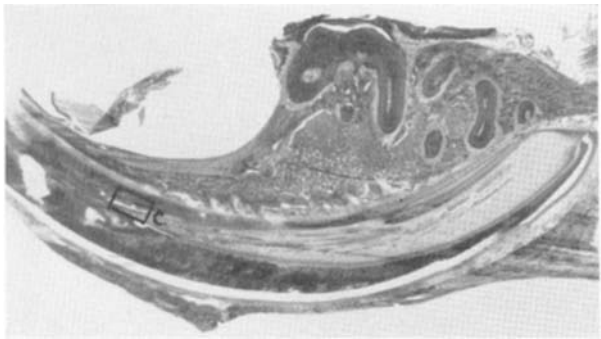
Histological.

A. The Radicular Invagination.

On the histological sections, corresponding to the hard-tissue border described above, an invaginal malformation, or formation resembling a dens in dente, is seen in the upper as well as in the lower maxilla, figs. 2 a and b, the appearance of the invagination depending upon the location of the section. Fig. 3 shows a higher magnification of a portion of fig. 2 a. It is seen from this that owing to its localization the central area of the invagination is not, as is otherwise the case in most dental invaginations in man, lined with enamel, and cannot be. Fig. 3 further shows the structure of the invagination: on both sides it is surrounded by pulp



a



b

Figs 2 a and b. Low power magnification of histologic sections of lower and upper maxillae. In both cases the radicular invagination is shown.

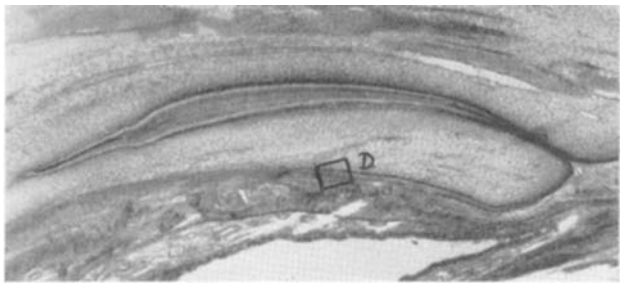


Fig. 3. Higher magnification of the invagination of Fig. 2 a. It is seen that the invagination has a pale predentine zone on either side of the invagination.

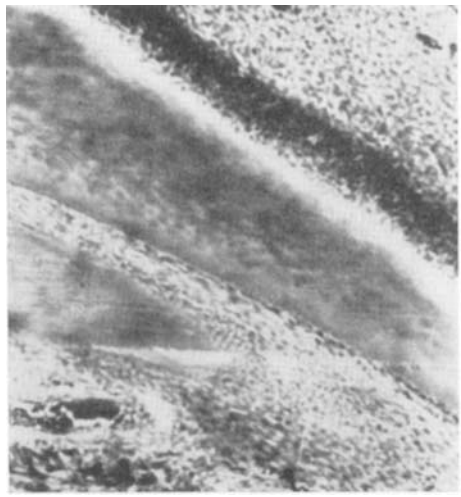


Fig. 4. Higher magnification of the apical portion of the invagination. It is seen that centrally in the invagination the connective tissue is a direct offshoot from the lingual periodontal connective tissue. Original magnification 8 × 10.

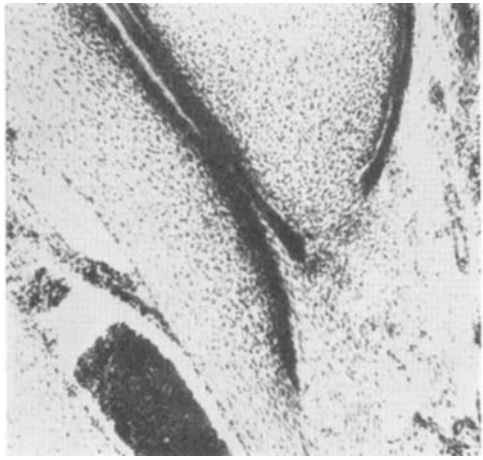


Fig. 5. The apical portion of the invagination from a section which shows plainly, that we are concerned with an invagination of the Hertwig root epithelial sheath. Original magnification 8 × 10.

tissue which apparently is normal in structure. Next follow — also on both sides — a well developed odontoblastic layer, a narrow predentine zone, and, finally, dentin which is normal in structure. Centrally in the invagination tissue is found, the ap-

pearance of which looks exactly like that of periodontal connective tissue. On one of the sections the connection with the periodontal connective tissue outside the tooth can be clearly followed, fig. 4. The periodontal connective tissue centrally in the invag-

Fig. 6. Higher magnification of the area in Fig. 3 marked D. The course of the dentinal tubules is oblique in relation to the predentine zone. Original magnification 40 × 10.

ination has been able to deposit a thin layer of cement on either side of the lumen. A study of fig. 5 will give information about the pathogenesis of the invagination; the illustration shows a slit in the oral, or lingual part, of Hertwig's root epithelial sheath. In conclusion should be stated that the structure of the invagination is identical in the upper and lower jaws.

B. The Atypical Hard-Tissue Formation.

The other peculiar pathologic-anatomical change is the very structure of the dentin and the isolated hard-tissue formation in the pulp. As the upper and the lower jaw do not present the same pathological changes, separate descriptions of them will be given in the following.

a. Upper Incisor.

Because of the presence of the invagination, the shape of the lingual dentin in particular becomes different from the normal. From the apical beginning and as far as to the incisal boundary

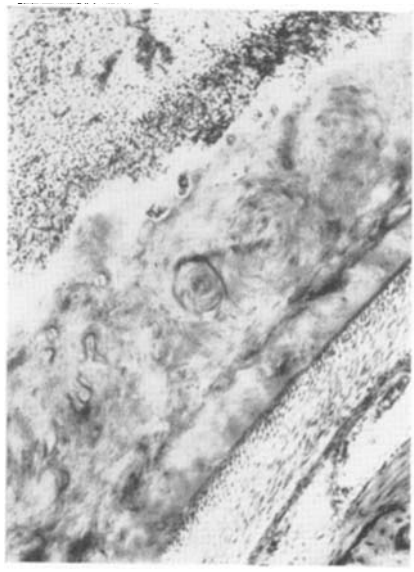


Fig. 7. Higher magnification of the area in Fig. 2 a marked E. Peripherally a homogeneous dentinal zone, and centrally a very irregular dentinal structure. Original magnification 8 × 10.

of the invagination, the lingual border of dentin is very narrow, fig. 3. Not only the shape but also the structure is thoroughly changed. The course of the dentinal tubules is very oblique, fig. 6, occasionally horizontal, and in certain areas the layer of odontoblasts is entirely missing, a phenomenon which is very conspicuous at the "incisal edge" of the invagination. In this dentin the number of dentinal tubules has diminished and the dentine appears homogeneous; furthermore, in this region too, no predentine is seen. Immediately after the tip of the invagination, a kind of secondary dentin is deposited on top of the narrow dentinal border just described. There are well defined odontoblasts, a predentine zone and a somewhat irregular canalicular structure. In the incisal direction the structure becomes more irregular, and cellular inclusions occur; in some few places the structure is suggestive of dentin with interstitial denticles, fig. 7.

This most irregular structure of the dentin is predominant in the whole anterior half of the tooth, cf. fig. 2 a.

The labial dentin presents normal conditions from the basal part and as far as to the hypoplastic defect caused by the hypophysectomy. Corresponding to this defect the mineralization of the

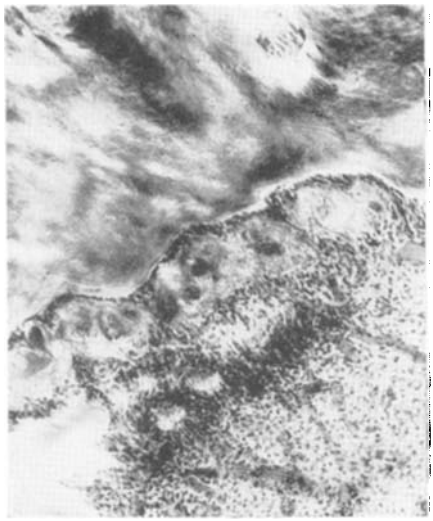


Fig. 8. Higher magnification of an area corresponding to the section of Fig. 2 a marked B. Note the irregular and isolated dentinal formation in relation to the labial dentin. Original magnification 8 × 10.

dentin is defective, but apart from this the structure is essentially normal up to about 2.7 mm from the defect in an incisal direction. After that the boundary between the pulp and the dentin becomes highly tortuous and scallop-formed, and at a distance of 25 μ from the dentin a hard-tissue formation of irregular structure occurs in the pulp, fig. 8. The formations are practically spherical with lamellated structure, and they take Hansen's collagen stain. Thus we are not concerned with pure precipitations of calcium but with the embedding of calcium in a preformed matrix. The isolated areas rapidly become confluent, and pulpal to them a further formation of "secondary dentin" takes place. In these atypical hard-tissue formations inclusions of cells and vessels occur, fig. 9. By the continued growth of the incisor a fusion takes place between the labial and the lingual dentin.

In the apical third the structure of the pulp connective tissue

appears normal except for a moderate hyperemia, which will be dealt with in greater detail on p. 311. The number of pulp cells in relation to the intercellular substance is not changed. Around the middle of the tooth abnormal depositions of calcium may be

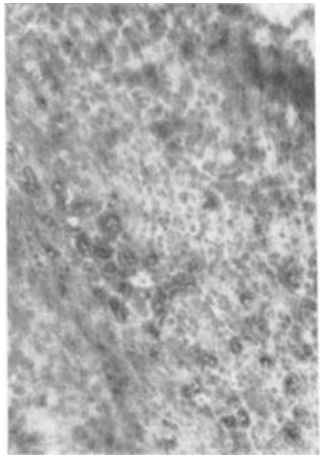


Fig. 9. Area from the labial dentin in the incisal portion of the upper incisor. Note the numerous cellular inclusions. Original magnification 8 × 10.

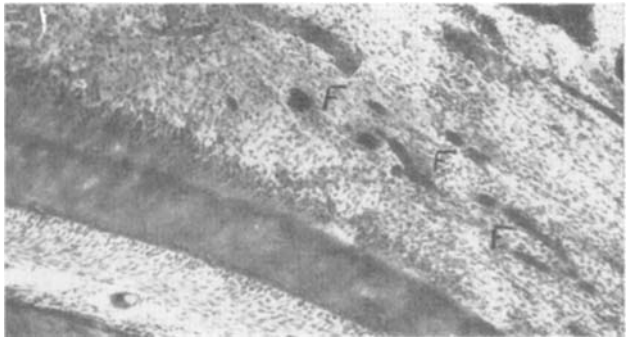


Fig. 10. Amorphous calcifications (F) in relation to the lingual dentin in the pulp of the upper incisor. Original magnification 8 × 10.

observed in the pulp itself. Small amorphous calcifications without any demonstrable structure, fig. 10, as well as a hard-tissue formation, which must be characterized as bone tissue are seen. The latter change occurs at the transition between the middle and incisal thirds. It measures 0.67 mm in length and 80 μ in width

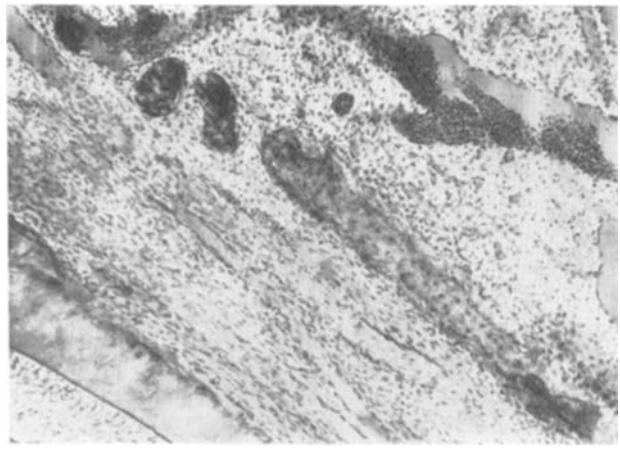


Fig. 11. Higher magnification of area corresponding to the area in fig. 2 a marked A showing the long bone spicule and the two smaller pieces of bone. Original magnification 8 × 10.

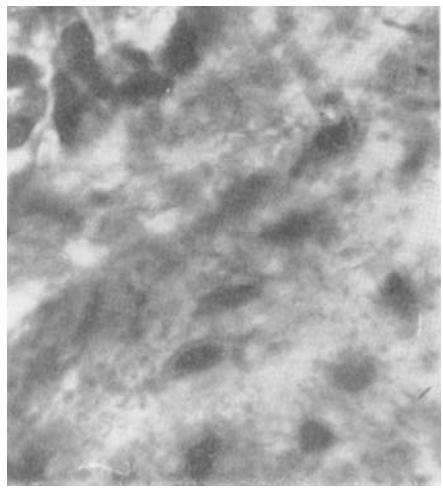


Fig. 12. Higher magnification of the cells in the long bone spicule in fig. 11. The cells are of the same appearance as those occurring in normal bone tissue. Original magnification 90 × 10. Immersion.

and is characterized by a great richness in cells, fig. 11. The distal areas are of a clearly fibrillary structure while the internal areas are more homogeneous and richer in calcium. By higher magnification, fig. 12, it is seen that the cells bear a clear re-

Fig. 13. The incisal edge of the upper incisor with the exposed pulp showing greatly dilated vessels. Original magnification 8 × 10.

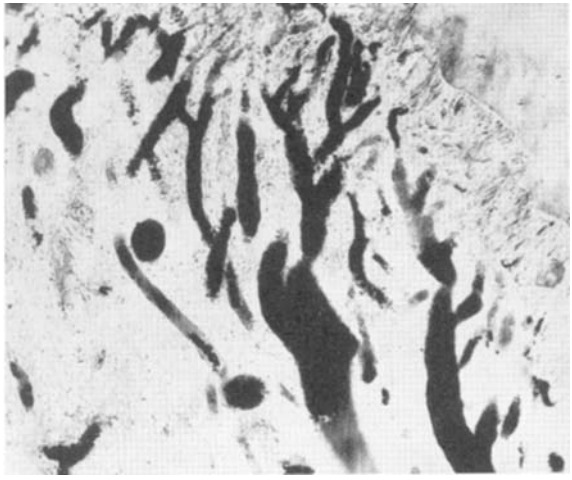


Fig. 14. Area from the labial dentin showing the greatly marked dilatation of the vessels. Original magnification 8 × 10.

semblance to osteoblasts embedded in bone matrix. On the basis of the findings it must be presumed that we are concerned with bone spicules. Incisal to the long bone spicule three other hard-tissue formations are in evidence; although they contain cells, they are not of the same typical bone structure. It is undoubtedly here a question of a tangential section of a similar bone tissue as the long spicule.

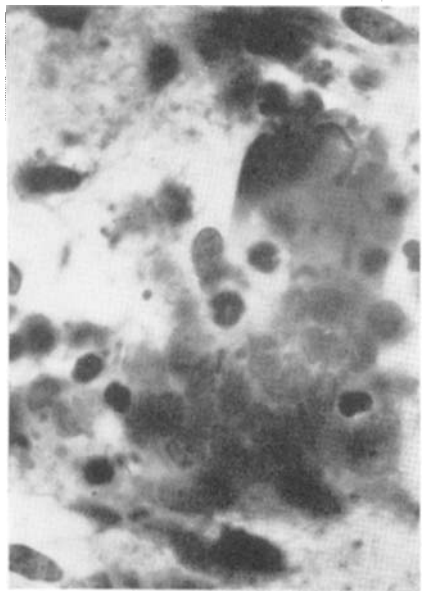


Fig. 15. Higher magnification of a dilated vessel with leucocytic emigrations. Original magnification 90 × 10. Immersion.

In the normal rat incisor an atrophy of the odontoblasts normally occurs at the transition between the middle and incisal thirds, and the lumen of the pulp is filled out with secondary dentin. In the rat incisor here described the incisal part of the pulp lumen has been somewhat reduced, although a central remnant of the pulp persists, extending right out to the incisal edge, fig. 13. The exposed pulp is — as was indeed to be expected — the seat of an inflammatory reaction with necrobiotic changes, which accounts for the hyperemia which is observable even in the apical third. Simultaneously with the hyperemia, fig. 14, an emigration of leucocytes from the vessels is seen, fig. 15.

β. Lower Incisor.

Also for the lower incisor it holds good that because of the invagination the lingual dentin border is very narrow; somewhat later than in the upper jaw a deposition of similar "secondary

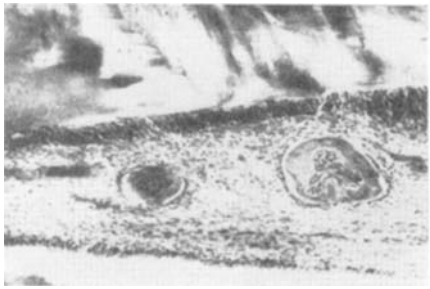


Fig. 16. Higher magnification of the area in fig. 2 b marked C. Two free dentinal formations are seen centrally in the pulp. Original magnification 8 × 10.

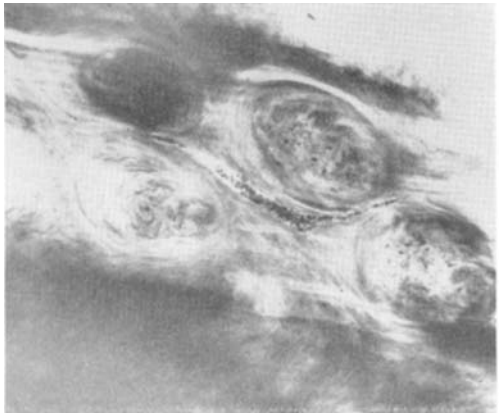


Fig. 17. Illustrations of denticles embedded in dentin in the incisal portion of the lower maxilla. Original magnification 8 × 10.

dentin" occurs. The labial dentin is more normal than in the upper jaw; the border between pulp and dentin is not so wavy, and the finer structure is normal. At the place of junction between the labial and lingual dentin pathological hard tissue formation is, however, present. This structure has presumably developed in the following manner: centrally in the incisal part of the pulp some peculiar pieces of hard tissue are formed. In the earliest stages,

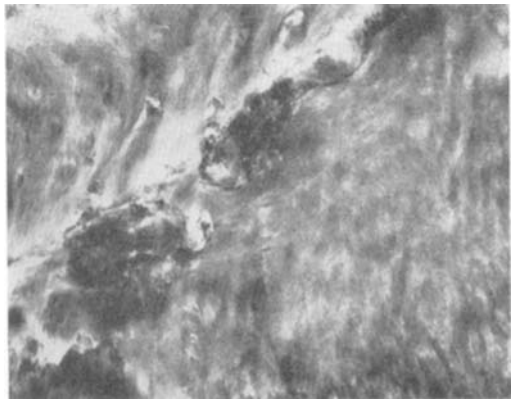


Fig. 18. Vascular and cellular inclusions in the lingual dentin of the lower incisor. Original magnification 8 × 10.

Fig. 19. Small bone spicule in the lower incisor. Original magnification 8 × 10.

fig. 16, there is, centrally in these, a tissue, rich in cells (forming hard tissue), lying closely adjacent to a pale "predentin zone"; the greater part is, however, occupied by a dentinlike substance of canalicular structure, which peripherally is provided with a pale border, against which there is a row of crowded cells. To judge by the dentinoid zones centrally and peripherally an active

hard tissue formation takes place in both directions. In the later stages the central lumen is filled out with hard tissue (dentin), and the denticle is surrounded by labial and lingual dentin, whereby a structure is produced resembling interstitial denticles, fig. 17. In addition to the interstitial denticles numerous cellular

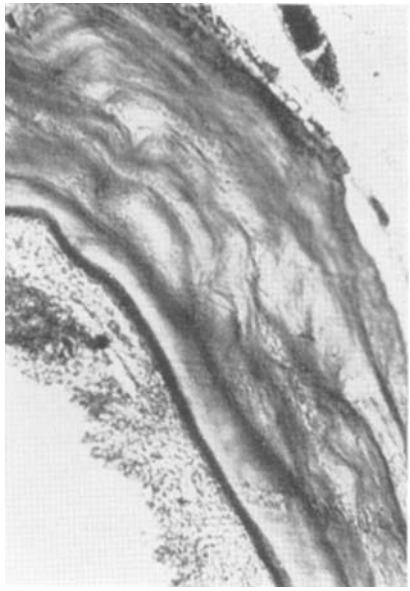


Fig. 20. Shows the characteristic dentin structure of a 05 — of a 2-year-old patient with osteogenesis imperfecta. Note the peripheral homogeneous zone. Original magnification 8 × 10.

inclusions are also seen, fig. 18. Except for the formations described above the pulp connective tissue is normal in structure. In the middle of the apical third there is, however, a formation of hard tissue resembling the bone spicule in the upper jaw, although it is not quite so highly differentiated, fig. 19. The pulp does not extend so far incisally as in the upper jaw, but hyperemia and some few leucocytic emigrations are in evidence all the same.

Discussion.

In a more detailed discussion of the case reported above the question will immediately be raised: what is the causal factor of these abnormities. To the author there is no doubt that the

invagination and the atypical hard tissue formation are entirely independent of the hypophysectomy. In none of the works published on hypophysectomy on rats (SCHOUR and VAN DYKE, 1932 (3); VEDANI, 1942 (4); HELD, 1944—45 (5); and BECKS, COLLINS, SIMPSON and EVANS, 1946 (6)) have changes been reported of a corresponding nature. Also as regards the radicular invagination no previous cases have — to the author's knowledge — been reported in rat incisors in the rest of the literature. As to the cause of this it is not possible to venture any definite opinion.

A hard tissue formation of a similar nature as that described here, has been previously reported by COOLIDGE, 1928 (1), who called the case a heterotopic ossification and registered it pathologically as an indirect, regressive metaplasia caused by the presence of vital epithelial cells in the pulp. The present case differs from COOLIDGE's case in that 1) it presents an identical condition in the lower jaw, 2) it presents at the same time a radicular invagination, and 3) apparently is without epithelial cells in the pulp. Unfortunately, it is not possible to prove that the finding of the invagination is independent of formation of hard tissue, but the author feels convinced that this is so, inter alia because, with the exceptions mentioned, the upper incisor here described, is completely like that described by COOLIDGE, which is without dens in dente. COOLIDGE's rat had been used in nutritional experiments extending over several months, and had only been given polished rice, to which COOLIDGE thinks the heterotopic ossification should be ascribed. In analogy to this the case here reported would have to be ascribed to the hypophysectomy, and that does not seem likely.

In certain pathologic conditions, *e. g.* vitamin A deficiency (SCHOUR, HOFFMAN and SMITH, 1941 (7)) an atypical hard tissue formation may be observed in the pulp of rat incisors, but unlike COOLIDGE's case and the one here reported the changes are present in all the experimental animals. In man a condition as the one here described is known, and is of the same rare occurrence. It is the so-called dentinogenesis imperfecta (synonymous with hereditary opalescent dentin). The expression was first used by SCHOUR and ROBERTS, 1939 (8), who described 3 cases of what had formerly been called hereditary opalescent dentin. In dentinogenesis imperfecta the dentin is irregular; the dentinal tubules are reduced in number, and have an irregular course. Disseminated in the dentin cellular inclusions are seen, and the intracellular

substance presents a granular appearance. It is a peculiar common feature of the structure of the dentin in all patients with dentinogenesis imperfecta that the peripheral dentin has a normal appearance, or, in any case, that it appears homogeneous. Precisely the same structure of the dentin is seen in patients with osteogenesis imperfecta, fig. 20, PINDBORG 1947 (9). A similar structure of the dentin has been described by RUSHTON, 1939 (10), under the name of dentinal dysplasia. Consideration of figs. 6, 7, 9, 13, and 18, makes it natural to draw a parallel between the human dentinogenesis imperfecta and the rat incisors here described. In addition to the purely pathological findings, the extremely rare occurrence of both cases lends support to the parallelism. About the dentinogenesis imperfecta it is known that it is hereditary; only in one case (PINDBORG, 1948, (11)), the mutation patient itself has been demonstrated. Unfortunately, there is no information as to whether the parents of the rat or its children have had the condition; however, whether or not this be the case, a mutation may very well have occurred, and the rare case thus have arisen in this manner, as a manifestation of a biological variation. The same thing may also have happened in COOLIDGE's case.

The conclusion must, therefore, be that the upper and lower incisors from an albino rat are an example from the animal world of dentinogenesis imperfecta.

Summary.

A case is reported of radicular invagination (dens in dente) and atypical hard tissue formation in the pulp of upper as well as lower incisors of an albino rat. The hard tissue formation consists, partly in the deposition of dentin-like substance in spherical formations with cellular inclusions, partly in the occurrence of bone spicules centrally in the pulp. The atypical hard tissue formation of dentin-like tissue is diagnosed as an example from the animal world of dentinogenesis imperfecta. It must be presumed that the radicular invagination and formation of new tissue are independent of one another.

Appreciation is expressed to Mrs. SOLVEJG FUGLEBAEK for making the sections and to C. M. PLUM, Ph. D., for taking the microphotographs.

Zusammenfassung.

Es wird ein Fall von radikulärer Invagination (dens in dente) und von atypischer Hartsubstanzbildung innerhalb der Pulpen sowohl der oberen als auch der unteren Schneidezähne eines weissen Rattes vorgelegt. Die Hartsubstanzbildung besteht teilweise in der Ablagerung eines dentinähnlichen Substanzes in Form kugelartiger Bildungen mit zellulären Einschlüssen und teilweise in der Erscheinung von Knochenspangen im Inneren der Pulpa. Die atypische Hartsubstanzbildung in Form des dentinähnlichen Substanzes wurde als Beispiel einer dentinogenesis imperfecta der Tierwelt aufgefasst. Es ist die Auffassung des Verfassers, dass die radikuläre Invagination und die Bildung des neuen Hartgewebes von einander unabhängig sind.

Résumé.

On rapporte un cas d'invagination radiculaire (dens in dente) et de formation de la matière calcifiée atypique dans la pulpe de l'incisive aussi bien supérieure qu'inférieure d'un rat blanc. La formation de tissu dur se compose d'une part de dépôt de substance dentinoïde en formations sphériques avec inclusions cellulaires, d'autre part d'apparition de travées osseuses centralement dans la pulpe. La formation de tissu dur atypique de substance dentinoïde est diagnostiquée comme un exemple animal de dentinogenesis imperfecta. Il faut supposer que l'invagination radiculaire et les formations de tissu dur soient indépendantes les unes des autres.

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