

Section of Odontology.

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A Melanotic Epithelial Odontome in a Child.

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KATHERINE W., aged 5½ months, was admitted to the Hospital for Sick Children, Great Ormond Street, in September, 1921, under the care of Mr. T. Twistington Higgins, F.R.C.S., for a swelling of the maxilla.

History.—According to the mother the swelling appeared in the front of the maxilla at about one month and had steadily increased in size. The baby had been fed on modified cow's milk. Its general condition was good and it did not appear to be affected by the tumour.

Examination.—The child was well nourished and apparently free from any pain. The tumour was situated on the anterior aspect of the maxilla in the incisor region, chiefly on the right side but extending to the left side also. It was about the size of a small walnut and pushed forward the upper lip (fig. 1). The mucous membrane was stretched over the tumour but was freely movable. The tumour felt uniformly

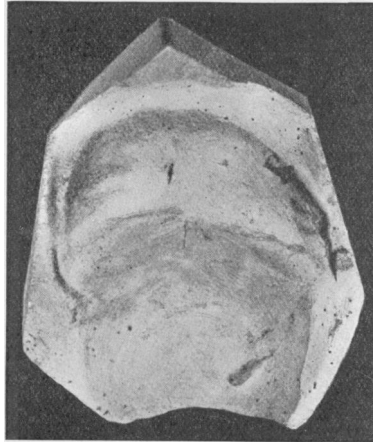


FIG. 1.

hard though not bony. It did not seem to be tender and there were no signs of inflammation. There were no teeth present on admission but during the child's stay in hospital previous to the operation the right upper deciduous central appeared. The labial surface presented through the gum, and it was evidently not a case of normal eruption but due to the growth of the tumour. A radiograph, unfortunately lost, showed that the tumour cast a moderately dense shadow much less dense than bone. There was a dense patch on the left side, evidently calcified, which resembled the imperfectly-formed crown of a tooth. There was no sign of the outer alveolar plate in the radiograph. Mr. Higgins asked one of us (A. T. P.)

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to see the case with him in the ward. It was agreed that probably the tumour was an odontome, though the exact variety was uncertain.

Operation.—October 21, 1921. The child having been anaesthetized, a flap of the stretched mucous membrane was raised over the tumour. It was found that the outer plate had been thinned to the consistency of tissue paper over the growth, but that it was still complete. Its thinness accounted for its apparent absence in the radiograph. This bone was removed as well as the thicker bone over the lateral margin of the tumour, so as to give access to the growth. It was found to be non-adherent to subjacent tissues except on its deep aspect. Here it was intimately united to the bone, spicules of which passed into its substance, and some force was needed to dislodge the tumour. The cavity was obliterated to some extent by crushing in the expanded bone, and the flap of mucous membrane was sutured into position with catgut. Recovery was uneventful and the child was discharged from hospital eleven days later.

Subsequent History of the Patient.—The patient was seen again by one of us (A. T. P.) in conjunction with Mr. Higgins a year later. The child was in perfect health and there was no sign of local recurrence or of metastasis. In view of the microscopic appearance of the tumour, to be described presently, an examination was made for pigmented patches in the mouth and elsewhere on the body but none were found. The teeth then present were $\frac{D \ B \ | \ A \ B \ D}{B \ A \ | \ A \ B}$. B | was twisted but well formed. The left incisors were in perfect alignment.

The child was again examined last week (October 21, 1925). She is now 4 years 6 months. She is a well developed, healthy child. All the deciduous teeth are present with the exception of the right upper central incisor. None of the permanent

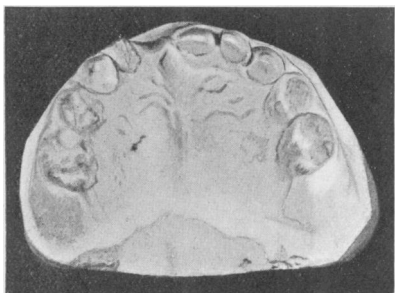


FIG. 2.

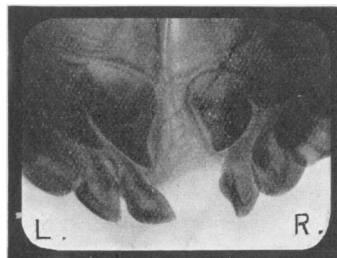


FIG. 3.

teeth have erupted. B | is twisted through a right angle with the lingual surface looking mesially. The arches are regular and the occlusion normal. The scar of the operation is visible on the right side of the frænum, and the lip is slightly attached to the gum by several narrow strands of tissue. The anterior surface of the bone above the missing central was concave, and this suggested that the permanent right central was absent. Elsewhere in the incisor region the outer plate was convex, this appearance suggesting that the other permanent incisors were present (fig. 2).

Radiographs were taken at the Hospital for Sick Children, both films and an antero-posterior plate, and prints from these have kindly been made by the Sister-in-charge. They show clearly that the right permanent central is absent. The left incisors are present and appear to be in normal position. The right lateral is present but the shadow suggests that it is twisted like the deciduous lateral. No sign of any tumour is visible (fig. 3).

EXAMINATION OF THE TUMOUR.

The growth preserved in 10 per cent. formol was of a blackish-grey colour. It measured 25×16 mm. and was invested by a thin, non-adherent capsule, through which the calcified mass shown in the drawing and the radiograph could be distinctly seen (fig. 4). The calcified body had a general resemblance to the crown of an incisor tooth. In addition to the larger calcified mass the radiograph showed several small calcified bodies scattered throughout its substance. The tumour was divided in the coronal plane by a sharp Gillette blade.

The cut surface showed a narrow, irregular cortex of a pale colour with a central, much darker zone. This zone was nearly black, but not uniformly so, being stippled with black dots spreading towards the periphery.

A small calcified body was seen to be embedded in the cut surface. A scraping from this examined in a drop of Farrant's solution under the microscope showed it to be composed of osteoid tissue.

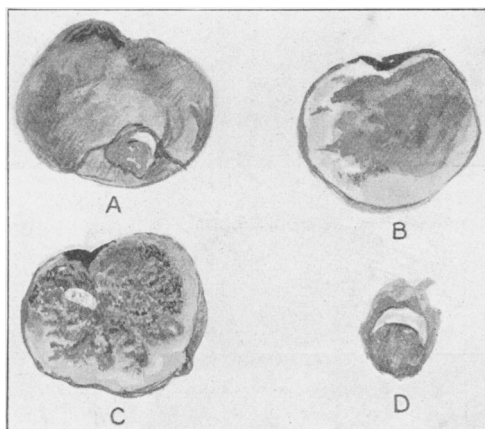


FIG. 4.—(a) Life-size drawing of the tumour; (b) coronal section through tumour; (c) coronal section showing distribution of pigmented area; (d) slightly enlarged drawing of the calcified mass of enamel on anterior aspect of the tumour.

Embedded in the outer surface of the tumour was a hard mass of what appeared to be enamel, of a yellowish-brown colour and mottled appearance, roughly resembling the crown of an incisor in shape and terminating abruptly above, where it was continuous with a semilunar-shaped mass of soft tissue of a whitish colour. When separated from the tumour this calcified body appeared to be a thin scale of enamel, and the soft tissue above it formed a sort of shallow sac beneath it reaching nearly to its exposed edge. As it appeared important to examine this shell without decalcifying (a process which would probably have destroyed it), it was cut on a freezing microtome, sections being taken in its long axis. Some fairly thin sections were obtained but the substance was decidedly hard and turned the edge of the knife.

Microscopic Appearance of Calcified Shell with Adjacent Tissue.

As was surmised the tissue turned out to be chiefly composed of enamel, very imperfectly formed. The prisms stained deeply both with van Gieson's stain and polychrome methylene blue. Intermixed with small masses of well-formed enamel were numerous calcospherites, and an enamel organ with ameloblasts, stratum

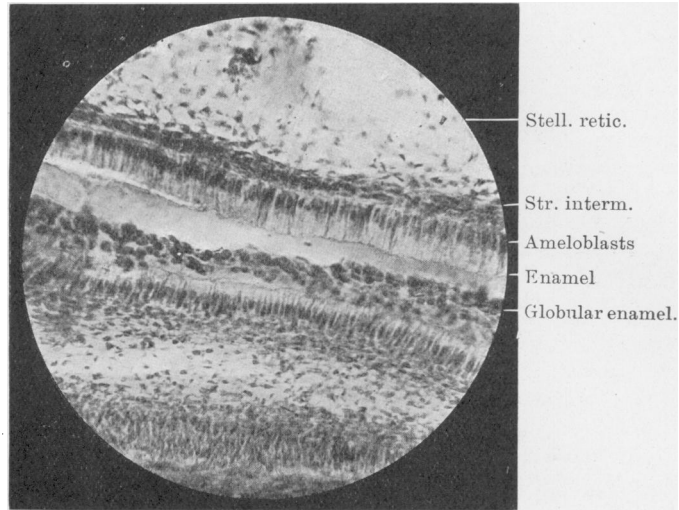


FIG. 5.—Folded enamel organ.

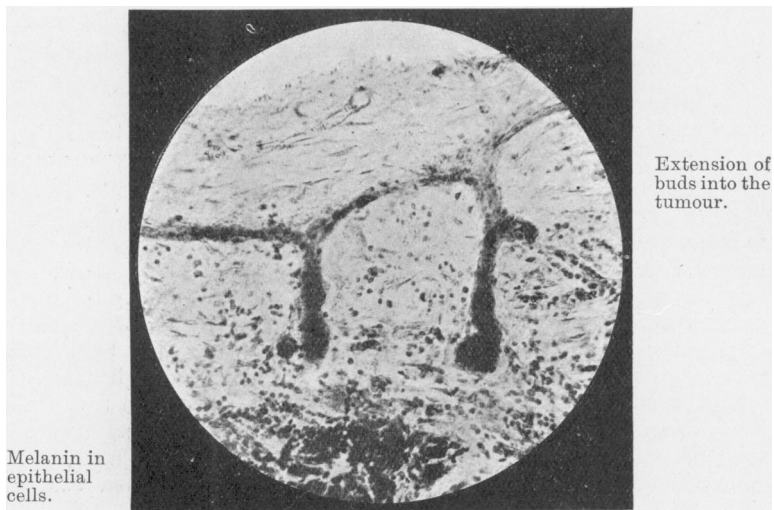


FIG. 6.—Epithelial band.

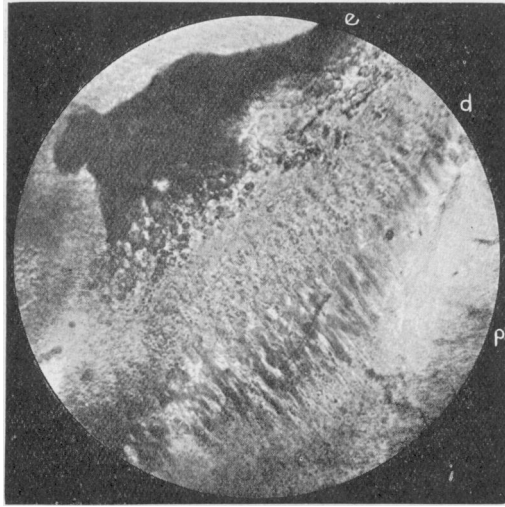


FIG. 7.—Showing globular enamel and malformed dentine ($\times 150$).
(*a*) Enamel; (*d*) dentine; (*p*) papilla.

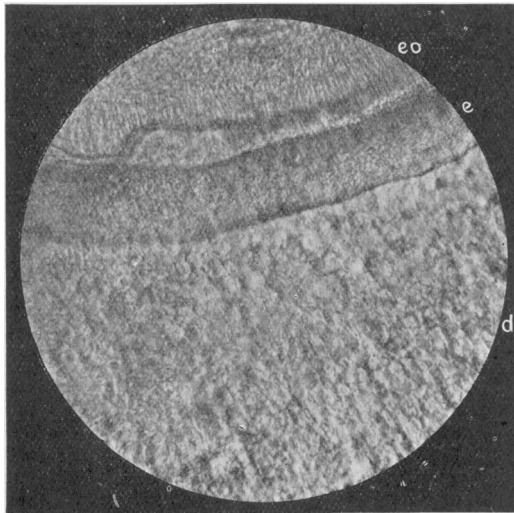


FIG. 8.—Band of enamel over globular dentine ($\times 150$).
(*e*) enamel; (*eo*) enamel organ; (*d*) dentine.

intermedium and a stellate reticulum, was found in connexion with the masses of enamel. In several places long columns of enamel organ were seen extending into the growth with alternating bands of forming enamel (fig. 5). These bands of enamel-organ cells form five distinct layers, and in one section a prolongation of the enamel organ is seen within the dental papilla, and the enamel-organ cells form a circular investment to what appears to be a calcifying body.

In several sections a narrow epithelial band was seen at the margin with numerous buds of epithelium extending into the growth, bearing a striking resemblance to a tooth-band with young tooth-buds growing from it (fig. 6). Portions of dental pulp were also seen, as well as some imperfectly formed dentine. This was small in amount compared to the abundant enamel everywhere surrounding it, which was chiefly made up of masses of globular calcospherites. In the imperfectly formed dentine the tubules can scarcely be detected but they are clearly visible in the odontogenetic zone. The whole of the calcified dentine appears to consist of globules and interspaces, which latter take the stain deeply and under a low power give the impression of irregularly formed bony tissue (figs. 7 and 8).

HISTOLOGY OF THE SOFT PART OF THE TUMOUR.

This shows the typical structure of an epithelial odontome or multilocular cyst. There are numerous cystic cavities of all sizes, surrounded by connective tissue which forms strongly defined septa between the cysts (figs. 9, 10). These septa show strands of connective tissue fibres and spindle-shaped connective tissue cells. Clumps and strands of large epithelial cells traverse the connective tissue in every direction. These cells are ill-defined, being much obscured by the dark pigment which is visible both within and between them. The cysts are occupied by a mass of cells with small, round nuclei. Some of the cells are vacuolated and the whole contents of the cystic cavities are enclosed in a delicate network. In many parts this fibrillar network appears to be continuous with fine fibres in the connective tissue of the septa, and in many places it stains differently to the enclosed cells. The smaller cysts are surrounded by epithelial cells, which appear quite black from the contained pigment present in the cytoplasm but not in the nucleus. The larger cysts in most cases have no epithelial lining and the contents are in close apposition with the surrounding connective tissue. A similar condition has been noted by the authors of the "Report on Odontomes" (p. 13) [1].

There can be no question here of the loss of the epithelium from the lining membrane by manipulation, for the sections were placed in formol and cut on the freezing microtome and not exposed to the action of heat and alcohol. There is no pigment in the cystic cavities in most places, but in one or two instances the cysts, instead of containing degenerated cells in the fibrillar stroma, are filled with large epithelial cells which are loaded with pigment granules (figs. 11, 12).

Toward the periphery of the growth small clumps of apparently cornified epithelial cells are met with.

The tumour showed a distinct investing capsule of connective tissue. This is a point of some significance in view of the benign character of the growth as proved by the subsequent history of the patient. The pigment appears to be melanin. It does not react to the Prussian-blue test and is therefore not an iron-containing pigment. It is very abundant and gives a blue-black appearance to the central part of the tumour. The outer portion of the growth contains but little pigment, which appears to extend in radiating lines toward the circumference. There are a few small scattered particles of bone within the connective tissue.

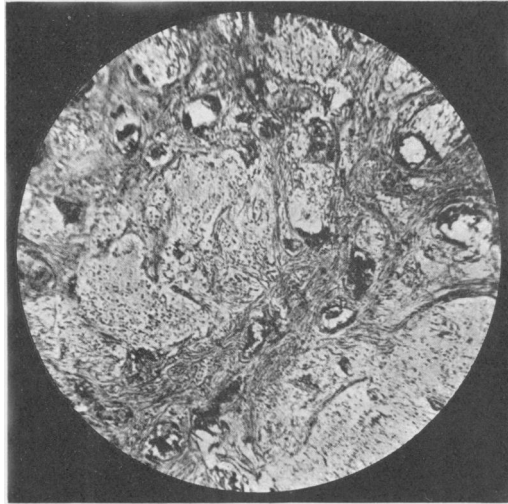


FIG. 9.—Alveoli and cysts ($\times 60$).

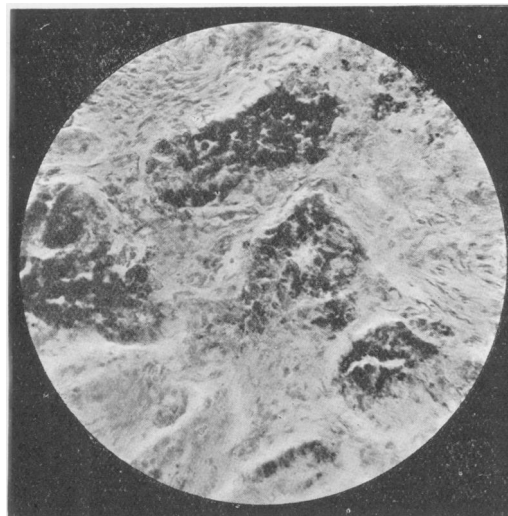


FIG. 10.—Alveoli with pigmented cells ($\times 150$).

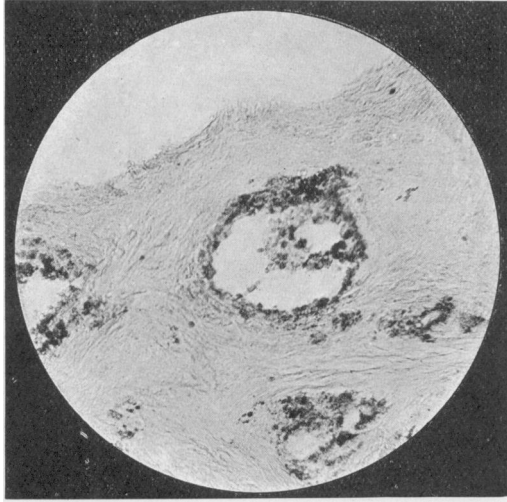


FIG. 11.—A small cyst lined with pigmented cells. Unstained preparation ($\times 150$).

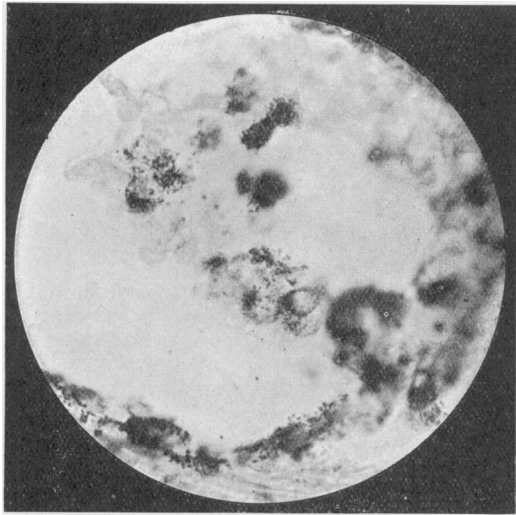


FIG. 12.—A portion of the cyst shown in fig. 9 ($\times 700$).

COMMENTARY.

This tumour is of great interest both as a melanoma and as a dental tumour. Considered as a melanoma it appears, as far as we can find, to be the first on record in which melanin has been found in an odontome. Another striking point is that the tumour has been proved on clinical grounds to be benign, in spite of the high degree of malignancy often shown by melanotic tumours. It is true that melanotic tumours are not always malignant, as in many cases of pigmented mole, which are usually quiescent in character. When they begin to increase they are usually rapidly malignant, though exceptions to this rule have been recorded. In grey horses, in whom melanomas are especially common, they are less malignant than in man. For an actively growing melanotic tumour such as this to prove benign is uncommon. No suspicion of its melanotic character was entertained at the time of operation and no attempt at radical removal was made, so that had the tumour been malignant it would almost certainly have given rise to metastases.

Concerning melanin itself, it is an iron-free pigment unconnected with hæmoglobin and containing sulphur. It is found in the skin of negroes and is present in the eye. Scattered collections of pigment cells may also be present in the brain, along the course of nerves and in the retroperitoneal and mesenteric connective tissue.

Two views have been put forward as to their origin [2, 3]. One is that the chromatophore cells are specific mesoblastic cells, though epithelial cells may also take on pigment formation. The other view, for which there appears to be greater support, is that the chromatophore cells are, as their name implies, only carriers of pigment which is derived from epithelial cells, or melanoblasts, derived from the deeper layers of the skin. Under normal conditions the cells are quiescent and the pigment formation small. This applies to stationary melanomata. The melanin is cytoplasmic and not nuclear in origin. It has been noted that in a rapidly growing melanoma the division of cells is in advance of the formation of the pigment, so that some of the secondary growths are not pigmented; this may perhaps explain the comparative absence of pigment in the peripheral part of this tumour. Melanomata usually arise in places where pigment cells exist, though they have been found in places where pigment is not normally found. In this connexion it may be noted that in many dogs the palate is pigmented in patches. Mr. W. G. Spencer [4] also states that congenital patches of pigment may be present on the hard palate and inner aspect of the cheek in dark races, such as the Dravidian races in India. They have been stated to appear for the first time in middle life, and to spread. The structure is that of a quiescent melanoma. New and Hansel [5] have recorded twenty-four cases of melanotic cancer of the hard palate. Pigment cells are also present in the olfactory epithelium, and a few cases of melanotic cancer have been recorded in the nose. It is suggestive to find that melanomata have occurred in regions so close to the site of this tumour as the nose and hard palate. Whether the tumour was melanotic from the commencement, or whether it began as an odontome and became secondarily melanotic, one cannot say. The general characteristics of the growth suggest that it undoubtedly arose as an aberration of the dental epithelium, yet its melanotic characters are so well marked as to suggest that they were present from the outset.

Considered as an epithelial odontome the tumour is of great interest, for it is possible to link it up with other examples of epithelial odontomes, and we would suggest that it sheds considerable light on the genesis of these growths. Most cases of multilocular cysts have occurred in adults when they have attained a large size and it has been difficult to arrive at a conclusion as to their origin. Malassez [6] supposed them to arise from the paradental epithelial rests. Eve [7] and Heath [8] considered that they arose from a downgrowth of the gum. Falkson [9], Bryk [10],

and Bland-Sutton [11] considered that they arose from an abnormal development of the enamel organ. This latter view is now generally accepted and is supported by the structure of this tumour. It has been further stated that the origin of these tumours may be either from the cells of the tooth-band or from the various layers of the enamel organ, and that the nature of the cells in the growth gives a clue to the cells from which it has been derived. Thus, epithelial odontomes containing stellate cells like the stellate reticulum, or cubical cells like those of the tooth-band or the outer cells of the enamel organ, have been described. We would suggest that such an inference, based on the appearance of the cells in the tumour, is fallacious, and that because cells resembling those of the stellate reticulum are present in the tumour it does not follow that they are derived from the stellate reticulum. That they arise from an aberration of the tooth-band or from the forming enamel organ during its active life seems probable, but that the nature of the cells gives a clue to the exact origin of the growth appears to us unlikely.

The bulk of this tumour consisted of alveoli, some with a wide lumen, others almost solid with cells. In this respect it resembles other examples of epithelial odontomes, especially those arising in young individuals before the growth had attained a large size and still retained some of its embryonic characteristics. But at one part this tumour presents very unusual characteristics, namely, in the region of the flake of enamel embedded in its surface. In this region we find enamel of an amorphous character, which is arranged in layers alternating with rows of enamel organ not unlike the arrangement of the enamel in the lower incisors of *Galeopithecus*. We also find a curious appearance like a tooth-band with downgrowths of epithelial buds resembling enamel organs. The resemblance is so close that it is difficult not to believe that we have here an aberrant tooth-band, though not necessarily the tooth-band proper, with a series of aberrant tooth-buds. From this part of the tumour it is possible to trace the gradual development of alveoli of varying sizes, many of which are lined with epithelial cells and are often so crowded with cells as to appear solid. This suggests that the tumour originated in this region, which still retains the characters of the primitive dental epithelium and that subsequently it assumed the characteristic appearance associated with multilocular disease. Malassez remarks with regard to these tumours that the tubes and solid strands may represent the commencing forms of these growths, while the cysts are the end-products. In large specimens the alveoli may fuse together to form large cavities.

The view that the tumour originated in the region of the flake of enamel is supported by the subsequent dental history of the child. All the deciduous incisors are present, with the exception of the right upper deciduous central which had been pushed through the gum by the growth of the tumour and was removed at the operation. This tooth was in every way normal. This tumour could not therefore have arisen in substitution of one of the deciduous incisors. But a recent radiograph shows that the right permanent central incisor is absent and we therefore suggest that this growth may be regarded as having arisen as an aberration of the enamel organ of this tooth. As already stated, the growth was first noticed at the age of one month and must therefore have arisen earlier than that. The tooth-bud of the permanent central appears at the twenty-fourth week of intra-uterine life and calcification commences during the first year. The enamel organ was not destroyed by the growth but was stimulated to an abnormal activity characterized by an irregular formation of cells and the deposition of ill-formed enamel. The view has been put forward that multilocular disease may arise as a downgrowth of the gums or that the growths may be endotheliomata. Most of these growths were first noted when they had attained a large size and their embryonic characters had been obscured. The knowledge obtained from a study of these tumours in early life, when they are small, would seem to afford little doubt of their origin from the dental epithelium. In an account of an epithelial odontome in a girl of $4\frac{1}{2}$ years which was recorded before

this Section by Mr. Warwick James and Dr. Graham Forbes [12], the early age of the patient and the early state of the tumour clearly revealed the dental origin of the growth. In our case, in which the tumour arose at an age when dental development was in a still more active state, its dental origin is even better marked.

Two other small points may be noted. This tumour is true to type in occurring in a female. It is, however, a little unusual in being situated in the maxilla, for most cases of multilocular disease have been found in the mandible. It is remarkable that so large a tumour in so young a subject should have occasioned such a small disturbance of tooth development that the only trace of it is a torsion of a deciduous lateral and the absence of a permanent central. Though this tumour adds to our knowledge of the pathology of the epithelial odontomes, yet it is in many respects so aberrant that it must, we think, be regarded as something of a pathological curiosity.

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