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A CONTRIBUTION TO THE KNOWLEDGE OF THE HISTOLOGY, HISTOGENESIS AND ETIOLOGY OF ADAMANTINOMAS

by

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MATERIAL

The case series of the investigation reported here comprised 36 patients attending four Stockholm hospitals[1] and the Royal School of Dentistry. The adamantinoma diagnosis was in each instance confirmed by histopathologic examination. Where doubt existed concerning the classification of the tumour the case was rejected. There were 7 such cases apart from the 36 mentioned. The chief difficulty lay in distinguishing adamantinomas from mixed tumours of the salivary gland type, craniopharyngeomas and certain types of carcinoma.

Of the 36 patients 19 were males and 17 females. In 26 instances the tumours were found in the lower jaw; the anterior, intermediate and distal parts of the jaw were involved in 3, 4 and 16 cases, respectively. One adamantinoma affected practically one half of the mandible, while in two cases the exact location was not stated. Of the maxillary tumours, 7 were in the molar region and 2 mainly, if not wholly, in the canine and premolar area; in one case there was no information concerning the site.

In 26 cases the ages were given at which the symptoms first appeared. The age distribution is shown in the table

[1] Radiumhemmet, St. Göran's Hospital, Sabbatsberg Hospital and Serafimer Hospital.

Ages of patients when the first symptom was observed

10—20 years	1	4 per cent
20—30 »	6	23 »
30—40 »	5	19 »
40—50 »	9	34 »
50—60 »	2	8 »
60—70 »	2	8 »
70—80 »	1	4 »

No statistical account of the clinical data will be given here as most of the cases have already been dealt with in this respect by *Hertz* (1951).

MORPHOLOGY

Adamantinomas are for the most part benign tumours. It is seldom that they display infiltrative development, and still more rarely do they metastasize. *Kimm & Baranoff* (1938) have been able to find mention of no more than 13 cases of metastasis in the whole voluminous literature on the subject.

Histologically the adamantinoma consists of epithelial cells growing in connective tissue stroma.

The tumour forms are divided into solid and cystic (generally polycystic). Most authors appear to be in agreement with the view that the growth begins as a solid and that the younger parts even of the developed tumour are solid (*Hesse,* 1913; *Mead,* 1940; *Cahn,* 1941; *Axhausen,* 1943, and *Hill,* 1945). The cysts are, then, formed with stellate epithelial cells as an intermediate stage. *Axhausen* (1943) and *Sonesson* (1950) are of the opinion that when a large cystic cavity is found early on, it is an ordinary dental cyst from which the adamantinoma has developed. *Thoma* (1944) states that a cystic tumour can become solid as a secondary stage by growth of tumour tissue within the cyst cavity itself. Referring to the frequency of occurrence of the two main forms, *Robinson* (1937) mentions that of 219 cases 57.5 per cent were cystic, 19.1 per cent solid and 24.2 per cent both cystic and solid. *Sonesson's* (1950) material contained 28 per cent wholly or predominantly solid.

The most detailed system of histologic classification has been compiled by *Thoma* (1944) and this will therefore be used here. Thoma's system specifies the following eight types.

1. *Epithelioma:* The epithelial cells show but a slight tendency to differentiate. They grow in cords or strands in a loose fibrous stroma and generally form a solid tumour with marked infiltrative growth.
2. *Stellate:* The tumour consists mainly of stellate epithelial cells of the type found in the developed enamel organ.
3. *Ameloblastic:* This type forms lobes or follicles with cells of the same type and arrangement as those of the mature enamel organ. Outermost are cylindrical cells, similar to ameloblasts, and then a layer of indifferent cells; in the centre are stellate cells. In contrast to ameloblasts the cylindrical peripheral cells do not form enamel but sometimes develop a narrow homogenous zone between their basal membrane and the surrounding stroma. This zone, that may vary in width, is stained yellow with van Gieson and is thought to be abortive enamel. It has not, however, the structure of enamel.

   Destruction of the stellate cells in the centre gives rise to microcysts in the follicles. Such small cysts occasionally fuse to give larger cystic formations.
4. *Acanthoma:* In the centre of the follicles is a differentiation of squamous or prickle epithelial cells with a tendency to the formation of epithelial pearls. Between these and the peripheral cylindrical or cuboid cells are layers of indifferent and stellate epithelium.
5. *Adamantinocarcinoma:* Carcinomatous development in an adamantinoma.
6. *Melanotic adamantoblastoma:* A rare type that contains pigmented epithelial cells.
7. *Haemangioadamantoblastoma:* Typical adamantinoma tissue with haemangiomas or blood-filled spaces surrounded by epithelium.
8. *Adenoadamantoblastoma:* The epithelium tends towards glandular structure and arrangement. Thoma believes it might be due to the potential ability of the oral epithelium to form both dental and glandular structures.

The material of the present investigation contains examples of *Thoma's* Types 1, 3, 4 and possibly 7 (Figs. 1, 2, 3 and 10, resp.). In the last instance blood-vessels are in places so numerous and large that they are to a great extent reducing the rest of the connective tissue. (Sites with such pronounced development are, however, not visible in the section reproduced here, which is included for another purpose).

Are Thoma's types all really variants of adamantinomas? *Ehrich* (1941) doubts whether this is the case.

Thoma's Type 3 is generally accepted as an adamantinoma[1]. Some authors — *Siegmund-Weber* (1926) and *Borst* (1928) — in fact describe only that type, and if the tumour were similar to the developed enamel organ in its formation it would, of course, bear some resemblance to Type 3.

Thoma's Types 4, 6, 7 and 8 are probably to be regarded as nothing more than variants of Type 3.

Types 1, 2 and 5 are sometimes not easy to diagnose. In Fig. 1, for example, the infiltrative epithelial strands show but little of the structure generally considered characteristic of adamantinomas. According to the scheme the tumour should belong to Type 1 and is indisputably an adamantinoma[2].

In the case of Type 8 there can hardly be any author to-day who would agree with Thoma that there is any question of

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[1] *Churchill* (1934) cautions against confusing this type of tumour with harmless epithelial proliferations that occasionally develop in the walls of an ordinary dental cyst. They consist of large aggregations of epithelial cells in which are enclosed small areas of connective tissue. Sometimes this tissue degenerates with the resultant formation of growths resembling epithelial follicles. The presence of blood-vessels in these false follicles serves, however, as a reliable confirmation of the differential diagnosis. One or two cases in the present material belong to this type (Fig. 4). There seem to be no grounds for denying, as Churchill would, that formations of this type are adamantinomas. They are — at least in the case of the present investigation — too extensive formations to be only proliferations of a non-tumour type. Moreover, they present in places a more generally accepted adamantinoma formation.

[2] With respect to some of the illustrations reproduced in this article it might be questioned whether the diagnosis of adamantinoma was correct. In all cases, however, this was fully confirmed by the presence of a more typical adamantinoma structure either in other parts of the tumour, or, in the case of relapse, in the original tumour or one of the relapses.

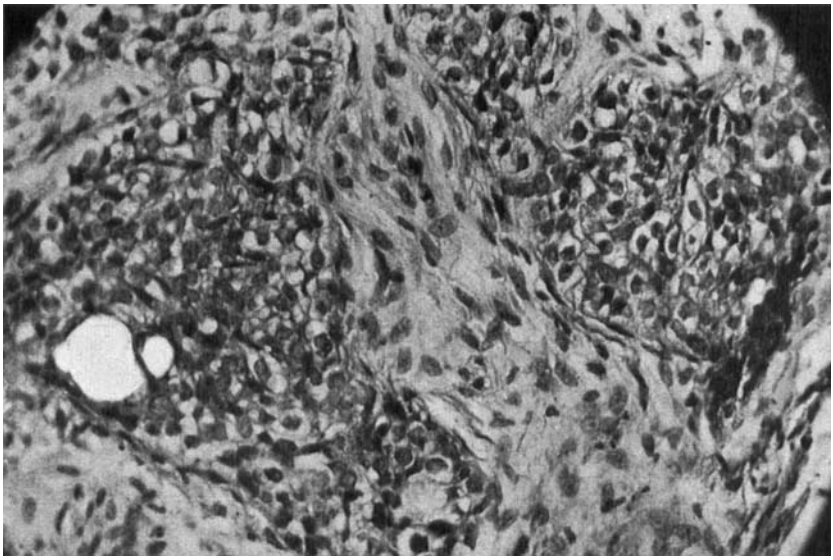

Fig. 1. Adamantinoma consisting of solid, epithelial formations, little differentiated, growing in connective tissue stroma. Corresponding roughly to Thoma's Type 1.
250 ×.

glandular tissue. *Borst* (1928), *Ringertz* (1938) and *Cahn* (1941) consider that the apparent glandular lumina is due only to the fact that in the small cysts nothing but the outer cuboid or cylindrical epithelium remains.

McGregor (1935) has attempted to establish histologic characteristics in malignancy of the tumour. To this end she has collected from the literature 28 malignant cases, 10 of which gave rise to metastasis and 13 being of a marked infiltrative character. In 5 cases the malignancy was visible only under the microscope. Of these tumours the atypical characteristics were:

1. Stroma rich in cells, in some instances as pronounced as in the fibrosarcomas;
2. Cuboid cells dominade over the cylindrical and stellate cells in the epithelium;
3. The epithelium dominates over the stroma. The epithelium ramifications bear some resemblance to the branches on a tree and are frequently intertwined.

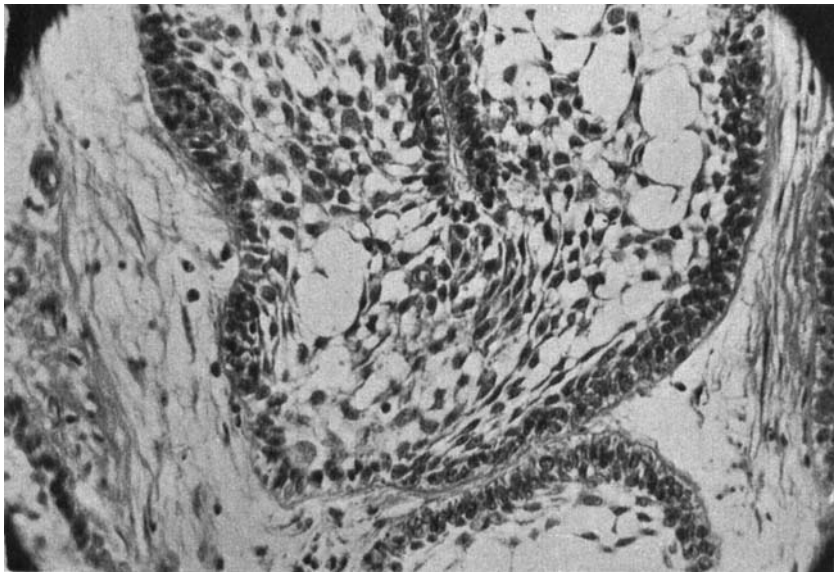

Fig. 2. Adamantinoma follicle with outermost cylindrical ameloblast-like cells. Inside are indifferent cells and stellate epithelium cells. 250 ×.

DENTAL EMBRYOLOGY

As a background to this account a brief outline of dental embryology will be given.

When the embryo is some 6½ weeks old the tooth development begins, the epithelium from the oral cavity growing into the underlying tissue to develop into the dental lamina. On this epithelial lamina bud-shaped swellings form by cell proliferation, these constituting the ectodermal primordia of the deciduous teeth. The epithelial bud then develops into the bell-shaped enamel organ, the inner surface of which corresponds to the shape of the future dental crown. On the lingual side of the deciduous enamel organ a further lamina forms, the successional lamina, which, just as the deciduous lamina, gives origin to the enamel of the permanent crown.

The fully developed enamel organ (the epithelial bell) is built up in the following manner. Outermost there is a layer of low cuboid cells with round nuclei; this is the outer enamel epi-

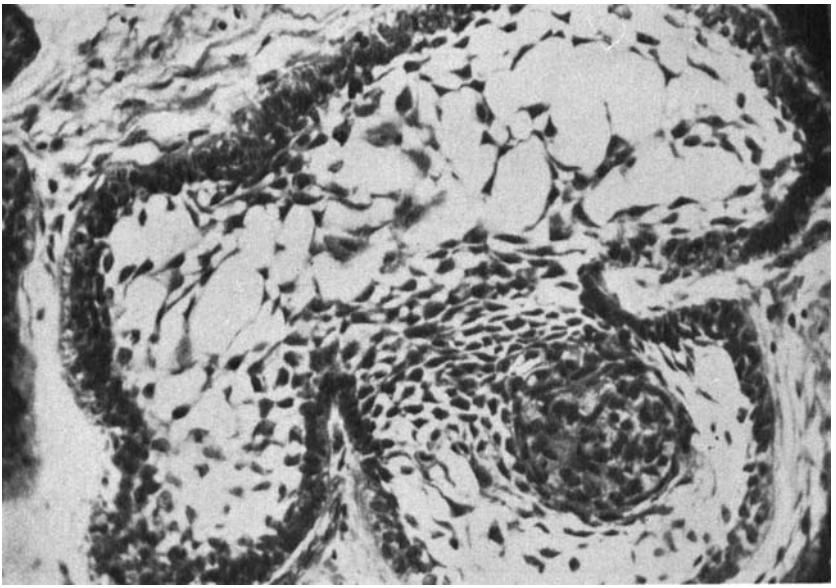

Fig. 3. Adamantinoma follicle containing an epithelium pearl. 250 ×.

thelium. Inside this is the enamel pulp, consisting of stellate epithelial cells which, with long processes, form a network the spaces of which are filled with a mucoid fluid. Next is the stratum intermedium, consisting of several layers of low squamous cells. Innermost there are the actual enamel-producing cells, the ameloblasts, arranged as a palissade of cylindrical cells. The nuclei of the ameloblasts lie at the periphery of the cells nearest the stratum intermedium. (A similar arrangement is sometimes found in the adamantinoma.)

In the invaginated part of the enamel organ lies the mesiodermal dental papilla from which the dentine-forming odontoblasts are differentiated. These lie peripherally in the dental papilla directly against the ameloblasts. The dentine formation begins just before the enamel. The enamel pulp atrophies and wholly disappears long before the enamel formation is complete.

From the free border of the enamel organ, where the outer and inner enamel epithelial cells meet, the epithelia grow down-

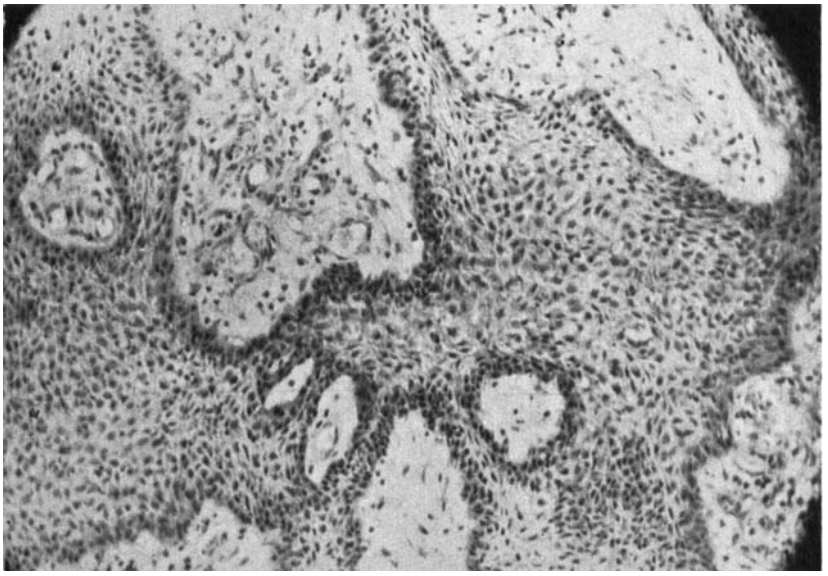

Fig. 4. Solid epithelium masses surrounding parts of connective tissue. Churchill calls these formations "epithelium proliferations" but in this case at least, it is an adamantinoma.
150 ×.

wards in a double-layered sheath around the future root. This sheath is later split up by ingrowing connective tissue, and the remnants (Malassez's rests) will lie in the periodontium during the whole life of the tooth. According to *Fischer* (1909) and *Müller* (1948) the rests are only apparent islands due to the direction of sectioning. In fact the individual rests are connected one with the other and with the basal layer of the gingiva in the form of a net. *Meyer* (1935) considers that this is the case only while the person is young. The network subsequently being destroyed, and the residual parts themselves becoming real cell islands.

From Meyer's photomicrographs (Fig. 5, for example) it is clearly seen that the basal cell layer of the mucosal epithelium continues immediately into the inner and outer enamel epithelium, and into the epithelial root sheath. The whole cell-row is distinguished from the surrounding cells by the fact that the cell nuclei have a higher chromatin content and are consequently

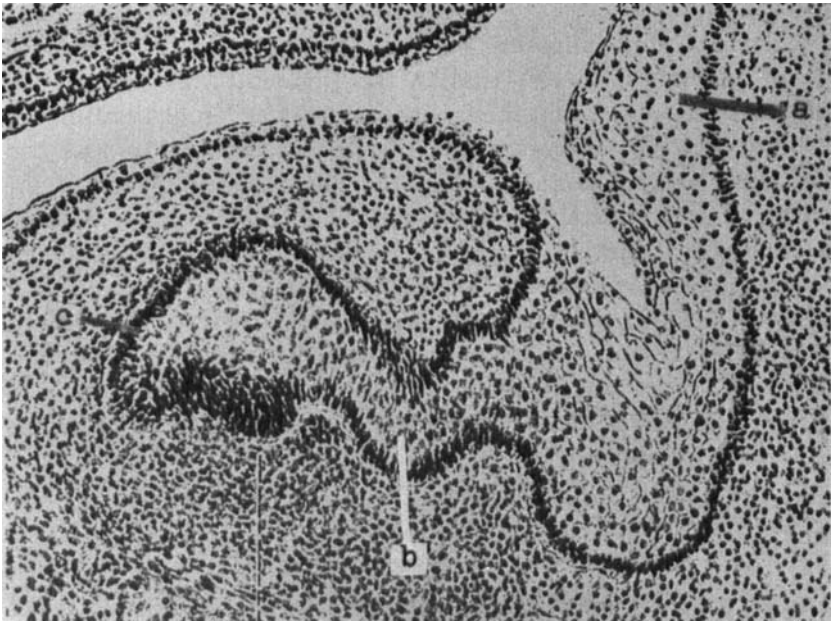

Fig. 5. Dental lamina and embryo of the enamel organ and the oral mucosa. It is seen that the darker basal cell layer of the oral epithelium is continuous with the dental lamina and the inner and outer oral epithelium. a = the oral mucosa epithelium, b = dental lamina, c = the enamel organ under development. (Figure from Wilhelm Meyer "Normal histology and development history of the human tooth", 1932; Carl Hanser-Verlag, München.

darker in colour. The cells in the future enamel pulp correspond directly to that part of the oral epithelium that lies peripherally to the basal cell layer (Fig. 5). (The intercellular fluid formation and the appearance of stellate cells in the enamel pulp belong to a later stage than that reproduced). This genetic connection between the cells in the different structures suggests that the adamantinoma might originate from several different epithelial cell formations, such as those of the gingiva and an ordinary dental cyst.

The dental germ eventually loses its connection with the oral epithelium, often leaving behind small groups of cells. These stratify concentrically (Serres pearls). Similar structures are found occasionally in adamantinomas (See Thoma's Type 4, Fig. 3).

HISTOGENESIS

Since the name adamantoblastoma (adamantinoma) is derived from adamantoblasts — that is, the enamel-forming cells — it might be supposed that these constitute the origin of the tumour. The majority of authors are in fact agreed that the tumour can originate in the dental lamina, the normal enamel organ, the supernumary enamel organ, rests of the enamel organ or malposed embryonal dental tissue. (*Magitot,* 1878; *Falkson,* 1879; *Krompecher,* 1918; *Simmons,* 1928; *Norberg,* 1930; *Kegel,* 1932; *Ringertz,* 1938; *Axhausen,* 1943; *Thoma,* 1944; *Geschickter & Copeland,* 1949; *Sonesson,* 1950, and *Hertz,* 1952.) None has, however, succeeded in giving any but indirect proof of such an origin. The most important evidence falls into one of the three following groups.

1. The similarity in structure between the tumour and the enamel organ is frequently striking. In other cases, however, — for example, some of the solid forms — some imagination is required if any such similarities are to be traced (Fig. 1). Even so, the structural likeness provides no definite proof. In the material of this investigation it has been possible to show that formations similar to the enamel pulp can also appear in other epithelial formations under certain conditions; for example, in cysts (Fig. 6). Further reference will be made to this below.

2. It has been shown that disturbances sometimes change the normal structure of the enamel organ; this in some ways suggests that tumours might originate here. *Churchill* (1934) has shown that the outer cell layer in the enamel organ can present irregularities in the form of local aggregations of cells or papillary proliferations. *Geschickter & Copeland* (1949) have kept pigs on a rickets-promoting diet and subsequently found defects in the dental germ, and particularly in the enamel organ. The ameloblast layer becomes irregular and parts of the cells become disconnected and isolated as islands.

3. That the tumour generally develops in the molar region is perhaps due to the fact that it is here that aberrant dental germs are most often found. It has been stated that negroes, who, more frequently than whites, grow a fourth molar, are more often troubled with adamantinomas. *Kegel* (1932) found in one hos-

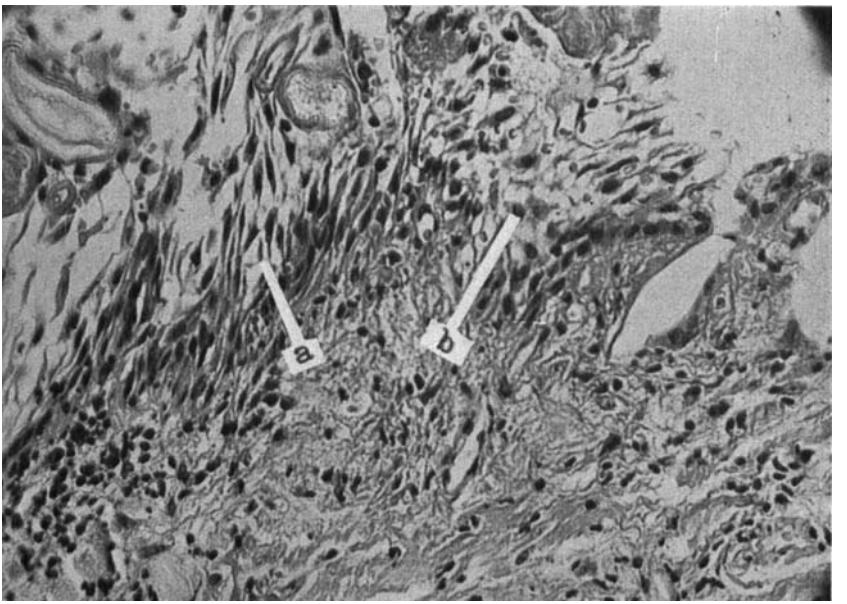

Fig. 6. Reticular (a) and vacuolar (b) degeneration of the epithelium in an ordinary follicular cyst with inflammatory cell infiltration in the walls. The changed epithelium cells bear a close resemblance to cells in some adamantinomas and cells in enamel pulp. Cf. Fig. 2. The rest of the cyst epithelium normal in appearance and without shrinkage. 250 ×.

pital that these were distributed among negroes and whites in the ratio of 11: 1. *Geschickter & Copeland* attributes the difference in frequency to the greater incidence of rickets among coloured people.

One factor that to some extent conflicts with the theory of the origin of adamantinomas in the enamel organ is the age of the patients. The age at which adamantinomas most frequently appear is so high — 40 to 50 years — that all the teeth will generally have erupted. Consequently the enamel organ will have disappeared, with the possible exception of an occasional supernumary germ.

The tumour does not form enamel or any other hard tissue although it should derive from the ameloblasts. *Hildebrand* (1890) in one case found a large quantity of tooth substance and complete teeth in the tumour mass; but it is not certain

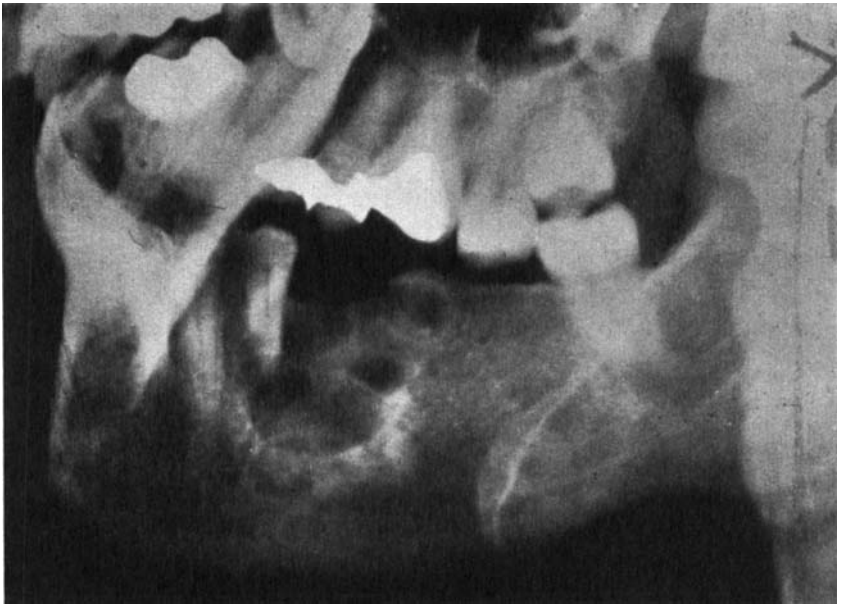

Fig. 7. Radiograph of typical adamantinoma, apparently originating in a periapical focus in a lower left first premolar.

from his description that this was in fact a case of adamantinoma. *Hertz* (1951) writes that in those cases where a complete tooth is found in the tumour it might have been formed in some way through the agency of the tumour. The more likely explanation is probably that it is a retained tooth that was already in existence before the tumour formed.

The reason that adamantinomas do not form hard substance is, according to *Schmidt* (1922), that the formation of enamel must be preceeded by the production of dentine. *Sonesson* (1950) suggests that the absence of enamel formation is due to the ameloblast-like cells remaining in an immature stage of development. They lack the capacity of developing into real enamel-forming ameloblasts.

Another possible origin of the adamantinoma is thought to be the Malassez rests in the periodontium. (*Krompecher,* 1918; *Morlets,* 1925; *Simmons,* 1928; *Ewing,* 1928; *Major* et. al., 1934; *Ringertz,* 1938; *Axhausen,* 1943, and *Thoma* 1944.) *Sonesson*

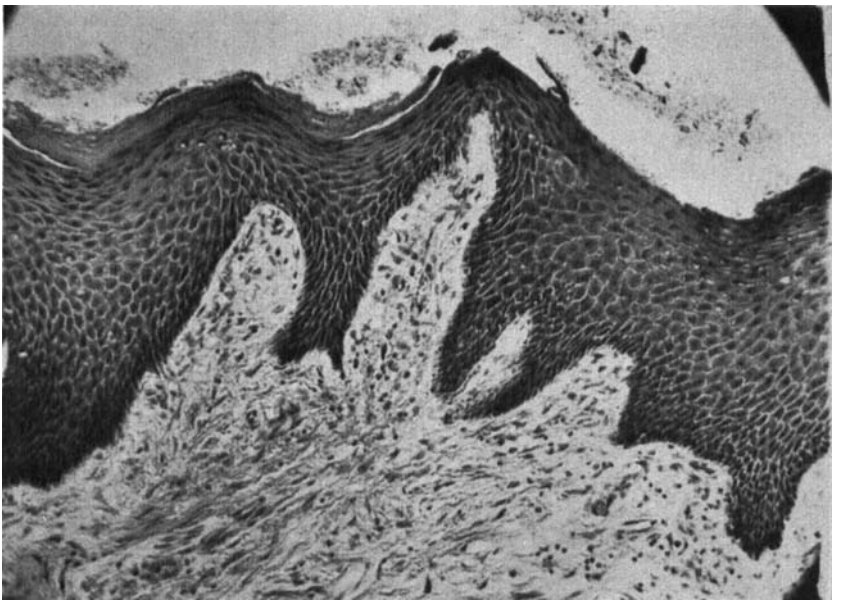

Fig. 8. Ordinary stratified squamous epithelium in a cyst wall. Only slight inflammatory cell infiltration in the underlying connective tissue. 250 ×.

(1950) points out that the youngest adamantinoma in his material — a macroscopically solid type, 5.8 mm diameter — was situated tightly against a tooth and thus had probably developed from Malassez rests in the periodontium. The origin of an adamantinoma in a radicular cyst (see below) would mean that the tumour does in fact arise from Malassez rests, although indirectly. The epithelia of the root cyst are of course derived in this way.

Radiographs of the material of this investigation have occasionally revealed a root tip involved by the adamantinoma, just as in apical periodontitis or cysts (Fig. 7); the destruction of the bone around the root tip is most pronounced. It would seem in such cases most likely that the apical part is the focus of origin of the tumour. The epithelial rests in the apical periodontal focus might for some reason have given rise to proliferations.

Another possible source of adamantinomas is the ordinary dental cyst; that is, a radicular or follicular cyst. The epithelium

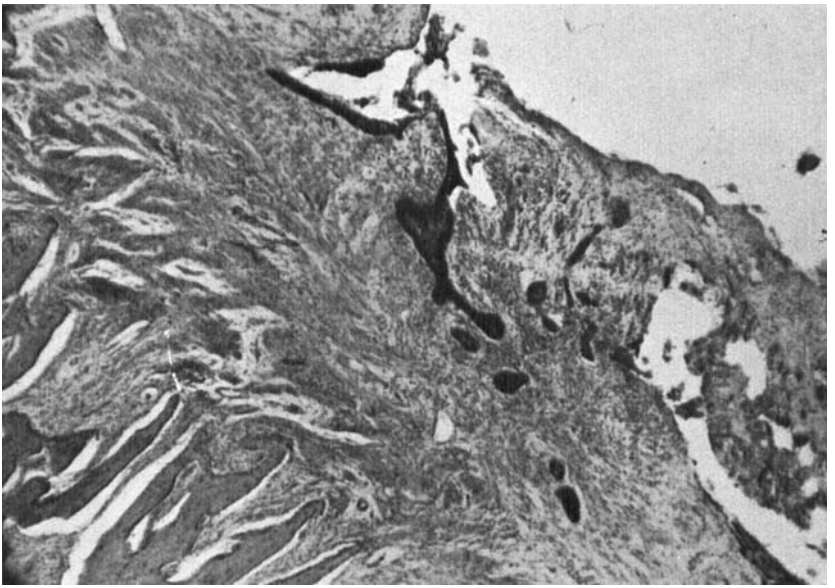

Fig. 9. Adamantinoma tissue in a cyst wall with inflammatory cell infiltration. From another part of the cyst of Fig. 8. The enlargement is smaller so as to take the whole tumour infiltrate in the cyst wall into the picture. Typical adamantinoma tissue is found in the bone outside the cyst. 44 ×.

in the former has its origin - - as stated above — in the rests of Malassez, while in the latter it consists of the rests of the enamel organ. *Thoma & Proctor* (1937) maintain that the adamantinoma in these cases can start either in the surface epithelial layer of the cyst wall, where the tumour proliferates into the cyst cavity in the form of mural adamantinoma, or is formed from the epithelium in the basal layer. In the latter case the tumour develops in the surrounding connective tissue and in the marrow spaces of the bone. Combinations of both modes of growth are to be found. *Axhausen* (1943) believes that adamantinomas often grow from ordinary cyst epithelia. He states that reticularization, foam cells and fluid formation in the cyst epithelium suggest the possibility of degeneration into adamantinomas. *Sonesson* (1950) would say that at least 25 per cent of all adamantinomas have formed in various types of odontogenic cysts. He calls these forms secondary adaman-

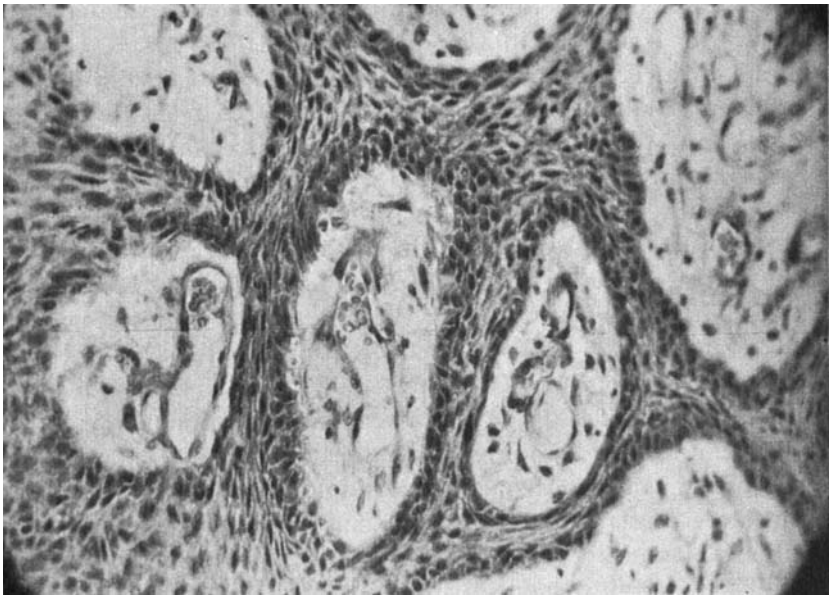

Fig. 10. Adamantinoma tissue closely resembling an oblique section from basal gingival epithelium (cf. Fig. 11). Note the rich vascularization in the connective tissue follicles. Elsewhere in the tumour the vessels are still more dominant, so that the tumour should probably be classed as Thoma's Type 7. 250 ×.

tinomas. Sonesson shares Axhausen's view that adamantinomas with a dominant cyst cavity arise in this manner.

What proof is there in the literature that adamantinomas originate in dental cysts? There have been many cases of adamantinoma with a retained tooth lying in the tumor, sometimes with the crown surrounded by a cyst in the tumour exactly as occurs in a follicular cyst. (*Dreybladt,* 1907; *v. Bakay,* 1909; *New,* 1915; *Wohl,* 1916; *Morlets,* 1925; *Bump,* 1927; *Cahn,* 1933; *Jacobs,* 1935; *Ringertz,* 1938; *Kimm & Baranoff,* 1938; *Thoma,* 1944; *Sonesson,* 1950; *Hertz,* 1951.)

Then there are relapses with the formation of adamantinomas after operations on what have appeared to be ordinary dental cysts. Such cases have been reported by *Becker* 1930, *Wigdortschik* 1932, *Axhausen* 1943 and *Sonesson* 1950. In this connection *Cahn* (1933) has suggested that if the liquid in a cyst with

adamantinoma degeneration is drained, there is a risk that the tumour will transform into a solid, more malign type.

It has also been intimated that in cases of relapse with the formation of adamantinomas it must have been from the outset a question of an adamantinoma, the diagnosis of ordinary dental cyst being incorrect. In the literature there are cases described, however, where both ordinary cystic epithelia and adamantinoma tissue were found at different sites in the same cyst wall, or in its immediate vicinity (*Schmidt,* 1922; *Schroff,* 1931; *Thoma & Proctor,* 1937; *Hankey,* 1937; *Axhausen,* 1943, and *Sonesson,* 1950). Such a case is also found in the present material (Figs 8 and 9). In a cyst, which in the slide had the size of a hazel nut, the wall in most places showed marked inflammatory cell infiltration and the epithelium was completely destroyed over large areas, with consequent ulceration. At one place in that cyst there remained typical ordinary cystepithelium, and at another, adamantinoma tissue was penetrating from the surface into the underlying connective tissue. This might well serve as convincing proof of the fact that adamantinoma degeneration can occur in an ordinary dental cyst. *Kegel* (1932) is of the opinion that the fluid pressure in the cystic adamantinoma would change the adamantinoma epitelium to ordinary cyst epithelium, but in the present case at least, this probability cannot be entertained. (Note the typical, well-formed epithelium with connective tissue papillas in Fig. 8).

In conclusion, there are also supporters of the view that adamantinomas can grow directly from the gingival epithelium (*Büchtemann,* 1881; *Eve,* 1883; *v. Bakay,* 1909; *Kuru,* 1911; *Krompecher,* 1918; *Kaufmann,* 1931; *Mc Gregor,* 1935; *Ringertz,* 1938; *Thoma,* 1944, and *Hertz,* 1951). Such a connection between the two tissues can naturally also occur secondarily if the tumour grows from the surroundings into the gingival epithelium. *Hertz* (1951) has presented histological evidence of a primary connection between the gingival epithelium and the tumour epithelium in 10 of 31 cases, and considers the gingival epithelium to be the most common origin of adamantinomas. In one case with 11 relapses it was possible to follow the downward growth of the tumour epithelium directly from the oral epithelium layer. In this case there seems to be no possibility of two independent

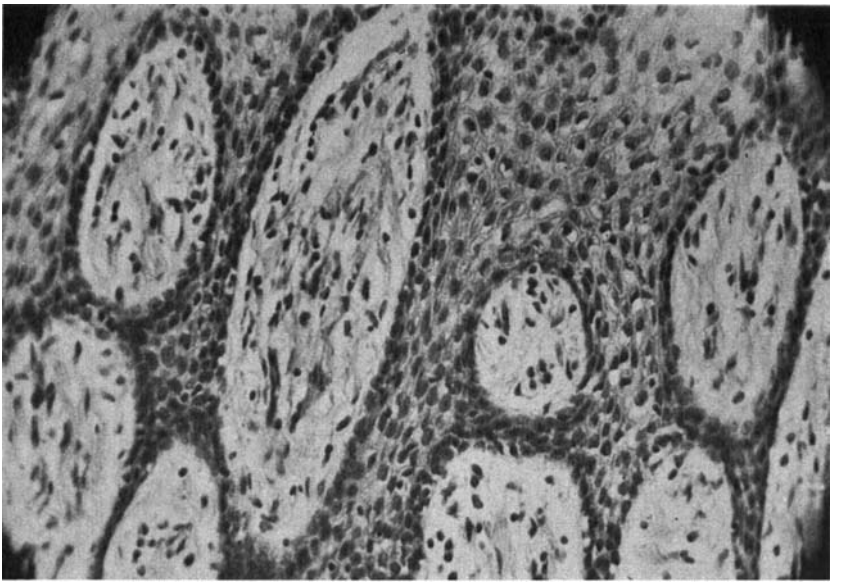

Fig. 11. Oblique section from basal layer of hyperplastic gingival epithelium. Closely resembling adamantinoma tissue in Fig. 10. 250 ×.

epithelial formations — the gingival epithelium and the tumour — having grown together as a secondary process. The photographs seem, moreover, to bear out Hertz's interpretation.

Striking proof of the genetic connection between gingival epithelium and adamantinoma tissue is to be found in one case in the present material. Sections of an adamantinoma (Fig. 10) show a remarkable similarity to oblique sections from basal gingival epithelium (Fig. 11). The tumour is of course not as a whole so regular in structure. In parts the boundary of the enclosed connective tissue follicles (the adamantinoma is of the solid type) is not so regularly oval as that of the gingiva. Epithelial septa incompletely dividing the connective tissue follicles are found in parts of the tumour; such formations are not to be found in slides of ordinary gingival tissue. The striking similarity certainly points to the fact that the gingiva in this case is the mother tissue of the tumour.

Further proof that the gingival epithelium can be the origin is provided by the fact that the tumour is occasionally growing

from the beginning as an epulis. There is an example of this in the present material. The case concerns a 59-year-old woman who had a small excess of gingival tissue removed by her dentist. After three months it had re-grown. An examination of the relapse showed the tumour to be polypous and situated with broad base on the gingiva behind the most posterior left molar. It was proved histologically to be an adamantinoma.

To summarize, it might be said that proof exists: —

that adamantinomas may form in ordinary dental cysts, this mode of origin probably being common;

that adamantinomas may developfrom the gingival epithelium;

that is is probable that the tumour can form from the débris of Malassez; and

that it is theoretically possible that the tumour can originate directly in the enamel organ.

That the adamantinoma can originate in different tissues is by no means strange if one recalls the development of the embryo. The gingival epithelium, the dental lamina, the enamel organ and the rests of Malassez are, of course, only different parts of the same embryonic tissue layer. The epithelium of dental cysts has the same origin. What are thought to be ameloblasts — the tumour's cylindrical, chromatin-rich basal cells — can, in fact, equally well be derived from the stratum germinativum in the gingival epithelium or from a corresponding layer in the other epithelial parts. Degenerative states in the epithelium roughly similar to enamel pulp can also occasionally be found in all the above-mentioned structures.

ETIOLOGY

Among the authors who have contributed to the literature on the etiology of adamantinomas the following are of interest in this connection.

Lindemann (1928) is of the opinion that the cause is to be found in disturbances of the development — unspecified — during the first and second dentitions.

Kimm & Baranoff (1938) point out that since the tumour is so often developing in connection with unerupted teeth the

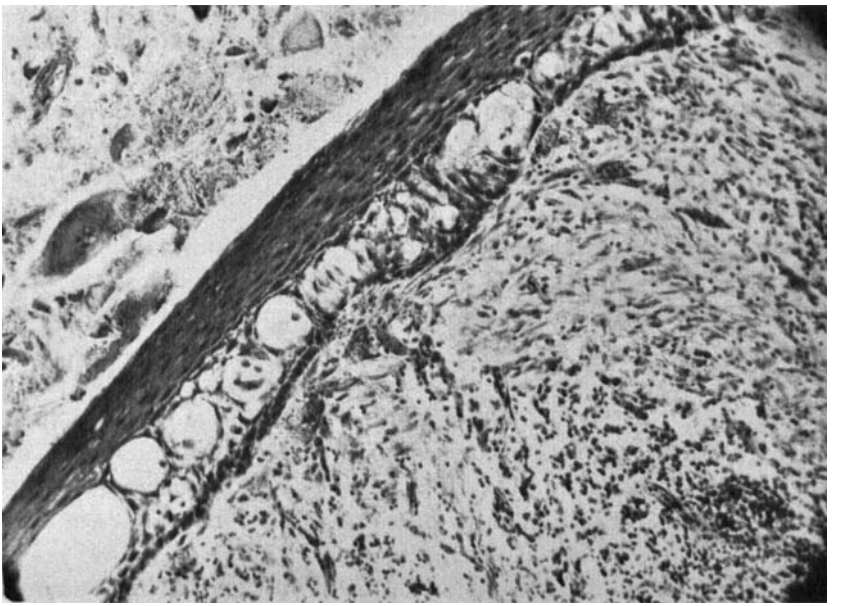

Fig. 12. Vacuolar degeneration of cyst epithelium in the neighbourhood of inflammatory cell infiltrate.
250 ×.

reason might lie in consequent pressure and nutritional disturbances.

Geschickter & Copeland (1949) consider rachitis to be a possible cause.

Hertz (1951) emphasizes trauma as an etiologic factor; extraction of teeth, for example, might give rise to adamantinomas or accelerate the growth of a tumour already in existence. Trauma and infection, possibly arising from carious teeth, would seem to be the etiologic factors that are most frequently named in the literature (e.g. *Eve,* 1883; *Blümm,* 1901; *Gentsch,* 1932 and *Robinson,* 1937).

To summarize, it may be said that the attempts to explain the etiology of the tumour found in the literature are offered more or less incidentally and are not founded on detailed evidence.

There are in the present material some cases where the tooth extraction wound showed no tendency to heal, and adamantinoma tissue was found on histologic examination. In such cases it

need not have been extraction trauma that gave rise to the tumour -- as Hertz in fact suggests. The teeth extracted were badly decayed and it might be supposed that chronic irritation from apical foci could equally well have been the cause of the tumour. Journals frequently note that teeth at the site of tumours have been decayed or that it had previously been necessary to make an incision of an abscess at the site where the tumour subsequently formed. It is impossible, unfortunately, to make a statistical study of a large part of the material in this very interesting connection because the journal entries are too scanty.

As has been pointed out earlier, one is entitled to assume that the follicular cyst is a common place of origin of adamantinomas. It might therefore be of interest to examine the coincidence of the predilection sites of follicular cysts and adamantinomas. The former occur most frequently in the region of the upper canines and lower third molars *(Bernick,* 1949). The latter is the most common for adamantinomas, too. On the other hand the tumour but seldom occurs in the region of the upper canines. Now and then, however, adamantinomas are found in follicular cysts even there, a fact illustrated by the following case history from the present material.

A 15-year-old boy received a blow on the left side of the jaw. After about six weeks the region became swollen, the swelling increasing rapidly in size. A little more than three months later an operation was undertaken. On incision a cyst was exposed, filled with a yellowish fluid, and in the cyst the crown of a retained tooth was seen --- an upper left canine. When extracting the tooth the cyst came away without difficulty. Histologic examination showed adamantinoma tissue in the cyst wall. (The case points, moreover, to trauma as an etiologic factor).

Why do adamantinomas form so much more frequently in the lower third molar region than near the upper canines? It is no doubt due to the fact that the epithelium of the follicular cyst does not transform simply to adamantinoma tissue. One can probably assume that the epithelium must first in some way be irritated before the tumour begins to form. So far as the author has been able to find in his investigation this irritation is frequently of an inflammatory nature. This provides a possible explanation of why adamantinomas are relatively common in

connection with retained lower third molars. Prolonged inflammatory states often develop in such cases. Similar inflammatory processes are very rare in the case of retained upper canines.

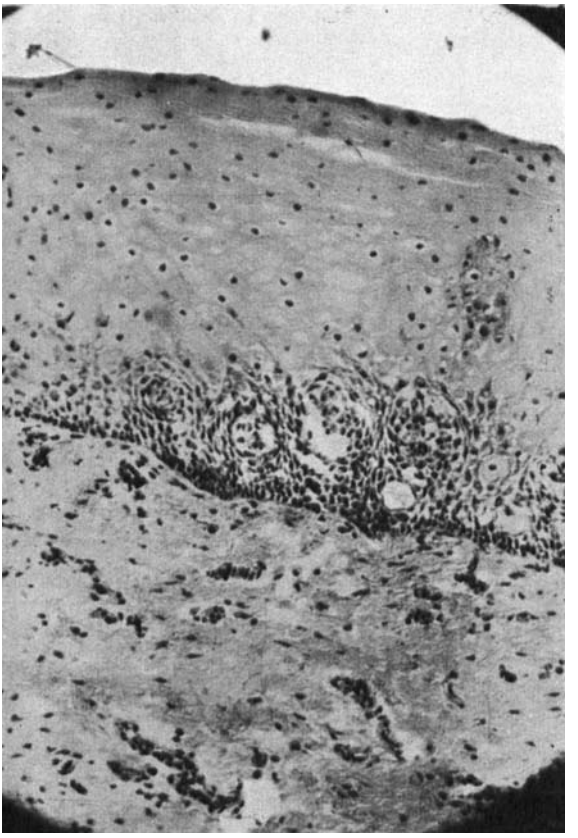

Fig. 13. Stratified squamous epithelium in the vicinity of an adamantinoma. The dark basal cells show a marked tendency towards proliferation at the same time as other parts of the epithelium degenerate and decompose with vacuole formation. Inflammatory cell infiltration in the underlying connective tissue. The adamantinoma probably arises in this way from ordinary epithelium by inflammatory irritation.
150 ×.

In order to study epithelial changes due to inflammatory irritation the present author has examined a number of microscopic slides of the gingiva and ordinary dental cysts. During this investigation it was clearly seen how the epithelium of the

gingiva and the cyst in the vicinity of inflammatory cell infiltration can change with the formation of vacuoles and stellate cells, thus resembling the characteristic forms of adamantinoma epithelium (Fig. 6). Note the similarity between the epithelial

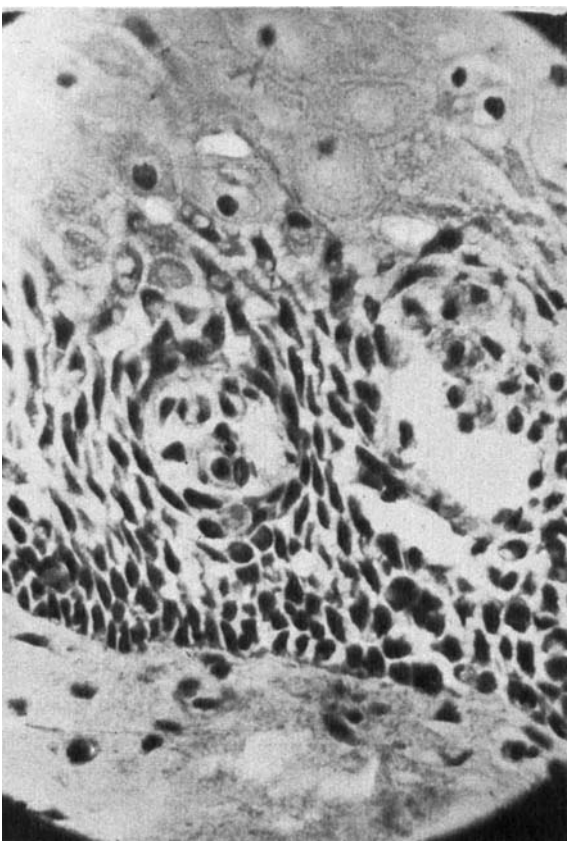

Fig. 14. Enlargement of detail in Fig. 13.
500 ×.

cells in Fig. 6 and the cells in the adamantinoma of Fig. 2. Such structural changes would be still more remarkable in ordinary epithelium near an adamantinoma if adamantinomas are of inflammatory genesis. The inflammatory irritation that in one place was so marked and prolonged that tumour growth began might also have had some influence on the epithelium in the

vicinity. This did in fact appear to be the case. In one preparate described earlier (Figs. 8 and 9) there were found in various places in the same cyst wall both ordinary cystic epithelia and adamantinoma proliferations. In the region of the normal epithelium the inflammatory cell infiltration was but slight, while around the adamantinoma tissue it was considerable. In this cyst a third epithelial part was found that might be most accurately characterized as a transition form between the two (Fig. 12). The epithelia show here marked signs of vacuolar degeneration but have not the character of a tumour. Here, too, inflammatory cell infiltration is found in the immediate vicinity.

Still closer similarity to the adamantinoma structure is found in the preparate illustrated in Figs. 13 and 14. These reveal stratified epithelium a short distance from an adamantinoma. The basal cells show marked proliferation while other parts of the epithelium are degenerating and decomposing. In the connective tissue under the epithelium there appear clear signs of round cell infiltration. It is quite probable that the earliest stages of an adamantinoma can arise in this way from ordinary epithelium by inflammatory irritation. That the inflammatory infiltrate is not caused by the epithelial change is to be seen from the fact that a developed adamantinoma is as a rule not surrounded by inflammatory cell infiltration.

It is not known, though, how the ordinary cells change when they become mother cells for a tumour. What is certain, however, is that when the tumour formation has commenced, supporting inflammation is no longer necessary.

SUMMARY

On the basis of a series of 36 cases of adamantinoma the author discusses the classification of the tumour into histological types.

With reference to the histogenesis of the adamantinoma it is asserted that the tumour may form in ordinary dental cysts and that this is probably a common mode of origin. It can be shown, however, that the tumour may develop from the gingival epithelium. It is probable that it can form from the débris of Malassez, and theoretically possible that it can have its origin directly in the enamel organ.

The histological changes that occur through inflammatory irritation of ordinary stratified squamous epithelium occasionally present so striking similarity to the adamantinoma structure that one is forced to assume that the tumour can, in fact, originate by such a process.

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